G.500 - PHS Human Subjects and Clinical Trials Information

The PHS Human Subjects and Clinical Trials Information form is used to collect information on human subjects research, clinical research, and/or clinical trials, including study population characteristics, protection and monitoring plans, and a protocol synopsis. This form accommodates the full spectrum of all types of clinical trials, including, but not limited to, exploratory/development, mechanistic, pilot/feasibility, early phase, efficacy, effectiveness, group-randomized, and others.

Read all the instructions in the Funding Opportunity Announcement (FOA) before completing this form to ensure your application meets all IC-specific criteria. If you are proposing a clinical trial, make sure your FOA accepts clinical trials (i.e., 'clinical trials required' or 'clinical trials optional').

The PHS Human Subjects and Clinical Trials Information form, together with the rest of your application, should include sufficient information needed for evaluation of the project, independent of any other documents (e.g., previous application). Be specific, describe each study clearly, and avoid redundancies. Be especially careful to avoid redundancies with your research strategy.

Quick Links

Complete the PHS Human Subjects and Clinical Trials Information form after you have completed the G.220 - R&R Other Project Information form. If you change your answer to the "Are Human Subjects Involved" question after you have started entering information into the PHS Human Subjects and Clinical Trials Information form, your data in the PHS Human Subjects and Clinical Trials Information form may be lost.

This form accommodates the full spectrum of all types of clinical trials, including, but not limited to, exploratory/development, mechanistic, pilot/feasibility, early phase, efficacy, effectiveness, group-randomized, and others.

Who should use the PHS Human Subjects and Clinical Trials Information form:

All applicants must use the PHS Human Subjects and Clinical Trials Information form regardless of your answer to the question "Are human subjects involved?" on the G.220 - R&R Other Project Information form.

If you answered "No" to the question "Are human subjects involved?" on the G.220 – R&R Other Project Information form, see the "If No to Human Subjects" section for instructions.

Additional Instructions for Training:

K12 and D43 applicants applying to FOAs that accept clinical trials (i.e., 'clinical trials required' or 'clinical trials optional'): Use the PHS Human Subjects and Clinical Trials Information Form to submit delayed onset studies, if applicable. Do not fill in Study Records. Follow the instructions in your FOA.

All other Training applicants: This form is not applicable and will not be available to you.

Note for studies involving only the secondary use of identifiable biospecimens or data: For studies where the only involvement of human subjects is the use of identifiable biospecimens or data originally collected for another purpose, complete the PHS Human Subjects and Clinical Trials Information form with information specific to the current study and not the original collection unless the information associated with the original collection is pertinent to the proposed study. If information about the original

collection is necessary, provide context and clearly distinguish between the current study and historical information.

Using the PHS Human Subjects and Clinical Trials Information form:

Follow instructions on the PHS Human Subjects and Clinical Trials Information form that are specific to your answer to the “Are Human Subjects Involved?” question on the G.220 R&R Other Project Information form. The PHS human Subjects and Clinical Trials Information form allows you to add study record(s) and/or delayed onset study(ies), as applicable.

Within each Study Record: PHS Human Subjects and Clinical Trials Information, you will add detailed information at the study level. Add a separate study record for each protocol involving human subjects proposed in your application. Do not duplicate studies within your application. Each study within the application should be unique. Each study record is divided into numbered sections:

- Section 1 – Basic Information
- Section 2 – Study Population Characteristics (includes Inclusion Enrollment Report)
- Section 3 – Protection and Monitoring Plans
- Section 4 – Protocol Synopsis
- Section 5 – Other Clinical Trial-related Attachments

The PHS Human Subjects and Clinical Trials Information form is dynamic and may eliminate sections that are not relevant to your application. The dynamic form behavior may not be enabled on all submission methods.

Additional Instructions for Career Development:

There are three primary situations by which K applicants can apply for human subjects and/or clinical trial research.

Career Development Award (CDA) applicants who are not proposing a clinical trial: Follow the standard instructions to complete the PHS Human Subjects and Clinical Trials Information form.

CDA applicants who are proposing an <u>independent</u> clinical trial: Follow the standard instructions to complete the PHS Human Subjects and Clinical Trials Information form. *If you are proposing an independent clinical trial, make sure you are applying to a FOA that requires clinical trials*.

CDA applicants who are proposing to gain clinical trial research experience under a mentor's supervision (i.e., you will not be leading an independent clinical trial): You will generally follow the standard instructions to complete the PHS Human Subjects and Clinical Trials Information form, but follow relevant Career Development instructions where they are given. *Make sure you are applying to a FOA that does NOT allow independent clinical trials, but does encourage a clinical trial research experience led by a mentor/co-mentor as part of your research career development.* Additionally, the mentor or co-mentor is required to include a statement to document leadership of the clinical trial. The statement must include the following:

- Source of funding;
- ClinicalTrials.gov identifier (e.g., NCT87654321); and
- A description of how the mentor or co-mentor's expertise is appropriate to guide the applicant in any proposed clinical trials research experience.

This statement should be included in the "Plans and Statements of Mentor and Co-Mentor(s)" attachment in the G.410 PHS 398 Career Development Award Supplemental form.

Additional Instructions for Fellowship:

Fellowship applicants are permitted to conduct research involving human subjects; however, they are NOT permitted to lead an independent clinical trial.

Fellowship applicants who are not proposing a clinical trial: Follow the standard instructions to complete the PHS Human Subjects and Clinical Trials Information form.

Fellowship applicants who are proposing to gain clinical trial research experience under a sponsor's supervision (i.e., you will not be leading an independent clinical trial): You will generally follow the standard instructions to complete the PHS Human Subjects and Clinical Trials Information form, but follow relevant Fellowship instructions where they are given. *Make sure you are applying to a FOA that does NOT allow independent clinical trials, but that does encourage a clinical trial research experience led by a mentor/co-mentor.* Additionally, the sponsor or co-sponsor is required to include a statement to document leadership of the clinical trial. The statement must include the following:

- Source of funding;
- ClinicalTrials.gov identifier (e.g., NCT87654321); and
- a description of how the mentor or co-mentor's expertise is appropriate to guide the applicant in any proposed clinical trials research experience.

This statement should be included in the "Sponsor and Co-Sponsor Statements" attachment of the G.430 PHS Fellowship Supplemental form.

Additional Instructions for Multi-project:

For multi-project applications with studies that are self-contained within a single component:

Overall Component: Do not complete a study record.

Other Component: Complete a separate study record for each human subjects study that is self-contained within a single component.

For multi-project applications with studies that span components:

Overall Component: Complete one study record for each study if it spans multiple components. This study record should include sufficient information for all components that are involved in the particular study. This might occur when an application includes a data coordinating center or recruitment core, or when participant assessments for one study are conducted across multiple components (e.g., the study includes an imaging core and clinical site).

Applicants must follow all policies and requirements related to formatting, proprietary information, human subjects, and clinical trials. See the following pages for more information:

- Format Attachments
- NIH Grants Policy Statement, Section 2.3.11.2: Confidentiality of Information
- NIH Grants Policy Statement, Section 2.3.11.2.2: The Freedom of Information Act

- Research Involving Human Subjects
- NIH's Clinical Trials website

Note: there are no page limits for any attachments in the PHS Human Subjects and Clinical Trials Information form.

PHS Human Subjects and Clinical Trials Information

Applicants must complete the human subjects questions on the R&R Other Project Information form prior to completing this form.

Are Human Subjects Involved? Yes/No

This field is pre-populated from the G.220 - R&R Other Project Information form. If the value in this field appears to be incorrect, you may correct it by adjusting it on the G.220 – R&R Other Project Information form.

Is the Project Exempt from Federal regulations? Yes/No

This field is pre-populated from the G.220 - R&R Other Project Information form. If the value in this field appears to be incorrect, you may correct it by adjusting it on the G.220 – R&R Other Project Information form.

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

This field is pre-populated from the G.220 - R&R Other Project Information form. If the value in this field appears to be incorrect, you may correct it by adjusting it on the G.220 – R&R Other Project Information form.

If No to Human Subjects

If you answered "No" to the question "Are Human Subjects Involved?" on the R&R Other Project Information form, answer the following question(s) about the use of human specimens or human data.

Does the proposed research involve human specimens and/or data?

Select "Yes" or "No" to indicate whether the proposed research involves human specimens and/or data.

Applications involving the use of human specimens or data may not be considered to be research involving human subjects, depending on the details of the materials to be used. To help determine whether your research is classified as human subjects research, refer to the **Research Involving Private Information or Biological Specimens** flowchart.

Note: If you answered "No" to the "Does the proposed research involve human specimens and/or data?" question, skip the rest of the PHS Human Subjects and Clinical Trials Information form unless otherwise directed by your FOA.

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

If you answered "Yes" to the "Does the proposed research involve human specimens and/or data?" question, you must provide a justification for your claim that no human subjects are involved.

Attach the justification as a PDF file. See NIH's Format Attachments page.

This justification should include:

- information on who is providing the data/biological specimens and their role in the proposed research;
- a description of the identifiers that will be associated with the human specimens and data;
- a list of who has access to subjects' identities; and
- information about the manner in which the privacy of research participants and confidentiality of data will be protected.

Note: once you have attached the justification, skip the rest of the PHS Human Subjects and Clinical Trials Information form unless otherwise directed by your FOA.

If Yes to Human Subjects

If you answered "Yes" to the question "Are Human Subjects Involved?" on the R&R Other Project Information form, add a study record for each proposed study involving human subjects by selecting "Add New Study" or "Add New Delayed Onset Study," as appropriate.

Other Requested Information

Who may provide Other Requested Information:

Follow the instructions below and any instructions in your FOA to determine whether you are permitted to include the "Other Requested Information" attachment.

Format:

Attach this information as a PDF file. See NIH's Format Attachments page.

Content:

Renewal applications: When preparing a renewal (or resubmission of a renewal), you can provide a list of ongoing studies or ClinicalTrials.gov identifiers (e.g., NCT87654321).

Additional Instructions for Multi-project:

For multi-project applications with studies that span components:

Overall Component: Describe the components involved with the study.

Other Components: Each component should include an attachment that indicates that the details of the study are included in the Overall component within this attachment.

Study Record(s)

Using the Study Record Attachment(s) Form:

Add a study record for each proposed study involving human subjects. If your study is a delayed onset study, see the delayed onset study(ies) instructions.

For all submission methods, the Study Record is used to collect human subjects study data. However, the steps to add a Study Record attachment(s) may vary with the submission method. For example, from the ASSIST Human Subjects and Clinical Trials tab, use the 'Add New Study' button to access the data entry screens to enter study record information directly into ASSIST. With other submission methods, you may have to extract a blank copy of the Study Record for completion offline.

After you complete each study record(s), you must add it to the PHS Human Subjects and Clinical Trials Information form. The exact process of adding your study record to the form will vary with submission method.

The PHS Human Subjects and Clinical Trials Information form accommodates up to 150 separate Study Records.

Format:

All attachments must be PDF files. The study records are already fillable PDFs when extracted. Do not alter the format of the study record file. Use unique file names for each human subject study record.

Content:

Follow the instructions in the "Study Record: PHS Human Subjects and Clinical Trials Information" section below.

Delayed Onset Study(ies)

If any of your human subjects studies meet the agency definition of "delayed onset human subject study," enter the information as instructed below. For any study that you include as a delayed onset study in this section, do not fill out a full study record, as the delayed onset record is sufficient.

Notes on delayed onset studies:

- Delayed onset does NOT apply to a study that can be described but will not start immediately (i.e., delayed start).
- If you have multiple delayed onset studies, you can include them together in a single Delayed Onset Study.

For additional guidance on whether a study meets the criteria to be considered "delayed onset," refer to the Supplemental Instructions, Part II, Section 2. Scenario D: Delayed-Onset Human Subjects Research.

Study Title

This field is required.

The Study Title can have a maximum of 600 characters.

Enter a brief, unique title that describes the study the participants will be involved in. If there is more than one study (i.e., you are including more than one study record in your application), each must have a unique Study Title.

Note on multiple delayed onset studies: If you are including multiple delayed onset studies in one delayed onset study entry, you may enter "Multiple Delayed Onset Studies" as the title of this record.

Anticipated Clinical Trial?

This field is required.

Check this box if you anticipate that this study will be a clinical trial. For help determining

whether your study meets the definition of clinical trial, see the Clinical Trial Questionnaire below.

Read your FOA carefully to determine whether clinical trials are allowed in your application.

Note on multiple delayed onset studies: If you are including multiple delayed onset studies in one delayed onset study entry, and you anticipate that any of these studies will be a clinical trial, answer "Yes" to the "Anticipated Clinical Trial?" checkbox.

Additional Instructions for Career Development:

CDA applicants who are proposing to gain clinical trial research experience under a mentor's supervision (i.e., you will not be leading an independent clinical trial): Do not check the "Anticipated Clinical Trial?" box.

Additional Instructions for Fellowship:

Do not check the "Anticipated Clinical Trial?" box. Fellowship FOAs do not allow clinical trials.

Justification Attachment

This attachment is required.

Attach the justification as a PDF file. See NIH's Format Attachments page.

- All delayed onset studies must provide a justification explaining why human subjects study information is not available at the time of application.
- If NIH's single Institutional Review Board policy will apply to your study, this justification must also include information regarding how the study will comply with the policy and state that you will provide an sIRB plan prior to initiating any multi-site study.
- If NIH's policy on the Dissemination of NIH-Funded Clinical Trial Information will apply to your study, this justification must also include the dissemination plan.

Note on multiple delayed onset studies: If you are including more than one delayed onset study in any given delayed onset study entry, address all the included studies in a single justification attachment.

Study Record: PHS Human Subjects and Clinical Trials Information

Section 1 - Basic Information

Who must complete "Section 1 – Basic Information:"

"Section 1 – Basic Information" is required for all studies involving human subjects.

1.1 Study Title (each study title must be unique)

The “Study Title” field is required.

The Study Title can have a maximum of 600 characters.

Enter a brief title that describes the study the participants will be involved in. If there is more than one study (i.e., you are including more than one study record in your application), each one must have a unique study title. The first 150 characters will display in the application image bookmarks.

Note: when registering a clinical trial in ClinicalTrials.gov, all study titles across your organization must be unique.

1.2 Is this Study Exempt from Federal Regulations? (Yes/No)

The “Is the Study Exempt from Federal Regulations” question is required.

Indicate whether the study is exempt from Federal regulations for the Protection of Human Subjects.

For more information, see the NIH’s Exempt Human Subjects Research infographic.

1.3 Exemption Number

The “Exemption Number” field is required if you selected “Yes” to the “Is this Study Exempt from Federal Regulations?” question.

Select the appropriate exemption number(s) for this particular study. Multiple selections are permitted.

For more information:

The categories of research that qualify for exemption are defined in the Common Rule for the Protection of Human Subjects. These regulations can be found at 45 CFR 46.

Need help determining the appropriate exemption number? Refer to NIH's Research Involving Human Subjects Frequently Asked Questions.

