Template for Preparing Protections for Human Subjects

As required by federal regulations (45 C.F.R.46- https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html) and NIH policy, applications that propose to involve human subjects must address the following:

1) the risk to subjects
2) the adequacy of protections against risk
3) potential benefits of the research to subjects and others
4) the importance of the knowledge to be gained
5) For clinical trials – data and safety monitoring plan and a data and safety monitoring board for Phase III trials.

Please follow the outline below for preparing your human subjects section. Addressing the points below will ensure that you have included all necessary content in your document.

1) Risk to Human Subjects

a. Human Subjects Involvement, Characteristics, and Design
   - Describe the proposed involvement of human subjects in the work outlined in the Research Strategy section.
   - Describe and justify the characteristics of the subject population, including their anticipated number, age range, and health status if relevant.
   - Describe and justify the sampling plan, as well as the recruitment and retention strategies and the criteria for inclusion or exclusion of any subpopulation.
   - 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. Note that ‘prisoners’ includes all subjects involuntarily incarcerated (for example, in detention centers) as well as subjects who become incarcerated after the study begins.
   - If relevant to the proposed research, describe procedures for assignment to a study group. As related to human subjects protection, describe and justify the selection of an intervention’s 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 the project(s) described in the application.
   - Indicate who will have access to individually identifiable private information about human subjects.
   - Provide information about how specimens, records, and/or data are collected, managed, and protected as well as whether material or data that include individually identifiable private information will be collected specifically for the proposed research project.
c. **Potential Risks**
   - Describe the potential risks to subjects (physical, psychological, financial, legal, or other), and assess their likelihood and seriousness to the human subjects.
   - Where appropriate, describe alternative treatments and procedures, including the risks and potential benefits of the alternative treatments and procedures, to participants in the proposed research.

2. Adequacy of Protection Against Risks

a. **Recruitment and Informed Consent**
   - Describe plans for 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.
   - If a waiver of some or all of the elements of informed consent will be sought, provide justification for the waiver.

   NOTE: informed consent document(s) need not be submitted to the PHS agencies unless required.

b. **Protections Against Risk**
   - Describe planned procedures for protecting against or minimizing potential risks, including risks to privacy of individuals or confidentiality of data, and assess their likely effectiveness.
   - Research involving vulnerable populations, as described in the DHHS regulations, Subparts B-D must include additional protections. Refer to DHHS regulations, and OHRP guidance:
     - [Additional Protections for Pregnant Women, Human Fetuses and Neonates](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#subpartb)
     - [Additional Protections for Prisoners](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#subpartc)
     - [OHRP Subpart C Guidance](http://www.hhs.gov/ohrp/policy/index.html#prisoners)
     - [Additional Protections for Children](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#subpartd)
     - [OHRP Subpart D Guidance](http://www.hhs.gov/ohrp/policy/index.html#children)
   - Where appropriate, discuss plans for ensuring necessary medical or professional intervention in the event of adverse effects to the subjects. Studies that involve clinical trials (biomedical and behavioral intervention studies) must include a general description of the plan for data and safety monitoring of clinical trials and adverse event reporting to the IRB, HRSA and others, as appropriate, to ensure the safety of subjects.

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 in the anticipated benefits to research participants and others.
4. Importance of the Knowledge to be Gained
   • Discuss the importance of the knowledge gained or 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.

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 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.

5. Data and Safety Monitoring Plan
   • If the proposed research includes a clinical trial, create a heading entitled "Data and Safety Monitoring Plan."
   • Provide a general description of a monitoring plan that you plan to establish as the overall framework for data and safety monitoring.
   • Describe the entity that will be responsible for monitoring and the process by which Adverse Events (AEs) will be reported to the Institutional Review Board (IRB), the funding I/C, and the Food and Drug Administration (FDA) in accordance with Investigational New Drug (IND) or Investigational Device Exemption (IDE) regulations. Be succinct. Contact the FDA (https://www.fda.gov/) and also see the following web site for more information related to IND and IDE requirements: https://www.fda.gov/biologicsbloodvaccines/developmentapprovalprocess/investigationalnewdrugordeviceexemptionideprocess/default.htm

   The frequency of monitoring will depend on potential risks, complexity, and the nature of the trial; therefore, a number of options for monitoring trials are available. These can include, but are not limited to, monitoring by a:

   a. PD/PI (required)
   b. Institutional Review Board (IRB) (required)
   c. Independent individual/safety officer
   d. Designated medical monitor
   e. Internal Committee or Board with explicit guidelines
   f. Data and Safety Monitoring Board (DSMB). PHS specifically requires the establishment of Data and Safety Monitoring Boards (DSMBs) for multi-site clinical trials involving interventions that entail potential risk to the participants, and generally for 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.

   • A detailed Data and Safety Monitoring Plan must be submitted to the applicant's IRB and subsequently to the funding IC for approval prior to the accrual of human subjects.
For additional information and references on research with human subjects please see the following links: