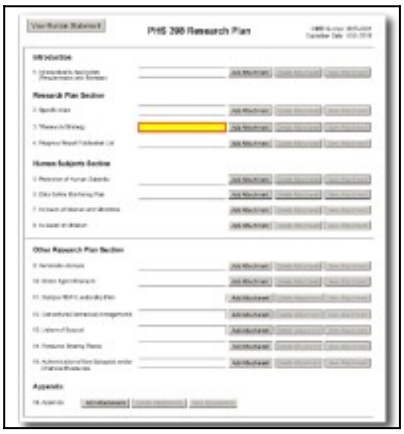
G.500 - PHS Human Subjects and Clinical Trials Information

The PHS Human Subjects and Clinical Trials Information form is used only for applications involving NIH-defined human subjects research, clinical research, and/or clinical trials.

This form collects information, including study title, exemption number, protection plans, monitoring plans (IRB, Data and Safety Monitoring, and Clinical Monitoring), study population characteristics (including Recruitment and Retention Plans and Inclusion Enrollment Reports, etc.), and trial synopsis.



View larger image

Quick Links

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

Use the PHS Human Subjects and Clinical Trials Information Form if you answered “Yes” to the question “Are human subjects involved?” on the G.220 - R&R Other Project Information Form. This answer will pre-populate at the beginning of this form.

Using the PHS Human Subjects and Clinical Trials Information Form:

The PHS Human Subjects and Clinical Trials Information Form is dynamic and will eliminate questions and/or sections that are not relevant to your application as you proceed through the questions. For example, some sections of the PHS Human Subjects and Clinical Trials Information Subform are required for all applications with research that involves human subjects, while others are required only when the project includes a clinical trial. Therefore, if you answer “No” to any the “Clinical Trial Questionnaire” questions, then all of “Section 3 - Clinical Trial Synopsis” and “Section 4 - Other Clinical Trial-related Attachments” will be unavailable, as you do not need to address those questions.

You must complete a separate PHS Human Subjects and Clinical Trials Information Subform for each clinical trial/clinical research/research involving human subjects study that you propose in your application.

Read all the instructions in the FOA before completing this form to ensure your application meets all IC-specific criteria.

Applicants must follow all policies and requirements related to proprietary information, page limits, and formatting. See the following pages for more information:

- **Format Attachments**
- **Page Limits**
- **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**

PHS Human Subjects and Clinical Trials Information Landing Page

Please complete the human subjects section of the Research & Related 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.

Is the Project Exempt from Federal regulations? Yes/No

This field is pre-populated from the G.220 - R&R Other Project Information Form.

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

This field is pre-populated from the G.220 - R&R Other Project Information Form.

If No to Human Subjects

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

This field is required if you answered "No" to “Are Human Subjects Involved? (from R&R form)”.

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

If Yes, provide an explanation of why the proposed study does not constitute 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.

PHS Human Subjects and Clinical Trials Information Sub-form for each Study

Introductory Fields

1. Study Title (must be unique)

This field is required.

The Study Title can have a maximum of 250 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 Sub-form in your application), provide a separate Study Title for each.

2. Delayed Onset Study? (Yes/No)

This field is required.

Check the appropriate box to indicate whether the study is considered delayed onset. If the study is delayed onset, select "Yes". If the study is not delayed onset, select "No".

“Delayed onset” generally means that a study has not been developed and cannot be described in terms of human subjects’ protections and inclusion. If human subjects research is anticipated within the period of the award but plans for involvement of human subjects cannot be described in the application, then “delayed onset” applies. The kinds of human subjects research activities that lack definite plans are often

- institutional awards where the selection of specific projects is made by the institution after award,

- research networks or multi-site studies where protocols to be conducted are determined after all sites have been selected, or
- projects in which the involvement of human subjects depends upon initial work in the award such as completion of instruments, animal studies, or purification of compounds.

Delayed onset does NOT apply to a study that can be described but will not start immediately.

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.

If you have answered “Yes” to the “Delayed Onset Study?” question, the subsequent sections of that particular PHS Human Subjects and Clinical Trials Information sub-form will be disabled. Complete only the remainder of the “Introductory Fields” section for this study. In addition, you should include a statement that the study meets the criteria for delayed onset human subjects research and that if awarded, the applicant will inform the awarding component about how they will comply with the NIH sIRB policy prior to initiating any multi-site study. Additionally, you must complete additional PHS Human Subjects and Clinical Trials Information sub-forms for other studies, if applicable.

