NIH Clinical Trial Initiatives: How it Impacts NLM Data Science and Biomedical Informatics Research

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Overview

To enhance the stewardship of research involving human subjects, NIH is implementing the following:

All Research Involving Human participants

- ✓ New human subject information forms
- ✓ Single IRB for multi-site studies
- ✓ Certificates of confidentiality for all research that uses "identifiable, sensitive info"

Research that Meets NIH Definition of a Clinical Trial

- ✓ Training in Good Clinical Practice (GCP)
- ✓ Clinical trial specific FOAs
- ✓ New review criteria
- ✓ Expanded registration and reporting in ClinicalTrials.gov

Why are changes being made?

Ensure public trust in…

- Scientific rigor
- Transparency
- Ethical oversight
- NIH stewardship of public funds

Changes for All human subject research

New PHS Human Subjects and Clinical Trials Information Form

- ✓ FORMS-E Application Package is required for due dates on or after January 25, 2018
- ✓ Consolidates human subject data that used to be spread over several forms
- ✓ Collects information at the study level and incorporates new structured data fields

Changes for All Human Subject Research

Single IRB for multi-site research involving human participants

- ✓ Applies to grant applications with due dates on or after January 25, 2018.
  All human subject research that involves multiple sites will require a single Institutional Review Board to be used in the ethical review of non-exempt human subjects research protocols funded by NIH. The goal is to streamline the IRB process and enable IRBs to concentrate their efforts on the review of single site protocols.

Changes for All human subject research

Certificates of Confidentiality

- ✓ These certificates are designed to protect research participants by limiting the disclosure of identifiable, sensitive information.

- ✓ In the past there was a process for obtaining these certificates. Beginning October 1, 2017 all NIH funded research that collects identifiable, sensitive information and began or was ongoing on or after December 13, 2016 is considered to have been issued a certificate of confidentiality as part of the terms of award.

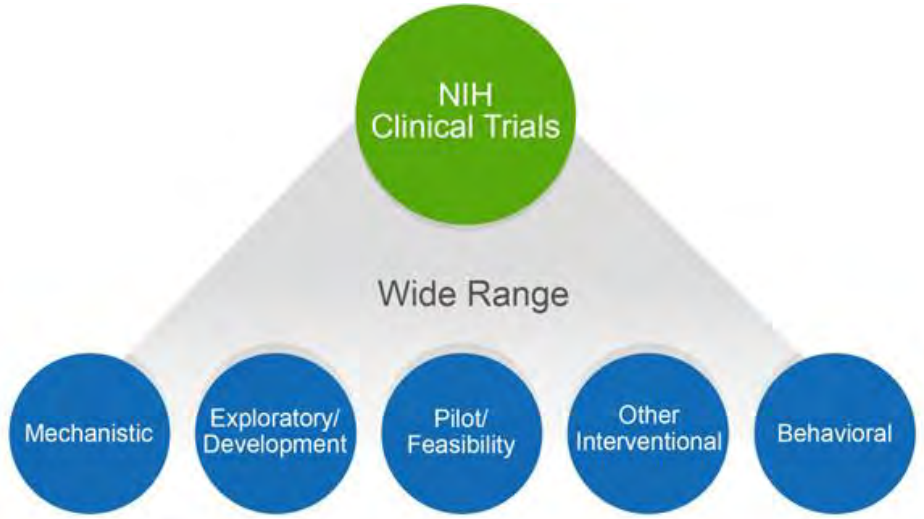
Changes that apply to clinical trials research

- ✓ Training in Good Clinical Practice (GCP)
- ✓ Clinical trial Specific FOAs
- ✓ New review criteria
- ✓ Expanded registration and reporting in ClinicalTrials.gov

Is my study a clinical trial?

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.



Is my study a clinical trial?

1. Does the study involve human subjects?
2. Are the participants prospectively assigned to an intervention?
3. Is the study designed to evaluate the effect of the intervention on participants?
4. Is the effect that will be evaluated health-related biomedical or behavioral outcome?