The Office of Human Research Protections (OHRP) guidance states that appropriate use of exemptions described in 45 CFR 46 should be determined by an authority independent from the investigators (for more information, see OHRP's Frequently Asked Questions). Institutions often designate their Institutional Review Board (IRB) to make this determination. Because NIH does not require IRB approval at the time of application, the exemptions designated often represent the opinion of the PD/PI, and the justification provided for the exemption by the PD/PI is evaluated during peer review.

1.4 Clinical Trial Questionnaire

The Clinical Trial Questionnaire is required.

Note: the following are **NOT** considered clinical trials:

- Surveys
- Questionnaires
- User preferences
- Focus groups
- Secondary research with biospecimens or health information
- Educational studies

Note for mechanistic studies: Many mechanistic studies (i.e., those designed to understand a biological or behavioral process, the pathophysiology of a disease, or the mechanism of action of an intervention) meet the NIH definition of a clinical trial.

Answer "Yes" or "No" to the following questions to determine whether this study involves a clinical trial. Answer the following questions based only on the study you are describing in this study record.

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

If you answered "Yes" to all the questions in the Clinical Trial Questionnaire, this study meets the definition of a clinical trial.

Refer to the table below for information about what sections of this form are required, optional, or not permitted based on your answers to Question 1.4 Clinical Trial Questionnaire.

Form Section	If you answered "yes" to all the questions in the Clinical Trial Questionnaire	If you answered "No" to any of the questions in the Clinical Trial Questionnaire
Section 2 – Study Population Characteristics	Required	Required
Section 3 – Protection and Monitoring Plans	Required	Required
Section 4 – Protocol Synopsis	Required	Do not complete
Section 5 – Other Clinical Trial-related Attachments	Required	Do not complete

Additional Instructions for Career Development:

CDA applicants who are proposing to gain clinical trial research experience under a mentor's supervision (i.e., you will not be leading an independent clinical trial): Even if you answered "Yes" to all the questions in the Clinical Trial Questionnaire, only certain fields of the HS/CT form are required because the study is not an independent clinical trial. Follow the additional instructions for Career Development throughout the "Study Record: PHS Human Subjects and Clinical Trials Information" instructions.

Additional Instructions for Fellowship:

Fellowship applicants who are proposing to gain clinical trial research experience under a mentor's supervision (i.e., you will not be leading an independent clinical trial): Even if you answered "Yes" to all the questions in the Clinical Trial Questionnaire, only certain fields of the HS/CT form are required because the study is not an independent clinical trial. Follow the additional instructions for Fellowship throughout the "Study Record: PHS Human Subjects and Clinical Trials Information" instructions.

For more information:

- the OER Glossary's definition of an NIH-defined clinical trial
- the NIH's decision tool will help determine whether your study is an NIH-defined clinical trial
- Your study may also be subject to additional regulations. Read NIH's What NIH Grantees Need to Know About FDAAA.

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

If a clinical trial has already been entered into ClinicalTrials.gov, enter the ClinicalTrials.gov identifier (e.g., NCT87654321) for this trial.

If you are building on an existing study (e.g., ancillary study), enter the ClinicalTrials.gov identifier only for the ancillary study, not the parent study.

Section 2 - Study Population Characteristics

Who must complete "Section 2 - Study Population Characteristics:"

All of "Section 2 – Study Population Characteristics" is required for all human subjects studies unless, on Question 1.3 "Exemption Number," you selected certain exemptions, as detailed below:

- If you selected only **Exemption 4** and no other exemptions: "Section 2 – Study Population Characteristics" is not required.
- If you selected any combination of the following exemptions, and no other exemptions: "Section 2 – Study Population Characteristics" is required, except certain questions, as noted in the individual field instructions below.
    - **Exemption 4,**
    - **Exemption 7, and/or**
    - **Exemption 8.**

2.1 Conditions or Focus of Study

At least 1 entry is required, and up to 20 entries are allowed.

Identify the name(s) of the disease(s) or condition(s) you are studying, or the focus of the study. If available, use appropriate descriptors from NLM's Medical Subject Headings (MeSH) so the application can be categorized. Include an entry for each condition.

2.2 Eligibility Criteria

List the study's inclusion and exclusion criteria. To provide a bulleted list, use a dash followed by a space ("- ") at the start of each bullet. Further explanation or justification should be included in the Recruitment and Retention plan.

Your text entry is limited to 15,000 characters.

2.3 Age Limits

Minimum Age

Enter the numerical value for the minimum age a potential participant can be to be eligible for the study. Provide the relevant units of time (i.e., years, months, weeks, days, hours, or minutes). If there is no lower limit or no lower limit is known, enter "N/A (No Limit)."

Maximum Age

Enter the numerical value for the maximum age a potential participant can be to be eligible for the study. Provide the relevant units of time (i.e., years, months, weeks, days, hours, or minutes). If there is no upper limit or no upper limit is known, enter "N/A (No Limit)."

2.4 Inclusion of Women, Minorities, and Children

Format:

Attach this information as a PDF file. See NIH's Format Attachments page.

Content:

Organize your attachment into two sections, following the headings and specified order below, and discuss each of the points listed below. Start each section with the appropriate section heading – "Inclusion of Women and Minorities" and "Inclusion of Children." Also include any additional information requested in the FOA.

You will also have to complete an Inclusion Enrollment Report (IER). Note that you may need to include multiple IERs for each study. Refer to the instructions for the IER below for more information.

1. Inclusion of Women and Minorities

Address the following points:

- Describe the planned distribution of subjects by sex/gender, race, and ethnicity.
- Describe the rationale for selection of sex/gender, racial, and ethnic group members in terms of the scientific objectives and proposed study design. The description may include, but is not limited to, information on the population characteristics of the disease or condition under study.
- Describe proposed outreach programs for recruiting sex/gender, racial, and ethnic group members.
- Inclusion and Excluded Groups: Provide a reason for limiting inclusion of any group by sex/gender, race, and/or ethnicity. In general, the cost of recruiting certain groups and/or geographic location alone are not acceptable reasons for exclusion of particular groups. See the Inclusion of Women and Minorities as Participants in Research Involving Human Subjects - Policy Implementation Page for more information.

Existing Datasets or Resources. If you will use an existing dataset, resource, or samples that may have been collected as part of a different study, you must address inclusion, following the instructions above. Generally, you must provide details about the sex/gender, race, and ethnicity of the existing dataset/resource and justify the details as appropriate to the scientific goals of the proposed study.

For more information about what is considered an existing dataset or resource for inclusion policy, see the NIH FAQs on Monitoring Inclusion When Working with Existing Datasets and/or Resources.

NIH-Defined Phase III Clinical Trials. If the proposed research includes an NIH-Defined Phase III Clinical Trial, the "Inclusion of Women, Minorities, and Children" attachment MUST address plans for how sex/gender, race, and ethnicity will be taken into consideration in the design and valid analysis of the trial. See the instructions for "Valid Analysis" and "Plans to test for Differences in Effect among Sex/gender, Racial, and/or Ethnic Groups" below.

Additional information about valid analysis is available on the NIH Policy and Guidelines on The Inclusion of Women and Minorities as Subjects in Clinical Research page.

Valid Analysis (for NIH-Defined Phase III Clinical Trials only):

Address the following issues for ensuring valid analyses:

- Inclusive eligibility criteria – in general, the cost of recruiting certain groups and/or geographic location alone are not acceptable reasons for exclusion of particular groups
- Allocation of study participants of both sexes/genders and from different racial and/or ethnic groups to the intervention and control groups by an unbiased process such as randomization;
- Unbiased evaluation of the outcome(s) of study participants; and
- Use of unbiased statistical analyses and proper methods of inference to estimate and compare the intervention effects by sex/gender, race, and/or ethnicity, particularly if prior evidence strongly suggests that such differences exist.