If you have answered "No" to the “Delayed Onset Study?” question, you must complete the rest of the PHS Human Subjects and Clinical Trials Information sub-form.

3. Is the Study Exempt from Federal Regulations? (Yes/No)

Select 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.

4. Exemption Number

If you selected “Yes” to the “Is the Study Exempt from Federal Regulations?” question, select the appropriate exemption number for this particular study.

5. Clinical Trial Questionnaire

Answer “Yes” or “No” to the following questions to determine whether or not this study involves a clinical trial.

5.a. Does the study involve human participants?

5.b. Are the participants prospectively assigned to an intervention?

5.c. Is the study designed to evaluate the effect of the intervention on the participants?

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

If you answered “Yes” to all the questions in the Clinical Trial Questionnaire, complete all subsequent sections of the sub-form. If you answered “No” to any of the questions in the

Clinical Trial Questionnaire, complete only the first two sections (Section 1- Study Population Characteristics and Section 2- Protection and Monitoring Plans) of the PHS Human Subjects and Clinical Trials Information sub-form.

For more information:

See NIH Glossary for the definition of clinical trials and the NIH Definition of a Clinical Trial Decision Tree.

Section 1 - Study Population Characteristics

1.1 Conditions or Focus of Study

Enter a brief statement about the primary disease or condition being studied or the focus of study.

Include 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) controlled vocabulary thesaurus or terms from another vocabulary, such as the Systematized Nomenclature of Medicine—Clinical Terms (SNOMED CT), that has been mapped to MeSH within the Unified Medical Language System (UMLS) Metathesaurus.

1.2 Inclusion Criteria

List the study's inclusion criteria.

1.3 Exclusion Criteria

List the study's exclusion criteria.

1.4 Age Limits

Enter the minimum and maximum age of the study population and provide the relevant units of time.

Minimum Age

The numerical value for the minimum age a potential participant can be to be eligible for the study.

Maximum Age

The numerical value for the maximum age a potential participant can be to be eligible for the study.

1.5 Inclusion of Women, Minorities, and Children

Who must complete the "Inclusion of Women, Minorities, and Children" attachment:

Include an “Inclusion of Women, Minorities, and Children” attachment if you answered “Yes” to the question “Are human subjects involved?” on the Section G.220 - R&R Other Project Information Form and the research does not fall under Exemption 4.

Additional Instructions for Training:

Skip the “Inclusion of Women, Minorities, and Children” field, as inclusion does not apply to Training applications.

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.

1. Inclusion of Women and Minorities

In the sections for the inclusion of women and the inclusion of minorities, address the following points. There may be reasons why the proposed sample is limited by sex/gender, race, and/or ethnicity. This should be addressed as part of the following points.

- Describe the planned distribution of subjects by sex/gender, race, and ethnicity and complete the Inclusion Enrollment Report (IER). You may need to include multiple IERs for each study. 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. Refer to the instructions for the IER below for more information.
- 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 as subjects. This is particularly important if difficulty recruiting certain groups is anticipated.

You may also choose to address the following points regarding inclusion and excluded groups. In general, the cost of recruiting certain groups and/or geographic location alone are not acceptable reasons for exclusion of particular groups. This should be considered when developing outreach plans. Establishing collaborations or other arrangements to recruit may be necessary.

- Inclusion of certain individuals would be inappropriate with respect to their health;
- The research question addressed is only relevant to certain groups or there is a gap in the research area;

- Evidence from prior research strongly demonstrates no difference on the basis of sex/gender, race, and/or ethnicity;
- Sufficient data already exist with regard to the outcome of comparable studies in the excluded group(s) and duplication is not needed in this study;
- A certain group(s) is excluded or severely limited because the purpose of the research constrains the applicant's selection of study subjects (e.g., uniquely valuable stored specimens or existing datasets are limited by sex/gender, race, and/or ethnicity; very small numbers of subjects are involved; or overriding factors dictate selection of subjects, such as matching of transplant recipients, or availability of rare surgical specimens); and/or
- Representation of specimens or existing datasets cannot be accurately determined (e.g., pooled blood samples, stored specimens, or datasets with incomplete sex/gender documentation are used), and this does not compromise the scientific objectives of the research.