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FAQs and Case Studies available to help applicants decide
https://grants.nih.gov/ct-decision/index.htm

Is my study a clinical trial?

1. Does the study involve human subjects? Yes
2. Are the participants prospectively assigned to an intervention? Yes
3. Is the study designed to evaluate the effect of the intervention on participants? Yes
4. Is the effect that will be evaluated health-related biomedical or behavioral outcome? Yes

If ALL 4 answers are YES then your study is considered a clinical trial

FAQs and Case Studies available to help applicants decide

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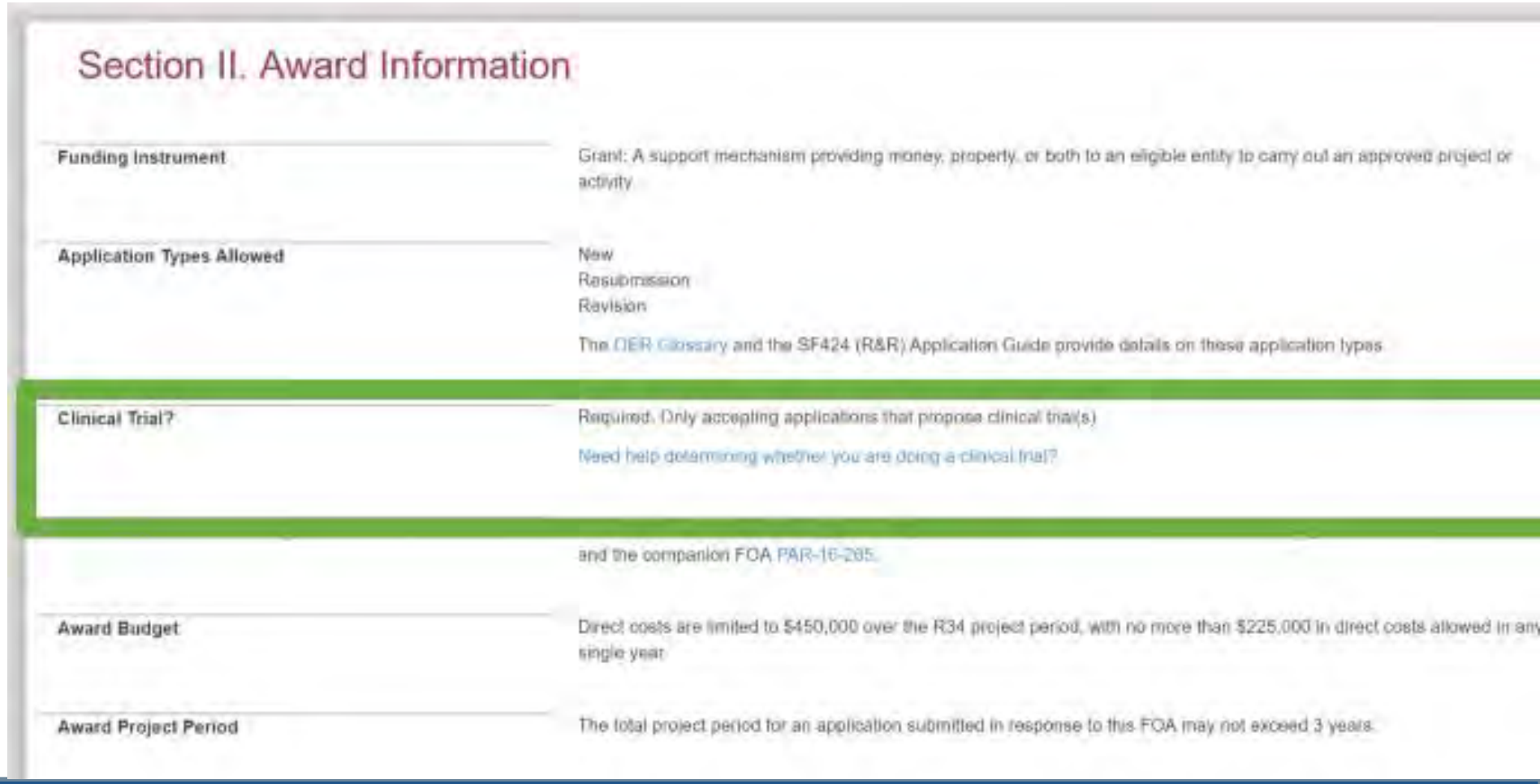
Good Clinical Practice (GCP) Training

- ✓ All NIH – funded investigators involved in the conduct, oversight or management of clinical trials must receive Good Clinical Practice training
- ✓ The goal is to ensure the safety, integrity, and quality of clinical trials
- ✓ Policy is effective January 1, 2017. Training should be refreshed every 3 years

All clinical trials MUST be submitted to a funding opportunity announcement that allows clinical trials

Beginning
January 25, 2018

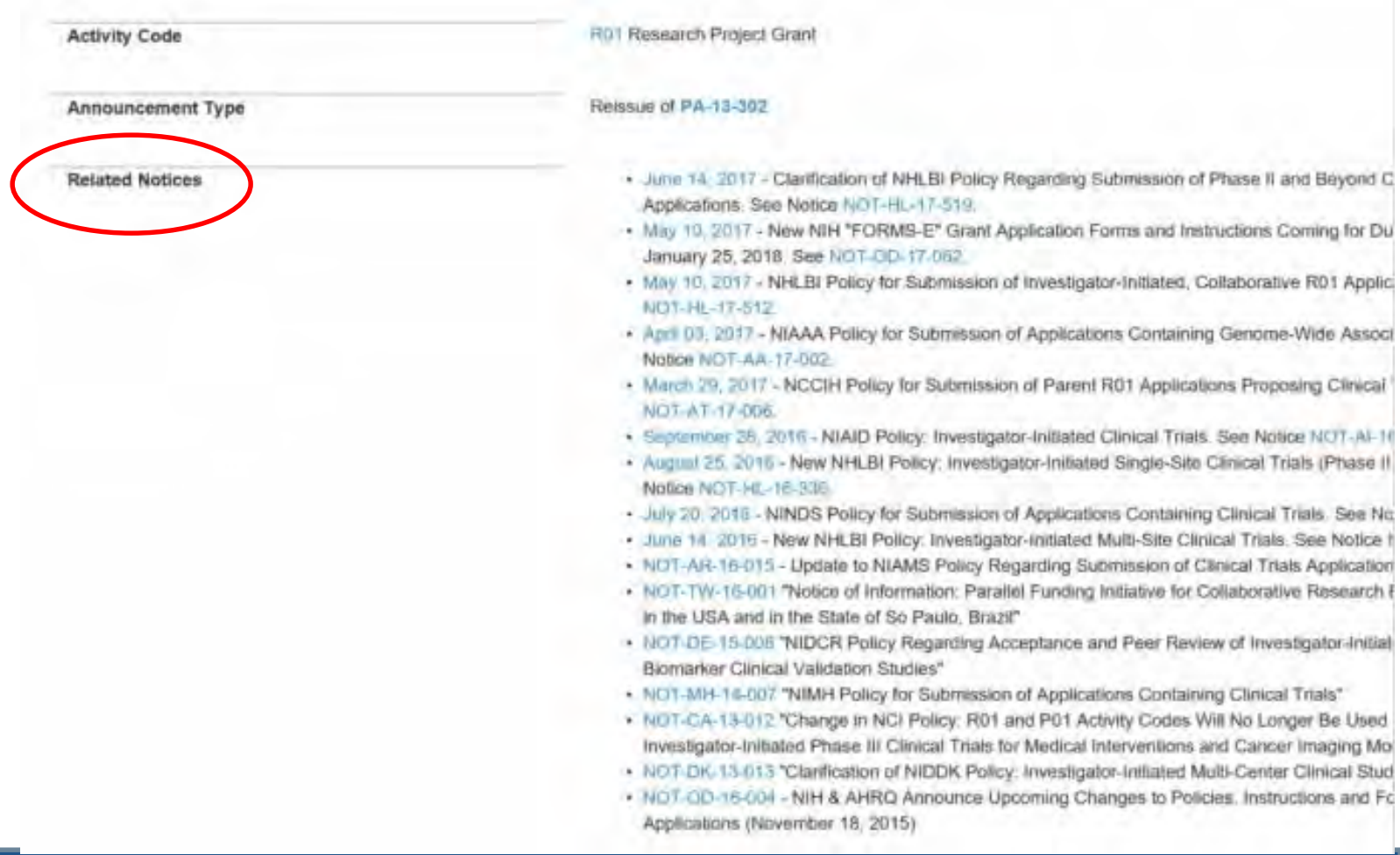


Section II. Award Information

Funding Instrument	Grant: A support mechanism providing money, property, or both to an eligible entity to carry out an approved project or activity
Application Types Allowed	New Resubmission Revision The OER Glossary and the SF424 (R&R) Application Guide provide details on these application types
Clinical Trial?	Required. Only accepting applications that propose clinical trial(s) Need help determining whether you are doing a clinical trial?
	and the companion FOA PAR-16-285.
Award Budget	Direct costs are limited to $450,000 over the R34 project period, with no more than $225,000 in direct costs allowed in any single year
Award Project Period	The total project period for an application submitted in response to this FOA may not exceed 3 years.

All clinical trials MUST be submitted to a funding opportunity announcement that allows clinical trials

Review the Related Notices in the Funding Opportunity Announcement



Activity Code	R01 Research Project Grant
Announcement Type	Reissue of PA-13-302