Plan to Test for Differences in Effect among Sex/gender, Racial, and/or Ethnic Groups (for NIH-Defined Phase III Clinical Trials only):

Applicants also should address whether they plan to test for differences in effect among sex/gender, racial, and/or ethnic groups and why such testing is or is not appropriate.

This plan must include selection and discussion of one of the following analysis plans:

- Plans to conduct analyses to detect significant differences in intervention effect among sex/gender, racial, and/or ethnic subgroups when prior studies strongly support these significant differences among one or more subgroups, or
- Plans to include and analyze sex/gender, racial, and/or ethnic subgroups when prior studies strongly support no significant differences in intervention effect between subgroups. (Representation of sex/gender, racial, and ethnic groups is not required as subject selection criteria, but inclusion is encouraged.), or
- Plans to conduct valid analyses of the intervention effect in sex/gender, racial, and/or ethnic subgroups (without requiring high statistical power for each subgroup) when the prior studies neither support nor negate significant differences in intervention effect among subgroups.

2. Inclusion of Children

For the purposes of the Inclusion of Children, individuals under 18 are defined as a child; however, exclusion of any specific age or age range group (e.g., older adults) should be justified in this section. In addition, address the following points:

- Children are expected to be included in all NIH-defined clinical research unless there are scientific or ethical reasons not to include them. Discuss whether children (as a whole or a subset of individuals under 18) will be included or excluded. If children will be included, include a rationale for selecting a specific age range of children, if relevant. If children will be excluded, provide a rationale for exclusion. See the NIH Policy and Guidelines on the Inclusion of Children as Participants in Research Involving Human Subjects for additional information about circumstances that may justify the exclusion of children.
- Include a description of the expertise of the investigative team for working with children of the ages included, of the appropriateness of the available facilities to accommodate the children, and the inclusion of a sufficient number of children to contribute to a meaningful analysis relative to the purpose of the study.
- When children are involved in research, the policies under HHS' 45 CFR 46, Subpart D - Additional Protections for Children Involved as Subjects in Research apply and must be addressed in the Protection of Human Subjects attachment.

For more information:

- NIH's Policy Implementation Page on the Inclusion of Women and Minorities
- NIH's Policy Implementation Page on the Inclusion of Children
- HHS' 45 CFR 46 Subpart B – Additional Protections for Pregnant Women, Fetuses, and Neonates
- HHS' 45 CFR 46 Subpart D – Additional Protections for Children
- NIH Grants Policy Statement, Section 4.1.15.7: Inclusion of Children as Subjects in Clinical Research
- NIH Grants Policy Statement, Section 4.1.15.8: Inclusion of Women and Minorities as Subjects in Clinical Research and Reporting Sex/Gender, Racial, and Ethnic Participation

2.5 Recruitment and Retention Plan

Who must complete the "Recruitment and Retention Plan" attachment:

The "Recruitment and Retention Plan" attachment is required unless you selected any combination of the following exemptions, and no other exemptions, on Question 1.3 "Exemption Number:"

- E4,
- E7, and/or
- E8.

Format:

Attach this information as a PDF file. See NIH's Format Attachments page.

Content:

Describe how you will recruit and retain participants in your study. You should address both planned recruitment activities as well as proposed engagement strategies for retention.

2.6. Recruitment Status

Who must complete the "Recruitment Status" question:

The "Recruitment Status" question is required unless you selected any combination of the following exemptions, and no other exemptions, on Question 1.3 "Exemption Number:"

- E4,
- E7, and/or
- E8.

Content:

From the dropdown menu, select a single "Recruitment Status" that best describes the proposed study, based upon the status of the individual sites. If any facility in a multi-site study has an individual site status of "recruiting," then choose "recruiting" for this question. Only one selection is allowed. Choose from the following options:

- Not yet recruiting
- Recruiting
- Enrolling by invitation
- Active, not recruiting
- Completed
- Suspended
- Terminated (Halted Prematurely)
- Withdrawn (No Participants Enrolled)

2.7. Study Timeline

Who must complete the "Study Timeline" attachment:

The "Study Timeline" attachment is required unless you selected any combination of the following exemptions, and no other exemptions, on Question 1.3 "Exemption Number:"

- E4,
- E7, and/or
- E8.

Format:

Attach this information as a PDF file. See NIH's Format Attachments page.

Content:

Provide a description or diagram describing the study timeline. The timeline should be general (e.g., 1 year after notice of award), and should not include specific dates.

Note: Additional milestones or timelines may be requested as just-in-time information or post-award.

2.8. Enrollment of First Subject

Who must complete the "Enrollment of First Subject" question:

The “Enrollment of First Subject” question is required unless you selected any combination of the following exemptions, and no other exemptions, on Question 1.3 “Exemption Number:”

- E4,
- E7, and/or
- E8.

Content:

Enter the date (MM/DD/YYYY) of the enrollment of the first subject into the study. From the dropdown menu, select whether this date is anticipated or actual.

Inclusion Enrollment Report(s)

Who must complete the Inclusion Enrollment Report(s):

An Inclusion Enrollment Report is required for all human subjects studies unless, on Question 1.3 “Exemption Number,” you selected only Exemption 4 and no other exemptions.

Using the Inclusion Enrollment Report:

Each proposed study, unless it is falls under Exemption 4, must contain at least one Inclusion Enrollment Report (IER). However, more than one IER per study is allowed.

Once you have added an IER for a given study, you may edit, remove, or view it. You may also add additional IERs.

Note: The IER format should NOT be used for collecting data from study participants.

Note: You can add a maximum of 20 IERs per study record. These can be a combination of planned and cumulative reports.

Multi-site studies: Generally, if the application includes a study recruiting subjects at more than one site/location, investigators may create one IER or separate, multiple IERs to enable reporting by study or by site, depending on the scientific goals of the study and whether monitoring of inclusion enrollment would benefit from being combined or separated. At a minimum, participants enrolled at non-U.S. sites must be reported separately from participants enrolled at US sites, even if part of the same study. Please review the FOA to determine whether there are any other specific requirements about how to complete the IER.

Duplicative Inclusion Reports: It is important that the IER for a given study be associated with only one application and be provided only once in a given application (e.g., do not submit the same IER on both the data coordinating center and the research site). If submitting individual application(s) as part of a network or set of linked applications, please provide the IER with the individual site applications unless otherwise directed by the FOA.

Renewal applications: When preparing a renewal (or resubmission of a renewal), investigators should provide a narrative description regarding the cumulative enrollment from the previous funding period(s) as part of the progress report section of the research strategy attachment in the application. The IER should NOT be used for this purpose. If a given study will continue with the same enrollment or additional enrollment, or if new studies are proposed, provide a new IER for each as described in the instructions above.

Resubmission applications: If inclusion enrollment tables were provided in the initial submission application, and if those studies will be part of the resubmission application, complete the IER and submit

again with the resubmission application, regardless of whether the enrollment has changed or not. Also, provide any new (additional) IERs.

Revision applications: Provide an IER if new studies are planned as part of the Revision and they meet the NIH definition for clinical research.

Additional Instructions for Multi-project:

For multi-project applications with studies that are self-contained within a single component:

Other Component: Include the IERs with the component(s) that involves the study(s), unless otherwise directed by the FOA.

For multi-project applications with studies that span components:

Overall Component: Should the study span more than one component, include the IER with the study record in the Overall Component and insert a comment in the comment field of the IER to indicate what other components it is associated with.