Additional guidance for research utilizing existing datasets or resources is given below. In general, these will be studies meeting the NIH definition for clinical research with a prospective plan to analyze existing data and/or derive data from an existing resource and where no ongoing or future contact with participants is anticipated. More information about what is considered an existing dataset or resource for inclusion policy is available on the NIH FAQs on Monitoring Inclusion When Working with Existing Datasets and/or Resources.

- Inclusion must be addressed when conducting NIH-defined clinical research, even if the samples or data have already been collected as part of a different study. Details about the sex/gender, race, and ethnicity composition of the existing dataset/resource should be provided and justified as appropriate to the scientific goals of the proposed study.
- For the purposes of inclusion policy, an existing dataset may be constructed of different types of data, including, but not limited to,
    - survey data,
    - demographic information,
    - health information,
    - genomic information, and
    - data to be derived from existing samples of cells, tissues, or other types of materials that may have been previously collected for a different purpose or research question but will now be used to answer a new research question.

When NIH-Defined Phase III Clinical Trials Are Proposed:

If the proposed research includes an NIH-Defined Phase III Clinical Trial, the section on Inclusion of Women and Minorities also MUST address plans for how sex/gender, race, and ethnicity will be taken into consideration in the design and valid analysis of the trial. Valid analysis means an unbiased assessment which will, on average, yield the correct estimate of the difference in outcomes between two groups of subjects. Valid analysis

can and should be conducted for both small and large studies. A valid analysis does not need to have a high statistical power for detecting a stated effect.

Scientific Review Groups will assess each application as being acceptable or unacceptable with regard to the scientifically justified inclusion plans, including these additional requirements for NIH-defined Phase III clinical trials.

- Applicants should 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 (males and females) 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 differences exist.
- Applicants also should address whether they plan to test or not test for differences in effect among sex/gender, racial, and/or ethnic groups and why that is or is not appropriate. This may include supporting evidence and/or data derived from animal studies, clinical observations, metabolic studies, genetic studies, pharmacology studies as well as observational, natural history, epidemiology and/or other relevant studies. Additional factors may include planned primary and secondary outcomes and whether there are previous studies that support or negate the likelihood of differences between groups.
- The plans 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 policy, individuals under 18 are defined as a child; however, exclusion of any specific age or age range group should be justified in this section. In addition, address the following points:

- Specifically discuss whether children under the age of 18 (as a whole or a subset of individuals under 18) will be included or excluded. If children will be included, the discussion should include a rationale for selecting a specific age range of children, if relevant.
- Also include a description of the expertise of the investigative team for working with children at 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.

Justifications for Exclusion of Children: It is expected that children will be included in all NIH-defined clinical research unless one or more of the following exclusionary circumstances apply:

- The research topic to be studied is not relevant to children.
- Laws or regulations bar the inclusion of children in the research.
- The knowledge being sought in the research is already available for children or will be obtained from another ongoing study, and an additional study would be redundant. Documentation of other studies justifying the exclusions should be provided. NIH program staff can be contacted for guidance on this issue if the information is not readily available.
- A separate, age-specific study in children is warranted and preferable. Examples include:
    - The condition is relatively rare in children, as compared to adults (so extraordinary effort would be needed to include children). For rare diseases or disorders where the applicant has made a particular effort to assemble an adult population, the same effort would be expected of the applicant to assemble a similar child population; or
    - The number of children is limited because the majority are already accessed by a nationwide pediatric disease research network; or
    - Issues of study design preclude direct applicability of hypotheses and/or interventions to both adults and children (including different cognitive, developmental, or disease stages or different age-related metabolic processes). While this situation may represent a justification for excluding children, you should consider taking these differences into account in your study design and expanding the hypotheses tested or interventions planned, to allow inclusion of children.

- Insufficient data are available in adults to judge potential risk in children. Although children usually should not be the initial group to be involved in research studies, in some instances, the nature and seriousness of the illness may warrant their participation earlier based on careful risk and benefit analysis.
- Study designs are aimed at collecting additional data on pre-enrolled adult study subjects (e.g., longitudinal follow-up studies that did not include data on children).
- Other special cases can be justified by the applicant and assessed by the review group and the IC Director to determine whether it is acceptable.

