INSTRUCTIONS: HUMAN SUBJECTS AND CLINICAL TRIAL SECTION OF NIH GRANT

Does your research involve human subjects? According to DHHS regulations, the answer is "yes" if you obtain data or biological specimens through intervention or interaction with a living individual or you obtain identifiable private information about a living individual. If you answer "yes" to human subjects' involvement, there are required sections of the NIH application that must be written and a number of questions that must be answered. NIH does not require that you have IRB approval at the time of submission; however, you will need to have an IRB approval letter before the proposal is funded. The human subjects section of the NIH application has become more complex and detailed. Instructions are below.

Does any of the proposed research in the application involve human specimens and/or data?

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

Provide an explanation for any use of human specimens and/or data not considered to be human subjects research.

To help determine whether your research is classified as human subjects research, refer to the Research Involving Private Information or Biological Specimens flowchart: https://grants.nih.gov/grants/policy/hs/PrivateInfoOrBioSpecimensDecisionChart.pdf

For guidance, OHRP does not consider research involving only coded private information or specimens to involve human subjects as defined under 45 CFR 46.102(f) if the following conditions are both met:
1. the private information or specimens were not collected specifically for the currently proposed research project through an interaction or intervention with living individuals; and
2. the investigator(s) cannot readily ascertain the identity of the individual(s) to whom the coded private information or specimens pertain because, for example:
a. the investigators and the holder of the key enter into an agreement prohibiting the release of the key to the investigators under any circumstances, until the individuals are deceased (note that the HHS regulations do not require the IRB to review and approve this agreement);
b. there are IRB-approved written policies and operating procedures for a repository or data management center that prohibit the release of the key to the investigators under any circumstances, until the individuals are deceased; or
c. there are other legal requirements prohibiting the release of the key to the investigators, until the individuals are deceased.
This guidance applies to existing private information and specimens, as well as to private information and specimens to be collected in the future for purposes other than the currently proposed research. The following are examples of private information or specimens that will be collected in the future for purposes other than the currently proposed research: (1) medical records; and (2) ongoing collection of specimens for a tissue repository.

If you are using specimens but determine you are not conducting human subjects reesearch, provide an explanation that includes 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.

Delayed-Onset Human Subjects Research (see end of document for instructions if your study is delayed onset.

FOR ALL STUDIES THAT ARE NOT DELAYED ONSET
You must fill out a study record for each human subjects protocol you propose that is not delayed onset.

Section 1: Basic Information:

Title: maximum 600 characters; each human subjects study must have a unique title.

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

Is the study exempt from federal regulations?

Select the appropriate exemption number(s) for this particular study. Multiple selections are permitted. See link for information: Final Rule Human Subjects Research Exemptions- NIH Infographic

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. We request that PIs consult with the IRB prior to submission to obtain a research determination (if needed) and to identify if the study is exempt and if so, which exemption applies. This is critical to ensure that the information provided to NIH is correct.

Is the study a clinical trial? Answer "Yes" or "No" to the following four questions to determine whether this study involves a clinical trial. If you answer "Yes" to all questions, then your study is a clinical trial. (NOTE: Once you answer "no" to any of the questions, all the following questions must also answer "no" as the questions are sequentially ordered).

a. Does the study involve human participants? Yes/No

b. Are the participants prospectively assigned to an intervention? Yes/No

c. Is the study designed to evaluate the effect of the intervention on the participants? Yes/No

d. Is the effect that will be evaluated a health-related biomedical or behavioral out- come? Yes/No

Once you have determined if your study is a clinical trial, the chart below will guide you as to which sections you must fill out for the rest of the form.

Refer to the table below for information about what sections of this form are required, based on your answers to Question 1.4 "Clinical Trial Questionnaire.	**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**
Form Section		
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 if specified in the FOA	Do not complete

If your study is a clinical trial:

- provide the clinicaltrials.gov identifier number, if applicable. (NOTE: this is optional at submission time).

Section 2: Study Population Characteristics

NOTE: If you claimed exemption 4 only and no other exemptions, you do not have to fill out section 2. Exemption 4 studies should skip to Section 3. Section 2 must be filled out for all other human subjects projects, including other exemptions.