For more information:

Refer to the Inclusion of Women and Minorities as Participants in Research Involving Human Subjects - Policy Implementation Page.

1. Using an Existing Dataset or Resource? (Yes/No)

The “Using an Existing Dataset or Resource” question is required.

Indicate whether this study involves the use of an existing dataset or resource.

For additional guidance on what is considered an existing dataset, refer to the NIH FAQs on Monitoring Inclusion When Working with Existing Datasets and/or Resources.

2. Enrollment Location Type (Domestic/Foreign)

The “Enrollment Location Type” field is required.

Select whether the participants described in the IER are based at a U.S. or at a non-U.S. site. At a minimum, participants at U.S. and non-U.S. sites must be reported separately (i.e., on separate IERs), even if it is for the same study.

For additional guidance on how to complete the IER if you will be working with non-U.S. populations, refer to these FAQs on Monitoring Inclusion in Non-US Research Participants.

3. Enrollment Country(ies)

The “Enrollment Country(ies)” field is optional.

Indicate the enrollment country or countries for the participants. Multiple U.S. sites can be reported together in one IER. Foreign countries can be reported together in one IER. However, you must use separate IERs for U.S. and non-U.S. sites. You can add up to 200 countries per IER.

4. Enrollment Location(s)

The “Enrollment Location(s)” field is optional.

Indicate the type of enrollment location (e.g., hospital, university, or research center), not the name of the enrollment location.

Enrollment locations are typically where the research is conducted, and can be different from the recruitment site.

5. Comments

Your comments are limited to 500 characters.

Enter information you wish to provide about this IER. This includes, but is not limited to, addressing information about distinctive subpopulations if relevant to the scientific hypotheses being studied. If inclusion monitoring is conducted on another study or NIH grant (e.g., data coordinating center or research site), please indicate here.

Planned

Who must complete planned enrollment tables?

You must enter planned enrollment counts if your proposed study will **not** use an existing dataset or resource. Planned enrollment generally means that individuals will be recruited into the study and/or that individuals have already been recruited and continue to be part of the study.

For more information about what is considered an existing dataset or resource for inclusion policy, see the NIH FAQs on Monitoring Inclusion When Working with Existing Datasets and/or Resources.

Racial Categories

American Indian/Alaska Native:

These fields are required.

Enter the expected number of females and males (in the respective fields) who are both American Indian/Alaska Native **and** Not Hispanic or Latino. Enter the expected number of females and males (in the respective fields) who are both American Indian/Alaska Native **and** Hispanic or Latino.

Asian:

These fields are required.

Enter the expected number of females and males (in the respective fields) who are both Asian **and** Not Hispanic or Latino. Enter the expected number of females and males (in the respective fields) who are both Asian **and** Hispanic or Latino.

Native Hawaiian or Other Pacific Islander:

These fields are required.

Enter the expected number of females and males (in the respective fields) who are both Native Hawaiian or Other Pacific Islander **and** Not Hispanic or Latino. Enter the expected number of females

and males (in the respective fields) who are both Native Hawaiian or Other Pacific Islander **and** Hispanic or Latino.

Black or African American:

These fields are required.

Enter the expected number of females and males (in the respective fields) who are both Black or African American **and** Not Hispanic or Latino. Enter the expected number of females and males (in the respective fields) who are both Black or African American **and** Hispanic or Latino.

White:

These fields are required.

Enter the expected number of females and males (in the respective fields) who are both White **and** Not Hispanic or Latino. Enter the expected number of females and males (in the respective fields) who are both White **and** Hispanic or Latino.

More than One Race:

These fields are required.

Enter the expected number of females and males (in the respective fields) who both identify with more than one racial category **and** are Not Hispanic or Latino. Enter the expected number of females and males (in the respective fields) who both identify with more than one racial category **and** are Hispanic or Latino.

Total:

The total fields at the bottom will be automatically calculated and reflect the totals of all racial categories for females, males, and individuals of unknown/not reported sex/gender who are Not Hispanic or Latino and of all racial categories for females, males, and individuals of unknown/not reported sex/gender who are Hispanic or Latino. The “Total” fields in the right column will be automatically calculated to total all individuals.

Cumulative (Actual)

Who must complete cumulative (actual) enrollment tables?

You must enter cumulative enrollment counts if your proposed study will use an existing dataset or resource.

For more information about what is considered an existing dataset or resource for inclusion policy, see the NIH FAQs on Monitoring Inclusion When Working with Existing Datasets and/or Resources.

Racial Categories

American Indian/Alaska Native:

These fields are required.

Enter the number of females and males (in the respective fields) who are both American Indian/Alaska Native **and** Not Hispanic or Latino. Enter the number of females and males (in the respective fields) who are both American Indian/Alaska Native **and** Hispanic or Latino. Use the “Unknown/Not Reported” fields as needed (i.e., race and/or ethnicity is unknown).

Asian:

These fields are required.

Enter the number of females and males (in the respective fields) who are both Asian **and** Not Hispanic or Latino. Enter the expected number of females and males (in the respective fields) who are both Asian **and** Hispanic or Latino. Use the “Unknown/Not Reported” fields as needed (i.e., race and/or ethnicity is unknown).

Native Hawaiian or Other Pacific Islander:

These fields are required.

Enter the number of females and males (in the respective fields) who are both Native Hawaiian or Other Pacific Islander **and** Not Hispanic or Latino. Enter the expected number of females and males (in the respective fields) who are both Native Hawaiian or Other Pacific Islander **and** Hispanic or Latino. Use the “Unknown/Not Reported” fields as needed (i.e., race and/or ethnicity is unknown).

Black or African American:

These fields are required.

Enter the number of females and males (in the respective fields) who are both Black or African American **and** Not Hispanic or Latino. Enter the expected number of females and males (in the respective fields) who are both Black or African American **and** Hispanic or Latino. Use the “Unknown/Not Reported” fields as needed (i.e., race and/or ethnicity is unknown).

White:

These fields are required.

Enter the number of females and males (in the respective fields) who are both White **and** Not Hispanic or Latino. Enter the expected number of females and males (in the respective fields) who are both White **and** Hispanic or Latino. Use the “Unknown/Not Reported” fields as needed (i.e., race and/or ethnicity is unknown).

More than One Race:

These fields are required.

Enter the number of females and males (in the respective fields) who both identify with more than one racial category **and** are Not Hispanic or Latino. Enter the expected number of females and males (in the respective fields) who both identify with more than one racial category **and** are Hispanic or Latino. Use the “Unknown/Not Reported” fields as needed (i.e., race and/or ethnicity is unknown).

Unknown or Not Reported:

These fields are required.

Enter the number of females, males, and individuals of unknown/not reported sex/gender (in the respective fields) whose race is unknown/not reported **and** who are Not Hispanic or Latino. Enter the number of females, males, and individuals of unknown/not reported sex/gender (in the respective fields) whose race is unknown/not reported **and** who are Hispanic or Latino. Enter the number of females, males, and individuals of unknown/not reported sex/gender (in the respective fields) who are both of unknown/not reported race and of unknown/not reported ethnicity. Use the “Unknown/Not Reported” fields as needed (i.e., race and/or ethnicity is unknown).

Total:

The total fields at the bottom will be automatically calculated and reflect the totals of all racial categories for females, males, and individuals of unknown/not reported sex/gender who are Not Hispanic or Latino and of all racial categories for females, males, and individuals of unknown/not reported sex/gender who are Hispanic or Latino. Use the "Unknown/Not Reported" fields as needed (i.e., race and/or ethnicity is unknown). The "Total" fields in the right column will be automatically calculated to total all individuals.