For more information:

For more information, see:

- SI, Part II, Section 4.2.1
- NIH's Policy Implementation Page on the Inclusion of Women and Minorities
- NIH's Policy and Guidelines 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

1.6 Recruitment and Retention Plan

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

Include a "Recruitment and Retention Plan" attachment if you answered "Yes" to the question "Are human subjects involved?" on the Section G.220 - R&R Other Project Information Form and the research does not fall under Exemption 4.

Format:

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

Content:

Describe and justify the sampling plan, with particular emphasis on retention strategies.

For more information:

For more information, see:

- SI, Part II, Section 4.1.2

1.7. Recruitment Status

Enter or select a single "Recruitment Status" that best describes the human subjects research and/or clinical trial as a whole, based upon the status of the individual sites. If at least one facility in a multisite clinical study has an Individual Site Status of “Recruiting,” then the Overall Recruitment Status for the study must be “Recruiting.” Only one selection is allowed.

1.8. Study Timeline

Who must complete the “Study Timeline” attachment:

Include a “Study Timeline” attachment if you answered “Yes” to the question “Are human subjects involved?” on the Section G.220 - R&R Other Project Information Form. This attachment is required if this study involves a clinical trial, and is optional for all other human subject research.

Format:

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

Content:

Provide a description or diagram describing the timeline for study milestones.

Inclusion Enrollment Report(s)

Who should complete the PHS Inclusion Enrollment Report?

The Inclusion Enrollment Report (IER) is required for any study that involves NIH-defined clinical research.

Additional Instructions for Training:

Skip the IER, as inclusion does not apply to Training applications.

Using the IER:

You must complete an IER for each proposed study that is NIH-defined clinical research (this excludes studies that are considered Exemption 4). More than one IER is allowed. Additionally, if a study will conduct enrollment at both a U.S. site and a non-U.S. site, you will need to complete a separate IER for each site.

Once you have added an IER for a given study, you may edit, remove, or view it.

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

For more information on how to use the IER:

Refer to the Supplemental Instructions, Part II, Section 4.3: Instructions for Completing the PHS Inclusion Enrollment Report(s) for additional guidance on how and when to use the

Inclusion Enrollment Report. The Supplemental Instructions, Part II, Section 4.3 has general guidance as well as specific guidance for different application types, applications involving more than one study, and applications with multi-site studies.

Using an Existing Dataset or Resource (Yes/No)

This field is required.

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

Studies that use an existing dataset or resource generally means that investigators are utilizing data from a previous study or data bank. Additionally, these studies meet the NIH definition for clinical research, with a prospective plan to analyze existing data and/or derive data from an existing resource and where no ongoing or future contact with participants is anticipated.

Do NOT answer “Yes” for individuals previously recruited specifically for this study.

For more information:

- For additional guidance on what is considered an existing dataset, refer to Supplemental Instructions, Part II, Section 4.2: Inclusion of Women and Minorities
- NIH Frequently Asked Questions on Monitoring Inclusion when Working with Existing Datasets and/or Resources.

Enrollment Location Type (Domestic/Foreign)

This 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.

Enrollment Country(ies)

Indicate the enrollment country or countries for the participants.

Enrollment Location

This field is required.

Indicate the enrollment location for the participants on the IER. This is typically where the research is conducted, and can be different from the recruitment site.

Planned:

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. Use the “Unknown/Not Reported” fields only when reporting actual enrollment (i.e., your “Enrollment Type” is “Cumulative”).

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. Use the “Unknown/Not Reported” fields only when reporting actual enrollment (i.e., your “Enrollment Type” is “Cumulative”).

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. Use the “Unknown/Not Reported” fields only when reporting actual enrollment (i.e., your “Enrollment Type” is “Cumulative”).

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. Use the “Unknown/Not Reported” fields only when reporting actual enrollment (i.e., your “Enrollment Type” is “Cumulative”).

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. Use the “Unknown/Not Reported” fields only when reporting actual enrollment (i.e., your “Enrollment Type” is “Cumulative”).