2.1: Conditions or Focus of the Study: At least 1 entry is required, and up to 20 entries are allowed (enter each entry on its own line). Each entry is limited to 255 characters.

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. You must provide at least one entry, and may provide up to 20 entries.

Note: This field matches a ClinicalTrials.gov field (Primary Disease or Condition Being Studied in the Trial, or the Focus of the Study).

2.2: Eligibility Criteria (15,000 character limit): List the study's inclusion and exclusion criteria. To provide a bulleted list, use a dash (or other character) followed by a space ("- ") at the start of each bullet. Be sure to check the formatting in the assembled application image. Further explanation or justification should be included in the Recruitment and Retention plan.

2.3: Age Limits: 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

If there is no age lower age limit or no lower limit is known, enter "N/A". Also enter the numerical value of the maximum age a potential participant can be to be eligible for the study. If there is no upper limit, enter "N/A."

2.3a. Inclusion of Individuals Across the Lifespan

For the purposes of the Inclusion of Individuals Across the Lifespan, exclusion of any specific age or age range group (e.g., children or older adults) should be justified in this section. In addition, address the following points:

- Individuals of all ages are expected to be included in all NIH-defined clinical research unless there are scientific or ethical reasons not to include them. Discuss whether individuals will be excluded based on age and provide a rationale for the minimum and maximum age of study participants, if applicable. Additionally, if individuals will be excluded based on age, provide a scientific or ethical rationale for their exclusion. See the NIH Policy and Guidelines on the Inclusion of Individuals Across the Lifespan as Participants in Research Involving Human Subjects for additional information about circumstances that may justify the exclusion of individuals based on age.
- Include a description of the expertise of the investigative team for working with individuals of the ages included, the appropriateness of the available facilities to accommodate individuals in the included age range, and how the age distribution of participants will 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.

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:

https://grants.nih.gov/grants/funding/women_min/datasets_faq.htm

2.4 Inclusion of Women and Minorities:

- 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.

2.5 Recruitment and Retention Plan: 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. (NOTE: If you have selected "exemption 4" and no other exemptions, then you do not have to respond to this question.

2.6. Recruitment Status: 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: Provide a description or diagram describing the study timeline. The timeline should be general (e.g., "one 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.

You do not have to fill out this section if you selected exemption 4 or if your study is not a clinical trial.

2.8 Enrollment of First Subject: 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. If you selected exemption 4 or if you are using an existing database, you do not need to respond to this question.

INCLUSION/ENROLLMENT REPORT

Each proposed study, unless it falls under Exemption 4 (and only 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.

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 U.S. sites, even if they are 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 below.

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

Comments: In this section of the inclusion/enrollment report, you may 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 ENROLLMENT TABLE

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 on racial categories, see the NIH Glossary definition of Racial Categories. For more information on ethnic categories, see the NIH Glossary definition of Ethnic Categories.

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.

Section 3: Protection and Monitoring Plans

3.1 Protection of Human Subjects

For Human Subjects Research Claiming Exemptions: If you are claiming that your human subjects research falls under any exemptions and you have obtained IRB confirmation of the exemption, 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. Do not merely repeat the criteria or definitions themselves. As noted above, please refer to this link - Final Rule Human Subjects Research Exemptions- NIH Infographic -- to review exemption criteria.

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 write-up that is commensurate with the risks of the study, its size, and its complexity. Organize your write-up 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 given below.

Risks to Human Subjects

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.

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.

Adequacy of Protection against Risks

- 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.

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.

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

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.

Note: Financial compensation of subjects should not be presented as a benefit of participation in research.

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.

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?

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 training 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.

If yes, describe the single IRB plan:

For NIH Applicants, the single IRB plan is no longer required. The information on single IRB will be requested at JIT, if the application is to be funded.

For AHRQ applicants, the single IRB plan is required and should include the following elements:
If available, provide the name of the IRB that you anticipate will serve as the sIRB of record.
Indicate that all identified participating sites will agree 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 sIRB 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: 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.

3.3 Data and Safety Monitoring Plan: This plan is required if you answered "yes" to all the questions in the Clinical Trial Questionnaire and you are conducting a clinical trial This write up is optional for all other human subjects research.

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.

3.4 Will a data and safety monitoring board be appointed for this study:
This 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.