Related Notices	• June 14, 2017 - Clarification of NHLBI Policy Regarding Submission of Phase II and Beyond C Applications. See Notice NOT-HL-17-519. • May 10, 2017 - New NIH "FORMS-E" Grant Application Forms and Instructions Coming for Du January 25, 2018. See NOT-OD-17-062. • May 10, 2017 - NHLBI Policy for Submission of Investigator-Initiated, Collaborative R01 Applic NOT-HL-17-512. • April 03, 2017 - NIAAA Policy for Submission of Applications Containing Genome-Wide Associ Notice NOT-AA-17-002. • March 29, 2017 - NCCIH Policy for Submission of Parent R01 Applications Proposing Clinical NOT-AT-17-006. • September 28, 2016 - NIAID Policy: Investigator-Initiated Clinical Trials. See Notice NOT-AI-16 • August 25, 2016 - New NHLBI Policy: Investigator-Initiated Single-Site Clinical Trials (Phase II Notice NOT-HL-16-336. • July 20, 2016 - NINDS Policy for Submission of Applications Containing Clinical Trials. See No • June 14, 2016 - New NHLBI Policy: Investigator-Initiated Multi-Site Clinical Trials. See Notice • NOT-AR-16-015 - Update to NIAMS Policy Regarding Submission of Clinical Trials Application • NOT-TW-16-001 "Notice of Information: Parallel Funding Initiative for Collaborative Research in the USA and in the State of So Paulo, Brazil" • NOT-DE-15-006 "NIDCR Policy Regarding Acceptance and Peer Review of Investigator-Initial Biomarker Clinical Validation Studies" • NOT-MH-16-007 "NIMH Policy for Submission of Applications Containing Clinical Trials" • NOT-CA-13-012 "Change in NCI Policy: R01 and P01 Activity Codes Will No Longer Be Used Investigator-Initiated Phase III Clinical Trials for Medical Interventions and Cancer Imaging Mo • NOT-DK-13-013 "Clarification of NIDDK Policy: Investigator-Initiated Multi-Center Clinical Stud • NOT-OD-16-004 - NIH & AHRQ Announce Upcoming Changes to Policies, Instructions and Fo Applications (November 18, 2015)