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. Use the “Unknown/Not Reported” fields only when reporting actual enrollment (i.e., your “Enrollment Type” is “Cumulative”).

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 only when reporting actual enrollment (i.e., your “Enrollment Type” is “Cumulative”). The “Total” fields in the right column will be automatically calculated to total all individuals.

Cumulative (Actual)

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. Use the “Unknown/Not Reported” fields only when reporting actual enrollment (i.e., your “Enrollment Type” is “Cumulative”).

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. Use the “Unknown/Not Reported” fields only when reporting actual enrollment (i.e., your “Enrollment Type” is “Cumulative”).

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. Use the “Unknown/Not

Reported" fields only when reporting actual enrollment (i.e., your "Enrollment Type" is "Cumulative").

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. Use the "Unknown/Not Reported" fields only when reporting actual enrollment (i.e., your "Enrollment Type" is "Cumulative").

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. Use the "Unknown/Not Reported" fields only when reporting actual enrollment (i.e., your "Enrollment Type" is "Cumulative").

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. Use the "Unknown/Not Reported" fields only when reporting actual enrollment (i.e., your "Enrollment Type" is "Cumulative").

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 only when reporting actual enrollment (i.e., your "Enrollment Type" is "Cumulative").

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 only when reporting actual enrollment (i.e., your "Enrollment Type" is "Cumulative"). The "Total" fields in the right column will be automatically calculated to total all individuals.

Participant level data file (CSV):

Provide individual participant level age as a CSV file upload to the bottom of the Cumulative Inclusion Enrollment Report

Section 2 – Protection and Monitoring Plans

2.1 Protection of Human Subjects

Who must complete the "Human Subjects Protection Plan" attachment:

Include a "Human Subjects Protection Plan" attachment if you answered "Yes" to the question "Are human subjects involved?" on the Section G.220 - R&R Other Project Information form.

Format:

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

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

Content:

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 Human Subjects 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

- Describe and justify the involvement of human subjects in the proposed study.
- Describe the characteristics of the subject population, including their anticipated number, age range, and health status, if relevant.
- Also include the following information, if it is relevant to your specific 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), as well as subjects who become incarcerated after the study begins.
- Describe procedures for assignment to a study group. As related to human subjects protection, provide details about all planned interventions, such as dose, frequency, and administration.
- 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. Explain how data from the site(s) will be obtained, managed, and protected.

b. Sources of Materials

- Describe the research material obtained from living individuals in the form of specimens, records, or data.
- Describe any data that will be collected from human subjects for this particular study.
- Indicate who will have access to individually identifiable private information about human subjects.
- Provide information about how the specimens, records, and/or data will be collected, managed, and protected, as well as whether any individually identifiable private information will be collected specifically for the proposed research project.

c. Potential Risks

- Describe all the potential risks (physical, psychological, financial, legal, or other) to subjects posed by participation in this particular study, and assess their likelihood and seriousness to the human subjects.
- Where appropriate, describe alternative treatments and procedures, including their risks and potential benefits, to participants in the proposed research. When alternative treatments or procedures are possible, make the rationale for the proposed approach clear.

2. Adequacy of Protection Against Risks:

a. Recruitment and Informed Consent

Describe plans for the recruitment of subjects (where appropriate) and the process for obtaining informed consent. If the proposed studies will include children, describe the process for meeting requirements for parental permission and child assent.

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.

If a waiver of some or all of the elements of informed consent will be sought, provide justification for the waiver. Informed consent document(s) need not be submitted to the PHS agencies unless requested.

b. Protections Against Risk

Describe planned procedures for protecting against or minimizing all potential risks identified, including risks to privacy of individuals or confidentiality of data, and assess their likely effectiveness.

Describe how proposed research involving vulnerable populations meets the additional regulatory requirements described in the HHS regulations, Subparts B, C or D. Refer to HHS regulations, and OHRP guidance:

- HHS' Subpart B - Additional Protections for Pregnant Women, Fetuses, and Neonates
- HHS' Subpart C - Additional Protections Pertaining to Prisoners as Subjects
- OHRP Subpart C Guidance on Involvement of Prisoners in Research
- HHS' Subpart D - Additional Protections for Children:
- OHRP Guidance on OHRP Subpart D Guidance:

Where appropriate, discuss plans for ensuring necessary medical or professional intervention in the event of adverse effects to the subjects. Studies that involve (see definition of "clinical trial" under Part III Section 3), you must also include a Data and Safety Monitoring Plan. In this attachment, describe the plan for data and safety monitoring of the clinical trials and adverse event reporting to the IRB, the DSMB (if one has been established for the trial), the NIH, and others, as appropriate, to ensure the safety of subjects.