3.5 Overall Structure of the Study Team: This is required if you are conducting a clinical trial. This is optional for other human subjects research.

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: This section is required if you are conducting a clinical trial.

4.1.a. Detailed Description: Enter a narrative description of the protocol. Studies differ considerably in the methods used to assign participants and deliver interventions. Describe your plans for assignment of participants and delivery of interventions. You will also need to show that your methods for sample size and data analysis are appropriate given those plans. For trials that randomize groups or deliver interventions to groups, special methods are required; additional information is available at the Research Methods Resources webpage. The Narrative Study Description is not meant to be a repeat of the Research Strategy.
The narrative description is limited to 32,000 characters (but typically needs only 5,000 characters), should be written in layperson's terms, and may repeat some of the information in the Research Strategy.

4.1.b. Primary Purpose
Enter or selection from dropdown menu a single "primary purpose" that best describes the clinical trial 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.)

4.1.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 **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.

4.1.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. Device and behavioral intervention studies may select “Yes” here even if the answer above is “Other”.

For more information on how to answer this question for devices or behavioral interventions, refer to the relevant FAQ: https://grants.nih.gov/grants/ElectronicReceipt/faq_full.htm#5571

4.1.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.)

4.1.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

4.1.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

4.2 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.

NIH-Defined Phase III Clinical Trials: If the proposed research includes an NIH-Defined Phase III Clinical Trial, then outcomes for required analyses by sex/gender, race, and ethnicity should be entered.
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.
https://grants.nih.gov/grants/funding/women_min/guidelines.htm

4.3 Statistical Design and Power: 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

You will need to show that your methods for sample size and data analysis are appropriate given your plans for assignment of participants and delivery of interventions. For trials that randomize groups or deliver interventions to groups, special methods are required; additional information is available at the Research Methods Resources webpage:
https://researchmethodsresources.nih.gov/

4.4 Subject Participant 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.

4.5 Will the study use an FDA-regulated intervention?
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).

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.

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:** 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.

4.6 Is this an applicable clinical trial under FDAAA?

Select "Yes" or "No" to indicate whether the study is an applicable clinical trial (ACT) under the Food and Drug Administration Amendments Act (FDAAA).

For more information:
NIH Glossary’s definition of an applicable clinical trial
FAQs on the ClinicalTrials.gov & FDAAA

4.7 Dissemination Plan: 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 the following:

- 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;
- informed consent documents for the clinical trial(s) will include a specific statement relating to posting of clinical trial information at ClinicalTrials.gov; and
- 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.

Section 5: Other Clinical Trial-related Attachments

This section is only required for proposed clinical trials whose FOA specifies additional requirements. If the FOA does not specify additional requirements, do not include any additional attachments.

DELAYED ONSET HUMAN STUDIES

In rare situations, applications are submitted with the knowledge that human subjects will be involved during the period of support, but plans are so indefinite that it is not possible to describe the involvement of human subjects in the application. The kinds of 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.

If you anticipate conducting research involving human subjects but cannot describe the study at the time of application (i.e., your study is a delayed onset human subject study), enter a Delayed Onset Study Record as instructed below.

Generally, for any study that you include as a delayed onset study in this section, you will provide a study title, indicate whether the study is anticipated to include a clinical trial, and include a justification attachment. Since by definition, information for a delayed onset study is not available at the time of application, you will not be given the option to complete a full Study Record for a delayed onset study. For delayed onset studies, the Delayed Onset Study Record is sufficient.

The definition of delayed onset is: ***Human subjects research is anticipated within the period of award but definite plans for this involvement cannot be described in the application.***

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.

Study Title of Delayed Onset Study: This field is required. (600 character limit)

Enter a brief, unique title that describes the study the participants will be involved in. Each

study within your application must have a unique Study Title. The first 150 characters will display in the application image bookmarks.

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? Check this box if you anticipate that this study will be a clinical trial. (see four questions above).

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, check the "Anticipated Clinical Trial?" checkbox.

Justification for Delayed Onset: Write a justification that includes the following:

Explain why human subjects study information is not available at the time of application.

If NIH's Single Institutional Review Board (sIRB) policy will apply to your study, this justification must also include information regarding how the study will comply with the policy.

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.