Clinical trial review criteria

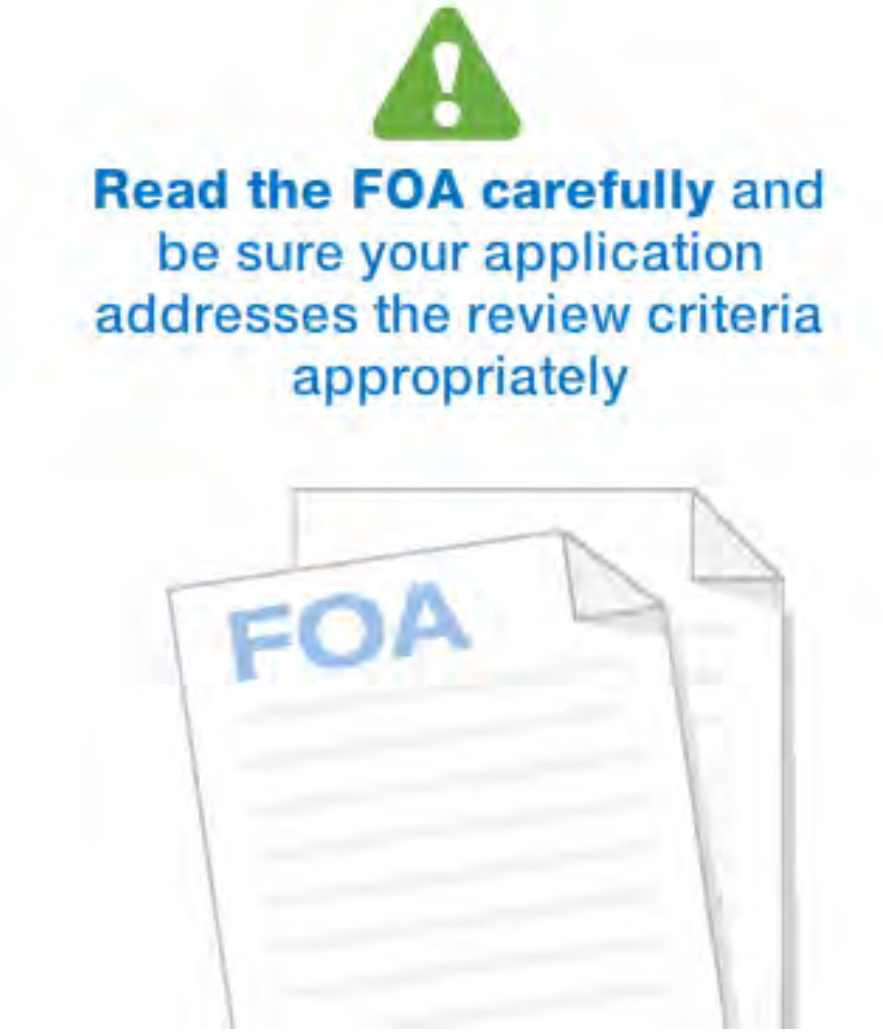
FOAs will include additional criteria:

Scored Review Criteria

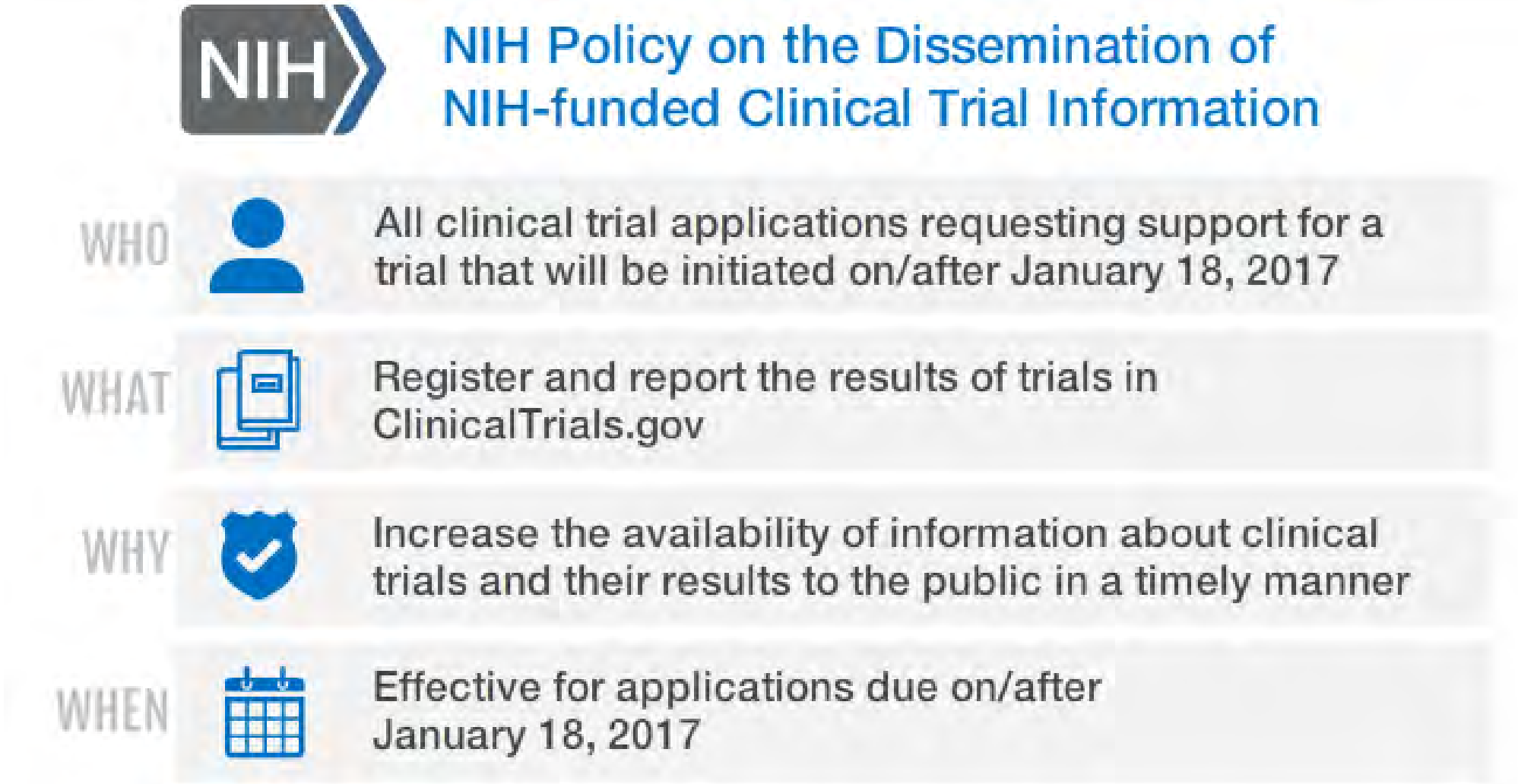
- ✓ Significance
- ✓ Investigator
- ✓ Innovation
- ✓ Approach
- ✓ Environment

Additional review Criteria

- ✓ Study Timeline



Registering and reporting results on Clinical Trials.gov



Registering and reporting results on Clinical Trials.gov

In order to comply with the NIH Policy on Clinical Trial Dissemination, awardees must:

- ✓ Submit a statement in the application that outlines a plan to comply with the expectations of the policy
- ✓ Register the clinical trial no later than 21 days after enrolling the first participant
- ✓ Update the trial with submitted information at least once a year
- ✓ Submit summary results no later than one year after primary completion date

Case Studies for determining whether a study is a clinical trial

https://grants.nih.gov/policy/clinical-trials/case-studies.htm

The study involves the recruitment of research participants suspected to have disease X. It is designed to compare the ability of 2 different widely used algorithms for digitally detecting tumors. A will be used in half of the patients; B will be used in the other half.

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1. Does the study involve human participants? Yes, the study involves human participants.

2. Are the participants prospectively assigned to an intervention? No, not in this context. The study is not intended to assess how the choice of detection algorithm modifies a health related biomedical or behavioral outcome.

X This study is not a clinical trial.

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1. Does the study involve human participants? Yes, the study involves human participants.
2. Are the participants prospectively assigned to an intervention? Yes, the participants are prospectively assigned to receive an intervention, one of two diagnostic devices.

