

Protection and Monitoring Plans for Human Subjects Research
Form E - of NIH Grant Applications due on or after January 25, 2018

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 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, etc. If the study is multicenter, discuss use of a single IRB for ethical review of all sites. If the study is a clinical trial (per the NIH definition), complete sections on data and safety monitoring and a DSMB. For detailed information, see <https://grants.nih.gov/grants/how-to-apply-application-guide/forms-e/general/g.500-phs-human-subjects-and-clinical-trials-information.htm>

To receive guidance on the protection of human subjects or guidance in the development of a monitoring plan, contact Marie Rape at 919-966-6844 or marie_rape@med.unc.edu.

3 - Protection and Monitoring Plans: For more information on protection of human subjects, see https://humansubjects.nih.gov/sites/hs/public_files/preparing_the_human_subjects_section.pdf

3.1 Protection of Human Subjects:

1. Risks to Humans 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; vulnerable populations; the procedures for assignment to a study group, and 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 have access to identifiers or link to the materials.
- Describe all the potential risks to subjects associated with each study intervention, procedure or interaction, including physical, psychological, social, cultural, financial, and legal risks; risks to privacy and/or confidentiality; or other risks. Discuss the risk level and the likely impact to subjects.
- Where appropriate, describe alternative treatments and procedures, including their risks and potential benefits. When alternative treatments or procedures are possible, make the rationale for the proposed approach clear.

2. Adequacy of Protection Against Risks

a. Informed Consent and Assent

- Describe recruitment of participants in the research. Describe 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.
- 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 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. Describe additional protections for vulnerable subjects.
- 'Prisoners' includes all subjects involuntarily incarcerated (for example, in detention centers): describe how proposed research meets the additional regulatory requirements, protections, and plans to obtain OHRP certification for the involvement of prisoners in research.
- Pregnant Women, Fetuses, and Neonates or Children: describe additional protections under Subparts B and D, provide a clear description of the risk level and additional protections necessary to meet the HHS regulatory requirements.

3. Potential Benefits

- 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.
- Monetary compensation of subjects should not be presented as a benefit of participation in research.

4. Importance of Knowledge

- 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 Multi-site human subject study

If 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, complete this section to address requirement to use of single IRB (sIRB). Include a plan with the following elements:

- Describe how you will comply with the [NIH Policy on the Use of sIRB for Multi-Site Research](#).
- Provide the name of the IRB that will serve as the sIRB of record.
- Indicate that all identified participating sites have agreed to rely on the proposed sIRB and that any sites added after award will rely on the sIRB.
- Briefly describe how communication between sites and the 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:** Do not include the authorization/reliance agreement(s) or the communication plan(s) documents in your application.

Clinical Trials (see section 1.4)

If the research is considered a clinical trial, additional sections will need to be completed. The NIH definition of a clinical trial is “A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.” To determine whether the study involves, answer the questions in the Clinical Trial Questionnaire

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

See <https://grants.nih.gov/grants/how-to-apply-application-guide/forms-e/general/g.500-phs-human-subjects-and-clinical-trials-information.htm#1.4>

If the study is a clinical trial, sections 3.3 – 3.5 (DSMP, DSMB, Structure of Study team), section 4 (Protocol Synopsis) and section 5 (Other Clinical Trial-related Attachments) will need to be completed. Additionally, the trial registered in ClinicalTrials.gov.

3.3 Data and Safety Monitoring Plan (DSMP)

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. Although a study may not be a clinical trial, it may have significant risks to participants, and it may be appropriate to include a DSMP. The DSMP should include:

- 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 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 DSMB is a formal, independent board of experts including investigators and biostatisticians that advise study investigators regarding the safety progression of a study. This monitoring option is typically required for phase III or multicenter trials; however, a DSMB may not be an appropriate option for other types of clinical trials.

3.4 Data and Safety Monitoring Board (DSMB), if applicable:

- 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. A DSMB may also be appropriate for Phase I and Phase II or other clinical trials if the studies are blinded (masked), employ high-risk interventions, or involve vulnerable populations.
- If a DSMB is used, describe the general composition of the Board without naming specific individuals.

3.5 Overall structure of study team

If the study is a clinical trial, 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).

4.0 Protocol Synopsis

If the study is a clinical trial, provide information about the protocol (Brief summary, study design, outcome measures, statistical design and power, subject participation, FDA regulated interventions, dissemination plan). All the questions in the "Protocol Synopsis" section are required. This is typically provided as an attachment or uploaded depending on the FOA instructions.

Protocol synopsis should include the following (document typically should not exceed 5 pages):

- Study objectives (primary, secondary, exploratory) and outcome measures
- Study design
- A description of the intervention to be tested (if applicable)
- Sample size, if not described in Protection of Human Subjects
- Study population (with key inclusion/exclusion criteria),
- Recruitment plan,
- Study procedures and evaluations, including safety assessments
- Overall study duration and duration of participant involvement.
- Process to be used for obtaining informed consent
- Draft data management plan
- Draft quality management plan
- Draft laboratory plan, including specimen handling, storage, tracking and processing
- Milestone plan for clinical study progress, including recruitment goals, interim analysis, data and safety monitoring

5.0 Other Clinical Trial-related attachments

Provide additional trial-related information only if your FOA specifically requests it. Include only attachments requested in the FOA, and use requested file names. If a specific file name is not given in the FOA, use a meaningful file name since it will become a bookmark in the assembled application image.