Section 3 – Protection and Monitoring Plans

Who must complete "Section 3 – Protection and Monitoring Plans:"

All of "Section 3 – Protection and Monitoring Plans" is required for all studies involving human subjects, unless otherwise noted.

3.1 Protection of Human Subjects

Format:

Attach this information as a PDF file. See NIH's Format Attachments page.

Do not use the "Protection of Human Subjects" attachment to circumvent the page limits of the Research Strategy.

For Human Subjects Research Claiming Exemptions:

If you are claiming that your human subjects research falls under any exemptions, you must include the following statement to indicate which exemptions you are claiming: "This human subjects research falls under Exemption(s) …". Clearly identify which exemption(s) (1, 2, 3, 4, etc.) you are claiming and justify why the research meets the criteria for the exemption(s) that you have claimed. This justification should explain how the proposed research meets the criteria for the exemption claimed and should not merely repeat the criteria or definitions themselves.

For Studies that involve Non-Exempt Human Subjects Research:

For any proposed non-exempt study involving human subjects, NIH requires a Protection of Human Subjects section that is commensurate with the risks of the study, its size, and its complexity. Organize your attachment into four sections, following the headings and specified order below, and discuss each of the points listed below. Start each section with the appropriate section heading – Risks to Human Subjects, Adequacy of Protection Against Risks, Potential Benefits of the Proposed Research to Research Participants and Others, and Importance of the Knowledge to be Gained. Also include any additional information requested in the FOA.

1. Risks to Human Subjects

a. Human Subjects Involvement, Characteristics, and Design

- Briefly describe the overall study design.
- Describe the subject population(s) to be included in the study; the procedures for assignment to a study group, if relevant; and the anticipated numbers of subjects for each study group.

- List any collaborating sites where human subjects research will be performed, and describe the role of those sites and collaborating investigators in performing the proposed research.

b. Study Procedures, Materials, and Potential Risks

- Describe all planned research procedures (interventions and interactions) involving study subjects; how research material, including biospecimens, data, and/or records, will be obtained; and whether any private identifiable information will be collected in the proposed research project.
- For studies that will include the use of previously collected biospecimens, data or records, describe the source of these materials, whether these can be linked with living individuals, and who will be able to link the materials.
- Describe all the potential risks to subjects associated with each study intervention, procedure or interaction, including physical, psychological, social, cultural, financial, and legal risks; risks to privacy and/or confidentiality; or other risks. Discuss the risk level and the likely impact to subjects.
- Where appropriate, describe alternative treatments and procedures, including their risks and potential benefits. When alternative treatments or procedures are possible, make the rationale for the proposed approach clear.

2. Adequacy of Protection Against Risks

a. Informed Consent and Assent

- Describe the process for obtaining informed consent. Include a description of the circumstances under which consent will be sought and obtained, who will seek it, the nature of the information to be provided to prospective subjects, and the method of documenting consent. When appropriate, describe how potential adult subjects' capacity to consent will be determined and the plans for obtaining consent from a legally authorized representative for adult subjects not able to consent.
    - **For research involving children:** If the proposed studies will include children, describe the process for meeting HHS regulatory requirements for parental permission and child assent (45 CFR 46.408). See the HHS page on Research with Children FAQs and the NIH page on Requirements for Child Assent and Parent/Guardian Permission.
- If a waiver of some or all of the elements of informed consent will be sought, provide justification for the waiver. Do not submit informed consent document(s) with your application unless you are requested to do so.

b. Protections Against Risk

- Describe planned strategies for protecting against or minimizing all potential risks identified, including strategies to manage and protect the privacy of participants and confidentiality of research data.
- Where appropriate, discuss plans for ensuring necessary medical or professional intervention in the event of adverse effects on participants.
- Describe plans for handling incidental findings, such as those from research imaging, screening tests, or paternity tests.

c. Vulnerable Subjects, if relevant to your study

Explain the rationale for the involvement of special vulnerable populations, such as fetuses, neonates, pregnant women, children, prisoners, institutionalized individuals, or others who may be considered

vulnerable populations. 'Prisoners' includes all subjects involuntarily incarcerated (for example, in detention centers).

Pregnant Women, Fetuses, and Neonates or Children

If the study involves vulnerable subjects subject to additional protections under Subparts B and D (pregnant women, fetuses, and neonates or children), provide a clear description of the risk level and additional protections necessary to meet the HHS regulatory requirements.

- HHS' Subpart B - Additional Protections for Pregnant Women, Fetuses, and Neonates
- HHS' Subpart D - Additional Protections for Children
- OHRP Guidance on Subpart D Special Protections for Children as Research Subjects and the HHS 407 Review Process

Prisoners

If the study involves vulnerable subjects subject to additional protections under Subpart C (prisoners), describe how proposed research meets the additional regulatory requirements, protections, and plans to obtain OHRP certification for the involvement of prisoners in research.

Refer to HHS regulations, and OHRP guidance:

- HHS' Subpart C - Additional Protections Pertaining to Prisoners as Subjects
- OHRP Subpart C Guidance on Involvement of Prisoners in Research

3. Potential Benefits of the Proposed Research to Research Participants and Others

- Discuss the potential benefits of the research to research participants and others.
- Discuss why the risks to subjects are reasonable in relation to the anticipated benefits to research participants and others.
- Please note that financial compensation of subjects should not be presented as a benefit of participation in research.

4. Importance of the Knowledge to be Gained

- Discuss the importance of the knowledge to be gained as a result of the proposed research.
- Discuss why the risks to subjects are reasonable in relation to the importance of the knowledge that reasonably may be expected to result.

For more information:

Refer to the NIH's Research Involving Human Subjects site.

See also the slideshow on Preparing the Human Subjects Section.

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

Select "Yes" or "No" to indicate whether this is a multi-site study that will use the same protocol to conduct non-exempt human subjects research at more than one domestic site. Select "N/A" only if any of the following apply (do not select "N/A" if none of the following apply):

- You answered "Yes" to "Question 1.2 Is this Study Exempt from Federal Regulations? (Yes/No)"

- You are a Career Development Applicant
- You are a Fellowship Applicant

Applicants who check “Yes” are expected to use a single Institutional Review Board (sIRB) to conduct the ethical review required by HHS regulations for the Protections of Human Subjects Research.

Note: The NIH sIRB policy applies to participating domestic sites. Foreign sites participating in NIH-funded, multi-site studies are not expected to follow this policy.

Additional Instructions for Career Development:

Check “N/A,” as the sIRB policy does not apply to career development awards.

Additional Instructions for Fellowship:

Check “N/A,” as the sIRB policy does not apply to fellowship awards.

For more information:

HHS regulations and requirements for the Protections of Human Subjects can be found at 45 CFR 46.

See NIH’s Single IRB Policy for Multi-site Research for more information.

If yes, describe the single IRB plan

Format:

Attach this information as a PDF file. See NIH’s Format Attachments page.

For each study within an application, you must include an sIRB attachment. Generally, one sIRB plan per application is sufficient. You may attach the same sIRB plan to different studies within one application, but each file name must be unique. Alternatively, you can refer to a previously attached sIRB plan in subsequent studies within your application. If a different sIRB will be used for each study within the application, you should attach a separate sIRB plan to each study (note that each file name must be unique).

Content:

If you are proposing a multi-site study that will use the same protocol to conduct non-exempt human subjects research at more than one domestic site, you are expected to include a plan for the use of an sIRB. The plan should include the following elements:

- Describe how you will comply with the NIH Policy on the Use of sIRB for Multi-Site Research.
- Provide the name of the IRB that will serve as the sIRB of record.
- Indicate that all identified participating sites have agreed to rely on the proposed sIRB and that any sites added after award will rely on the sIRB.
- Briefly describe how communication between sites and the single IRB will be handled.

- Indicate that all participating sites will, prior to initiating the study, sign an authorization/reliance agreement that will clarify the roles and responsibilities of the sIRB and participating sites.
- Indicate which institution or entity will maintain records of the authorization/reliance agreements and of the communication plan.
- NOTE: Do not include the authorization/reliance agreement(s) or the communication plan(s) documents in your application.
- NOTE: If your human subjects study meets the agency definition of "Delayed Onset," include information regarding how the study will comply with the NIH single Institutional Review Board (sIRB) policy prior to initiating any multi-site study in the delayed onset study justification.

For Studies with Legal-, Regulatory-, or Policy-based Claims for Exception as described by the sIRB Policy: Indicate that review by an sIRB will not be possible for all or some sites (specify which sites) because local IRB review is required by an existing federal/state/tribal law or policy. Include a specific citation to the relevant law, policy, or regulation.

For sites requesting an exception based on compelling justification: Indicate which site(s) is requesting an exception to the use of the sIRB and provide compelling justification based on ethical or human subjects protection issues or other well-justified reasons. NIH will determine whether to grant an exception following an assessment of the need. NOTE: If you intend to request an exception to the sIRB policy based on compelling justification, do not account for this exception in your proposed budget. The proposed budget must reflect any necessary sIRB costs without an exception (i.e., applicants should not assume that an exception will be granted when considering what sIRB costs to include in the budget).

For more information:

- NIH Office of Science Policy Clinical Research IRB Review page
- FAQs on NIH Policy on the Use of a Single IRB for Multi-Site Research Costs
- FAQs on Implementation of the sIRB policy
- NIH Guide Notice on the Final NIH Policy on sIRB

3.3 Data and Safety Monitoring Plan

A "Data and Safety Monitoring Plan" attachment is required if you answered "Yes" to all the questions in the "Clinical Trial Questionnaire." The "Data and Safety Monitoring Plan" attachment is optional for all other human subjects research.

For human subjects research that does not involve a clinical trial: Your study, although it is not a clinical trial, may have significant risks to participants, and it may be appropriate to include a data and safety monitoring plan. If you choose to include a data and safety monitoring plan, you may follow the content criteria listed below, as appropriate.

Format:

Attach this information as a PDF file. See NIH's Format Attachments page.

Content:

Additional Instructions for Career Development:

CDA applicants who are proposing to gain clinical trial research experience under a mentor's supervision (i.e., you will not be leading an independent clinical trial): Include only the following information in your data and safety monitoring plan (i.e., do not follow the general instructions for the data and safety monitoring plan):

- The names of the individual(s) or group that will be responsible for trial monitoring, (i.e., the lead investigator of the clinical trial).
- If applicable, the name of an independent safety monitor or a data and safety monitoring board.

Additional Instructions for Fellowship:

Fellowship applicants who are proposing to gain clinical trial research experience under a mentor's supervision (i.e., you will not be leading an independent clinical trial): Include only the following information in your data and safety monitoring plan (i.e., do not follow the general instructions for the data and safety monitoring plan):

- The names of the individual(s) or group that will be responsible for trial monitoring, (i.e., the lead investigator of clinical trial).
- If applicable, the name of an independent safety monitor, or a data and safety monitoring board.

For any proposed clinical trial, NIH requires a data and safety monitoring plan (DSMP) that is commensurate with the risks of the trial, its size, and its complexity. Provide a description of the DSMP, including:

- The overall framework for safety monitoring and what information will be monitored.
- The frequency of monitoring, including any plans for interim analysis and stopping rules (if applicable).
- The process by which Adverse Events (AEs), including Serious Adverse Events (SAEs) such as deaths, hospitalizations, and life threatening events and Unanticipated Problems (UPs), will be managed and reported, as required, to the IRB, the person or group responsible for monitoring, the awarding IC, the NIH Office of Biotechnology Activities, and the Food and Drug Administration.
- The individual(s) or group that will be responsible for trial monitoring and advising the appointing entity. Because the DSMP will depend on potential risks, complexity, and the nature of the trial, a number of options for monitoring are possible. These include, but are not limited to, monitoring by a:
    - PD/PI: While the PD/PI must ensure that the trial is conducted according to the approved protocol, in some cases (e.g., low risk trials, not blinded), it may be acceptable for the PD/PI to also be responsible for carrying out the DSMP.
    - Independent safety monitor/designated medical monitor: a physician or other expert who is independent of the study.

- Independent Monitoring Committee or Safety Monitoring Committee: A small group of independent experts.
- Data and Safety Monitoring Board (DSMB): a formal independent board of experts including investigators and biostatisticians. NIH requires the establishment of DSMBs for multi-site clinical trials involving interventions that entail potential risk to the participants, and generally, for all Phase III clinical trials, although Phase I and Phase II clinical trials may also need DSMBs. If a DSMB is used, please describe the general composition of the Board without naming specific individuals.

For more information:

- NIH Guide Notice on Policy for Data and Safety Monitoring
- NIH Guide Notice on Data and Safety Monitoring for Phase I and Phase II Trials
- NIH Grants Policy Statement, Section 4.1.15.6: Data and Safety Monitoring

3.4 Will a Data and Safety Monitoring Board be appointed for this study? Yes/No

The "Data Safety and Monitoring Board" question is required if you answered "Yes" to all the questions in the "Clinical Trial Questionnaire." This question is optional for all other human subjects research.

Check the appropriate box to indicate whether a Data Safety and Monitoring Board (DSMB) will be appointed for this study.

3.5 Overall Structure of the Study Team

The "Overall Structure of the Study Team" attachment is required if you answered "Yes" to all the questions in the "Clinical Trial Questionnaire." This question is optional for all other human subjects research.

Format:

Attach this information as a PDF file. See NIH's Format Attachments page.

Content:

Provide a brief overview of the organizational structure of the study team, particularly the administrative sites, data coordinating sites, enrollment/participating sites, and any separate laboratory or testing centers.

Note: do not include study team members' individual professional experiences (i.e., biosketch information).

Section 4 – Protocol Synopsis

Who must complete "Section 4 – Protocol Synopsis:

All the questions in the "Protocol Synopsis" section are required if you answered "Yes" to all the questions in the "Clinical Trial Questionnaire."

If you answered "No" to any question in the "Clinical Trial Questionnaire," do not provide information in

this section.

Additional Instructions for Career Development:

CDA applicants who are proposing to gain clinical trial research experience under a mentor's supervision (i.e., you will not be leading an independent clinical trial): Do not complete any of the "Section 4 - Protocol Synopsis" section.

Additional Instructions for Fellowship:

Do not complete any of the "Protocol Synopsis" section, as Fellowship FOAs do not allow clinical trials.

4.1. Brief Summary

Enter a brief description of objectives of the protocol, including the primary and secondary endpoints. The Brief Summary is limited to 5,000 characters.

4.2. Study Design

4.2.a. Narrative Study Description

Enter a narrative description of the protocol. Studies differ considerably in the methods used to assign participants and deliver interventions. Applicants will need to show that their methods are appropriate given their plans for assignment of participants, delivery of interventions, and data collection and analysis.

Describe how participants are assigned in groups or clusters (e.g., families, providers, clinics, schools, communities), and/or when interventions are delivered to groups or clusters, and/or how and when observations on individual participants are analyzed, and any special methods that are required for analysis and sample size.

The narrative description is limited to 32,000 characters.

For more information on assigning participants to groups, see the Trials that Randomize Groups or Deliver Interventions to Groups webpage.

4.2.b. Primary Purpose

Enter or select from the dropdown menu a single "Primary Purpose" that best describes the clinical trial. If you select "Other," indicate the primary purpose (e.g., analysis) in the space provided. Choose from the following options:

- Treatment
- Prevention
- Diagnostics
- Supportive Care
- Screening
- Health Services Research
- Basic Science
- Device Feasibility

- Other (If you select “Other,” provide a description in the space provided. Your response is limited to 255 characters.)

4.2.c. Interventions

Complete the “Interventions” fields for each intervention to be used in your proposed protocol. If an arm of the study to which subjects will be assigned (as discussed in in 4.2.a Narrative Study Description) includes more than one intervention (e.g., drug plus educational intervention), complete this section for each intervention. You can add up to 20 interventions.

Intervention Type: Enter or select from the dropdown menu the intervention type the clinical trial will administer during the proposed award. Choose from the following options:

- Drug (including placebo)
- Device (including sham)
- Biological/Vaccine
- Procedure/Surgery
- Radiation
- Behavioral (e.g., Psychotherapy, Lifestyle Counseling)
- Genetic (including gene transfer, stem cell and recombinant DNA)
- Dietary Supplement (e.g., vitamins, minerals)
- Combination Product
- Diagnostic Test
- Other

Name: Enter the name of the intervention. The name must be unique within each study record. The name is limited to 200 characters.

Description: Enter a description of the intervention. The description is limited to 1,000 characters.

4.2.d. Study Phase

Enter or select from the dropdown menu a "Study Phase" that best describes the clinical trial. If your study involves a device, choose “Other.”

Choose from the following options:

- Early Phase 1 (or Phase 0)
- Phase 1
- Phase 1/2
- Phase 2
- Phase 2/3
- Phase 3
- Phase 4
- Other (If you select “Other,” provide a description in the space provided. Your response is limited to 255 characters.)

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

Select "Yes" or "No" to indicate whether the study includes an NIH-defined Phase III clinical trial.

4.2.e. Intervention Model

Enter or select from the dropdown menu a single "Intervention Model" that best describes the clinical trial. If you select “Other,” provide a description in the space provided. Choose from the following options:

- Single Group
- Parallel
- Cross-Over
- Factorial
- Sequential
- Other (If you select “Other,” provide a description in the space provided. Your response is limited to 255 characters.)

4.2.f. Masking

Select "Yes" or "No" to indicate whether the protocol uses masking. Note that masking is also referred to as “blinding.”

If you answered “Yes” to the “Masking” question, select one or more types of masking that best describes the protocol. Choose from the following options:

- Participant
- Care Provider
- Investigator
- Outcomes Assessor

4.2.g. Allocation

Enter or select from the dropdown menu a single "Allocation" that best describes how subjects will be assigned in your protocol. If allocation is not applicable to your clinical trial, select “N/A” (e.g., for a single-arm trial). Choose from the following options:

- N/A
- Randomized
- Non-randomized

4.3. Outcome Measures

Complete the “Outcome Measures” fields for each primary, secondary, and other important measures to be collected during your proposed clinical trial. You may have more than one primary outcome measure, and you can add up to 50 outcome measures.

Name: Enter the name of the individual outcome measure. The outcome measure must be unique within each study record.

Type: Enter or select from the dropdown menu the type of the outcome measure. Choose from the following options:

- Primary – select this option for the outcome measures specified in your protocol that are of greatest importance to your study
- Secondary – select this option for outcome measures specified in your protocol that are of lesser importance to your study than your primary outcomes
- Other – select this option for additional key outcome measures used to evaluate the intervention.

Time Frame: Indicate when a measure will be collected for analysis (e.g., baseline, post-treatment).

Brief Description: Describe the metric used to characterize the outcome measure if the metric is not already included in the outcome measure name. Your description is limited to 999 characters.

4.4. Statistical Design and Power

Format:

Attach this information as a PDF file. See NIH's Format Attachments page.

Content:

Specify the number of subjects you expect to enroll, the expected effect size, the power, and the statistical methods you will use with respect to each outcome measure you listed in 4.3 Outcome Measures.

4.5 Subject Participation Duration

Enter the time (e.g., in months) it will take for each individual participant to complete all study visits. If the participation duration is unknown or not applicable, write "unknown" or "not applicable." The subject participation duration is limited to 255 characters.

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

Select "Yes" or "No" to indicate whether the study will use an FDA-regulated intervention (see the definition of "FDA Regulated Intervention" under the Oversight section of the ClinicalTrials.gov Protocol Registration Data Element Definitions for Interventional and Observational Studies page).

4.6.a. If yes, describe the availability of Investigational Product (IP) and Investigational New Drug (IND)/Investigational Device Exemption (IDE) status:

This attachment is required if you answered "Yes" to the "Will the study use an FDA-regulated intervention?" question.

Format:

Attach this information as a PDF file. See NIH's Format Attachments page.

Content:

Describe the availability of study agents and support for the acquisition and administration of the study agent(s). Please indicate the IND/IDE status of the study agent, if applicable, and whether the investigators have had any interactions with the FDA. If the study agent currently has an IND/IDE number, provide that information. Note that the awarding component may request consultation with the FDA and the IND/IDE sponsor about the proposed clinical trial after peer review and prior to award.

4.7 Dissemination Plan

Format:

Attach this information as a PDF file. See NIH's Format Attachments page.

For each study within an application, you must include a Dissemination Plan attachment. One Dissemination Plan per application is sufficient. You may attach the same Dissemination Plan to

difference studies within one application, but each file name must be unique. Alternatively, you can refer to a previously attached Dissemination Plan in subsequent studies within your application.

Content:

Explain briefly your plan for the dissemination of NIH-funded clinical trial information and address how the expectations of the policy will be met. The plan must contain sufficient information to assure that:

(1) the applicant will ensure that clinical trial(s) under the award are registered and results information is submitted to ClinicalTrials.gov as outlined in the policy and according to the specific timelines stated in the policy;
(2) informed consent documents for the clinical trial(s) will include a specific statement relating to posting of clinical trial information at ClinicalTrials.gov; and
(3) the recipient institution has an internal policy in place to ensure that clinical trials registration and results reporting occur in compliance with policy requirements.

NOTE: Do not include informed consent documents in your application.

NOTE: If your human subjects study meets the definition of "Delayed Onset," include the dissemination plan in the delayed onset study justification.

For more information:

See the NIH Policy on the Dissemination of NIH-Funded Clinical Trial Information.

Section 5 – Other Clinical Trial-related Attachments

Who must complete "Section 5 – Other Clinical Trial-related Attachments:"

If you answered "Yes" to all the questions in the "Clinical Trial Questionnaire:" Include an attachment only if your FOA specifies that an attachment(s) is required or permitted; otherwise, do not include any Other Clinical Trial-related attachments.

If you answered "No" to any question in the "Clinical Trial Questionnaire:" do not provide information in this section.

Additional Instructions for Career Development:

CDA applicants who are proposing to gain clinical trial research experience under a mentor's supervision (i.e., you will not be leading an independent clinical trial): Do not complete "Section 5 – Other Clinical Trial-related Attachments."

Additional Instructions for Fellowship:

Fellowship applicants proposing to gain clinical trial research experience under a mentor's supervision (i.e., you will not be leading an independent clinical trial: Do not complete "Section 5 – Other Clinical Trial-related Attachments."

5.1. Other Clinical Trial-related Attachments

Format:

Attach this information as a PDF file. See NIH's Format Attachments page.

A maximum of 10 PDF attachments is allowed in the "Other Clinical Trial-related Attachments" section.

Content:

Provide additional trial-related information only if your FOA specifically requests it.