Where appropriate, describe plans for handling incidental findings that may be uncovered as a result of the research, such as incidental findings from research imaging, results of screening tests, or misattributed paternity.

Note: Test articles (investigational new drugs, devices, or biologics) including test articles that will be used for purposes or administered by routes that have not been approved for general use by the Food and Drug Administration (FDA) must be named. State the following with respect to the proposed use of the test article:

- whether the 30-day interval between submission of applicant certification to the FDA and its response has elapsed or has been waived and/or
- whether use of the test article has been withheld or restricted by the FDA, and/or
- the status of requests for an Investigational New Drug (IND) or Investigational Device Exemption (IDE) covering the proposed use of the test article in the Research Plan.

3. Potential Benefits of the Proposed Research to Human Subjects 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.
- 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 may reasonably be expected to result.

For more information:

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

2.2 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?

Check "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.

Applicants 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 the NIH sIRB policy because the NIH sIRB policy does not apply to foreign sites.

Additional Instructions for Career Development:

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

Additional Instructions for Training:

Check "N/A," as the sIRB policy does not apply to research training 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.

Also see the NIH policy on the Use of sIRB for Multi-site Research for more information.

If yes, describe the single IRB plan:

This field is required if you answered “Yes” to the “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?” question.

Who must complete the “Single IRB Plan” attachment:

Include a “Single IRB Plan” attachment if you answered “Yes” to the “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?” question above.

Format:

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

Content:

If you are proposing a multi-site study involving nonexempt human subjects research research funded by the NIH, you are expected to include a plan for the use of a single Institutional Review Board (sIRB). The plan should include the following elements:

- Describe how the applicant 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 additional sites added after award will rely on the sIRB.
- Indicate that all participating sites will, prior to initiating the study, sign a reliance agreement that will include a communication plan for interactions between the sIRB and participating sites.
- Indicate which institution or entity will maintain records of the reliance/authorization agreements and of the communication plan.
- If the research project as a whole proposes multiple multi-site studies, one sIRB plan for all the studies is acceptable.

For Studies with Legal-, Regulatory-, or Policy-based Claims for Exception to the sIRB Policy: Indicate that review by a 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 more information:

Refer to the following sIRB policy resources for more information:

- Final NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research
- NIH Guide Notice on the Final NIH Policy on sIRB
- sIRB Frequently Asked Questions (FAQs)

2.3 Will a data and safety monitoring board be appointed for this study?

This field is required if you answered “Yes” to all the questions in the “Clinical Trial Questionnaire” in the “Introductory Fields” section above..

Check the appropriate box to indicate whether a data and safety monitoring board will be appointed for this study.

2.4 Data and Safety Monitoring Plan

Who must complete the “Data and Safety Monitoring Plan” attachment:

Include a “Data and Safety Monitoring Plan” attachment if you answered “Yes” to all the questions in the “Clinical Trial Questionnaire” in the “Introductory Fields” section above. If you answered “No” to any of the “Clinical Trial Questionnaire” questions, the “Data and Safety Monitoring Plan” question is optional .

Format:

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

Content:

For any proposed clinical trial, NIH requires a data and safety monitoring plan (DSMP) that is commensurate with the risks of the trial and its size and 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 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 investigators and biostatisticians.
- 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, smaller clinical trials may not require this oversight format, and alternative monitoring plans may be appropriate. If a DSMB is used, please describe the general composition of the Board without naming specific individuals.

For more information:

For more information on data and safety monitoring, see:

- 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

2.5 Overall structure of the study team:

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

Section 3 – Clinical Trial Synopsis

Who must complete the "Clinical Trial Synopsis" section:

If you answered "Yes" to all the questions in the "Clinical Trial Questionnaire" in the "Introductory Fields" section, you must complete the "Clinical Trial Synopsis" section. If you answered "No" to any of the questions in the "Clinical Trial Questionnaire" in the "Introductory Fields" section, the "Trial Synopsis" section will be disabled and you should skip it.

3.1. Objective

This field is required.

Enter a brief description of objectives, including the primary and secondary endpoints.

3.2. Study Design

3.2.a Narrative Study Description

This field is required. The narrative description can have a maximum of 250 characters.

Enter a narrative description of the clinical trial. Include a description of each of the arms to which subjects will be prospectively assigned.

3.2.b Primary Purpose

This field is required.

Enter or select a single "Primary Purpose" that best describes the clinical trial.

3.2.c Interventions

These fields are required.

Complete the “3.2.c Interventions” fields for each intervention to be used in your proposed clinical trial. If an arm of the study to which subjects will be prospectively assigned includes more than one intervention (e.g., drug plus educational intervention), complete this section for each intervention.

Intervention Type: Select the intervention type the clinical trial will administer during the proposed award. If the intervention type is on the drop down menu, select "Other" and indicate the intervention type in the space provided.

Name: Enter the name of the intervention here.

Description: Enter a description of the intervention here.

3.2.d Study Phase

This field is required.

Enter or select a single "Study Phase" that best describes the clinical trial. If you select “Other”, provide a description in the space provided.

Also, check "Yes" or "No" to indicate whether the study is or includes an NIH-defined Phase III clinical trial. See NIH Glossary for the definition of Phase III clinical trial.

3.2.e. Intervention Model

This field is required.

Enter or select a single "Intervention Model" that best describes the clinical trial. If you select “Other”, provide a description in the space provided.

3.2.f. Masking

This field is required.

Select one or more "Masking" that best describes the clinical trial. Masking is also referred to as “blinding.”

3.2.g. Allocation

This field is required.

Enter or select a single "Allocation" that best describes the clinical trial. If allocation is not applicable to your clinical trial, select “N/A”.

3.3. Outcomes or Measures

These fields are required.

Complete the “3.3 Outcome or Measures” fields for each primary, secondary, and other important measure to be collected during your proposed clinical trial. Primary measures are typically study endpoints. You can add as many outcomes as you need.

Name: Enter the name of the individual outcome or measure.

Type: Enter the name of the outcome or measure here.

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

Brief Description: Enter a brief description of the outcome or measure here.

3.4. Statistical Design and Power

Who must complete the “Statistical Design and Power” attachment:

The “Statistical Design and Power” attachment is required.

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 (per protocol, intent-to-treat) to compare groups with respect to the primary outcome measure. A more detailed analysis plan, including a valid analysis if an NIH defined Phase III Clinical Trial, should be included in the Research Strategy.

3.5. Subject Participation Duration

This field is required.

Enter the time it will take for each individual participant to complete all subject visits.

3.6 Will use an FDA-regulated intervention? Yes/No

Check "Yes" or "No" to indicate whether the protocol will use an FDA-regulated intervention.

3.6.a. If yes, Availability of Investigational Product (IP) and IND/IDE Status:

This field is required if you answered “Yes” to the “Is this protocol FDA-regulated” question.

If the protocol is FDA-regulated, describe the availability of study agents and support for acquisition and administration of study agent(s). Please indicate the IND/IDE status of the study agent, if applicable, and whether or not the investigators have had any interactions with the FDA. If the agent currently has an IND/IDE number, provide that information. Note that the NIH IC may request consultation with the FDA and the IND/IDE sponsor about the proposed clinical trial after peer review and prior to award.

3.7 Dissemination Plan

Who must complete the "Dissemination Plan" attachment:

The "Dissemination Plan" attachment is required.

Format:

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

Content:

The required plan can be a brief statement explaining whether the applicant intends to register and submit results information to ClinicalTrials.gov as outlined in the policy or to meet the expectations in another manner. It is important to remember that an NIH-funded clinical trial that meets the definition of an applicable clinical trial is subject to the regulations and, therefore, to the requirements regarding registration and submission of results information to ClinicalTrials.gov.

For more information:

For more information on data and safety monitoring, see the NIH Policy on the Dissemination of NIH-Funded Clinical Trial Information

Section 4 – Other Clinical Trial-related Attachments

4.1. Other Trial-related Attachments

A maximum of 10 PDF attachments is allowed in the "Other Trial-related Attachments" section. Attach a file(s) to provide additional trial-related information only in accordance with the FOA and/or these instructions.

Section 5 – Clinical Trial Milestone Plan

5.1. Have there been any anticipated or unanticipated serious adverse events?

This field is required.

Check the appropriate box to indicate whether a there have been any anticipated or unanticipated serious adverse events within this study.

5.2. Have adverse events occurred with greater than 5 percent frequency within any area of the clinical trial?

This field is required.

Check the appropriate box to indicate whether a there have been any adverse events that have occurred with greater than 5 percent frequency within any area of the clinical trial.

5.3. Study Start Date

This field is required.

Enter the study start date (month, day, and year) of the clinical trial. Select whether this date is anticipated or actual.

5.4. Study Primary Completion Date

This field is required.

Enter the study primary completion date (MM/DD/YYYY) of the clinical trial. Select whether this date is anticipated or actual.

5.5. Study Final Completion Date

This field is required.

Enter the study’s final completion date (MM/DD/YYYY) of the clinical trial. Select whether this date is anticipated or actual.

5.6. Finalization of clinical protocol (with program agreement, if applicable)

This field is required.

Enter the date (MM/DD/YYYY) of the finalization of the clinical protocol (with program agreement, if applicable). Select whether this date is anticipated or actual.

5.7. Registration of clinical trial in ClinicalTrials.gov

This field is required.

Enter the date (MM/DD/YYYY) of the registration of the clinical trial in ClinicalTrials.gov. Select whether this date is anticipated or actual.

5.8. Completion of regulatory approvals

This field is required.

Enter the date (MM/DD/YYYY) of the completion of regulatory approvals of the clinical trial. Select whether this date is anticipated or actual.

5.9. Enrollment of the first subject

This field is required.

Enter the date (MM/DD/YYYY) of the enrollment of the first subject into the clinical trial. Select whether this date is anticipated or actual.

5.10. Enrollment and randomization

This field is required.

Enter the enrollment and randomization date (MM/DD/YYYY) of each quartile (25%, 50%, 75%, 100%) of the projected study population. Select whether this date is anticipated or actual.

5.11. Completion of data collection time period

This field is required.

Enter the completion date (MM/DD/YYYY) of data collection of the clinical trial. Select whether this date is anticipated or actual.

5.12. Completion of primary endpoint data analyses

This field is required.

Enter the completion date (MM/DD/YYYY) of the analyses of the data for the primary endpoints of the clinical trial. Select whether this date is anticipated or actual.

5.13. Completion of secondary endpoint data analyses

This field is required.

Enter the completion date (MM/DD/YYYY) of the analyses of the data for the secondary endpoints of the clinical trial. Select whether this date is anticipated or actual.

5.14. Completion of final study report

This field is required.

Enter the date (MM/DD/YYYY) of the completion of the final study report of the clinical trial. Select whether this date is anticipated or actual.

5.15. Reporting of results in ClinicalTrials.gov

This field is required.

Enter the date (MM/DD/YYYY) that the results of the trial were reported to ClinicalTrials.gov. Select whether this date is anticipated or actual.

5.16. Provide the ClinicalTrials.gov identifier (e.g. NCT00654321) for this trial

This field is required.

Enter the ClinicalTrials.gov identifier (e.g. NCT00654321) for this trial.

5.17. Is this an applicable clinical trial under FDAAA?

This field is required.

Check the appropriate box to indicate whether this is an applicable clinical trial under FDAAA. If this is an applicable clinical trial, select "Yes". If this is not an applicable clinical trial, select "No".

5.15. Clinical Trials Registration and Reporting Certification

This field is required.

Check the appropriate box to indication if you agree or disagree with the following statement:

Assurance is hereby provided that the recipient and all investigators conducting NIH-funded clinical trials are in compliance with NIH policy on Dissemination of NIH-Funded Clinical Trial Information and that any clinical trial funded in whole or in part under this award has been registered in ClinicalTrials.gov. If not registered at the time of this submission, the clinical trial will be registered not later than 21 days after enrollment of the first participant. Summary results have been submitted to ClinicalTrials.gov or will be submitted not later than one year after the primary completion date, even if the primary completion date occurs after the period of performance.