

INSTRUCTIONS FOR HUMAN SUBJECTS AND CLINICAL TRIAL SECTION

Fill out the Human Subjects and Clinical Trials PDF as applicable to your project. Some questions require write in answers or choice of a drop down menu, while some require you to upload a pdf. Follow instructions below.

Are human subjects involved? If you are interacting with human subjects and/or have access to identifiable data, the answer will be “yes.” If you are using human de-identified specimens and/or data the answer may be “no” if the following two criteria are 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.*

If you meet these criteria, you will answer “no” to human subjects. You will then be asked:

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

Select “yes” or “no.” If the answer is yes, provide an explanation as to why your project meets the definition of “no human subjects” as described above. This justification should include: information on who is providing the data/biological specimens and their role in the proposed research; a description of the identifiers that will be associated with the human specimens and data; a list of who has access to subjects’ identities; and information about the manner in which the privacy of research participants and confidentiality of data will be protected.

This writeup will be uploaded in space provided. Since you are not doing human subjects research, you may skip the rest of the form.

If “yes” to human subjects research:

If you answer “yes” to human subjects, you will be asked if your project is exempt from federal regulations. You may find the definitions of the exemptions here:

https://humansubjects.nih.gov/sites/hs/public_files/exemption_infographic_v6_hs_internet.pdf.

The common exemption for biomedical research is Exemption #4 which states the following:

Exemption #4: Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

Study Record

If you have answered “yes” to human subjects (even if you claim an exemption), please create a “study record.” There are four sections to the Study Record.

Section 1: Basic Information:

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

1.2: Is the study exempt? Go to the following link to help determine if your study is exempt: https://humansubjects.nih.gov/sites/hs/public_files/exemption_infographic_v6_hs_internet.pdf
Or NIH frequently asked questions here: <https://humansubjects.nih.gov/from-applicants#exemptions>

1.3 If exempt, check exemption number.

1.4 Is the study a clinical trial? Answer “Yes” or “No” to the following questions to determine whether this study involves a clinical trial.

- 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

If you answered “Yes” to all the questions in the Clinical Trial Questionnaire, this study meets the definition of a clinical trial. If you are doing a clinical trial, then sections 2, 3 and 4, must be completed. Do not complete section 5.

Section 2: Study Population Characteristics

NOTE: If you claimed exemption 4, 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: Identify the names of the diseases or conditions 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.

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

2.4: Inclusion of Women, Minorities and Children: Your write-up should have two sections:

a. *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.

Existing Datasets or Resources. If you will use an [existingdataset](#), 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 [FAQsonMonitoringInclusionWhenWorkingwithExistingDatasetsand/orResources](#).

b. *Inclusion of Children*

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

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

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.

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.

2.8 Enrollment of First Subject: Enter the date (MM/DD/YYYY) of the enrollment of the first subject into the study. State whether the date is actual or anticipated.

INCLUSION/ENROLLMENT REPORT (IER)

Each proposed study, unless it falls under Exemption 4, must contain at least one Inclusion Enrollment Report (IER). Answer preliminary questions. Comments: In this section, 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.

There are two types of tables to fill out; choose which is relevant to your project:

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 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](#).

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

Section 3 is required for all human subjects studies, unless otherwise noted.

3.1: Protection of Human Subjects

For Human Subjects Research Claiming Exemptions: If you are claiming that your human subjects research falls under any exemption, justify why the research meets the criteria for the exemption(s) that you have claimed in this section. This justification should explain how the proposed research meets the criteria for the exemption claimed. Do not merely repeat the criteria or definitions themselves.

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

1. Risk to Human Subjects

a. Human Subjects Involvement, Characteristics, and Design

Briefly describe the overall study design. Describe the subject population(s) to be included in the study; the procedures for assignment to a study group, if relevant; and the anticipated numbers of subjects for each study group. List any collaborating sites where human subjects research will be performed, and describe the role of those sites and collaborating investigators in performing the proposed research.

b. Study Procedures, Materials, and Potential Risks

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

2. Adequacy of Protection against Risks

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

b. Protections against Risk

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

c. Vulnerable Subjects, if relevant to your study

Explain the rationale for the involvement of special vulnerable populations, such as fetuses, neonates, pregnant women, children, prisoners, institutionalized individuals, or others who may be considered vulnerable populations. 'Prisoners' includes all subjects involuntarily incarcerated (for example, in detention centers).

Pregnant Women, Fetuses, and Neonates or Children

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

HHS' [Subpart B - Additional Protections for Pregnant Women, Fetuses, and Neonates](#)

HHS' [Subpart D - Additional Protections for Children](#)

OHRP Guidance on Subpart D [Special Protections for Children as Research Subjects](#) and the [HHS 407 Review Process](#)

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

HHS' [Subpart C - Additional Protections Pertaining to Prisoners as Subjects](#)

OHRP Subpart C Guidance on [Involvement of Prisoners in Research](#)

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

- Discuss the potential benefits of the research to research participants and others.
- Discuss why the risks to subjects are reasonable in relation to the anticipated benefits to research participants and others.

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

4. Importance of the Knowledge to be Gained

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

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." If the answer is "yes" you must use a single IRB to review protocols at all sites.

3.3 **Describe how you will comply with the [NIH Policy on the Use of sIRB for Multi-Site Research](#).**

- Provide the name of the IRB that will serve as the sIRB of record.
- Indicate that all identified participating sites have agreed to rely on the proposed sIRB
- and that any sites added after award will rely on the sIRB.
- Briefly describe how communication between sites and the 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.

3.3 Data and Safety Monitoring Plan: 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. If your study is not a clinical trial, this section is optional. 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:
 - 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.
 - 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.
 - [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 mandatory if you are proposing a clinical trial. It is optional for other studies.

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

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 ONLY REQUIRED IF YOU MEET THE DEFINITION OF A CLINICAL TRIAL; IF YOU DO NOT MEET THAT DEFINITION, DO NOT FILL OUT SECTION 4).*

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

4.2 Study Design

a. Narrative Study 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 description is limited to 32,000 characters.

b. Primary Purpose: Select the 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.)

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.

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.)

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.)

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
- Allocation

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

- N/A
- Randomized
- Non-randomized

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

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

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

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

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

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

4.4 Statistical Design and Power: Specify the number of subjects you expect to enroll, the expected effect size, the power, and the statistical methods you will use with respect to each outcome measure you listed in [4.3 Outcome Measures](#). 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

4.5 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.

4.6 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.

4.7 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.