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1. Does the study involve human participants? Yes, the study involves human participants.
2. Are the participants prospectively assigned to an intervention? Yes, the participants are prospectively assigned to receive an intervention, one of two diagnostic algorithms.
3. Is the study designed to evaluate the effect of the intervention on the participants? Yes, the study is designed to evaluate the ability of the algorithms to diagnose disease X, and in that way to inform diagnosis and clinical management.

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1. Does the study involve human participants? Yes, the study involves human participants.
2. Are the participants prospectively assigned to an intervention? Yes, the participants are prospectively assigned to receive an intervention, one of two diagnostic devices.
3. Is the study designed to evaluate the effect of the intervention on the participants? Yes, the study is designed to evaluate the ability of the two commercially available devices to diagnose disease X, and in that way to inform diagnosis and clinical management.
4. Is the effect being evaluated a health-related biomedical or behavioral outcome? Yes, the effect being evaluated, the extent to which providing specific information to physicians informs the treatment of patients, is a health-related outcome.

\+ This study is a clinical trial.

Case Studies for determining whether a study is a clinical trial

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The study involves the recruitment of healthcare providers to assess the extent to which being provided with genomic sequence information about their patients informs their treatment of those patients towards improved outcomes.

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The study involves the recruitment of healthcare providers to assess the extent to which being provided with genomic sequence information about their patients informs their treatment of those patients towards improved outcomes.

1. Does the study involve human participants? Yes, both the physicians and the patients are human participants

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The study involves the recruitment of healthcare providers to assess the extent to which being provided with genomic sequence information about their patients informs their treatment of those patients towards improved outcomes.

1. Does the study involve human participants? Yes, both the physicians and the patients are human participants
2. Are the participants prospectively assigned to an intervention? Yes, physicians are prospectively assigned to receive genomic sequence information, which is the intervention.

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2. Are the participants prospectively assigned to an intervention? Yes, physicians are prospectively assigned to receive genomic sequence information, which is the intervention.
3. Is the study designed to evaluate the effect of the intervention on the participants? Yes, the study is designed to evaluate the effect of intervening with physicians, on the treatment they provide to their patients.

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3. Is the study designed to evaluate the effect of the intervention on the participants? Yes, the study is designed to evaluate the effect of intervening with physicians, on the treatment they provide to their patients.
4. Is the effect being evaluated a health-related biomedical or behavioral outcome? Yes, the effect being evaluated, diagnosis and clinical management of patients with disease X, is a health-related outcome.

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Case Studies for determining whether a study is a clinical trial

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The study involves evaluating different types of printed announcements to identify the best designs for ensuring comprehension and retention of information in adults. Visitors to public libraries will be selected at random and asked to read one of the two announcements and then to take a short survey to elicit their perspectives about readability.

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1. Does the study involve human participants? Yes, the visitors to the library are human participants.
2. Are the participants prospectively assigned to an intervention? No, not in this context. The study is not designed to determine whether the two announcements modify a health-related behavioral or biomedical outcome.

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The study involves randomizing individuals to different processes for informed consent. It is designed to assess the effectiveness of interactive and multimedia components in enhancing participants' understanding of the study's purpose and procedures.

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2. Are the participants prospectively assigned to an intervention? Yes, the participants are prospectively assigned to an intervention, different consent processes.

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2. Are the participants prospectively assigned to an intervention? Yes, the participants are prospectively assigned to an intervention, different consent processes.
3. Is the study designed to evaluate the effect of the intervention on the participants? Yes, the study is designed to evaluate the effect of different informed consent processes on understanding the study.

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2. Are the participants prospectively assigned to an intervention? Yes, the participants are prospectively assigned to an intervention, different consent processes.
3. Is the study designed to evaluate the effect of the intervention on the participants? Yes, the study is designed to evaluate the effect of different informed consent processes on understanding the study.
4. Is the effect being evaluated a health-related biomedical or behavioral outcome? Yes, enhanced comprehension of information is a health-related behavioral outcome.

+ This study is a clinical trial

Follow-up Actions

- ✓ Read the Funding Opportunity Announcements and the instructions very carefully
- ✓ Start the application process early
- ✓ Understand how these new policies will affect your application and award

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Pick up a copy of the links to more information