TEMPLATE PROTOCOL INSTRUCTIONS:

- *Use this "TEMPLATE PROTOCOL (HRP-503)"if this is an investigator-initiated study where a protocol document has not already been provided to you with relevant information for each applicable section listed in the Table of Contents (below).*
- *Depending on the nature of the research, some sections may not be applicable. If a section is not applicable, mark as "NA" or delete altogether. For example, research involving a retrospective chart review may have many sections marked as NA or deleted.*
- *When you create a protocol using this template, save an electronic copy with the protocol version date incorporated into the name of the document, e.g., LastName_Protocol_20160623.You will need to use the current electronic copy when making recommended changes and future modifications.*
- *As you are creating the protocol, remove all instructions in italics so they are not included in the final version of your protocol.*
- *Enter the protocol title and protocol version date in the header, so the header appears on each page.*
- *Please note that underlined items in this document are hyperlinked to additional information.*

STUDY TITLE:

Replace this italicized text with the full protocol title & include the title and version date in the header.

STUDY SPONSOR:

Specify study sponsor, if there is one. If the PI is acting as the study sponsor, i.e., an investigator-sponsor, insert PI's name here.

PRINCIPAL INVESTIGATOR

Refer to PI Eligibility on the Tufts Health Sciences IRB website. List only one PI:
Name
Department
Telephone Number
Email Address

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1. Study Schema

- *Include a diagram that provides a quick "snapshot" of the study. For examples of study schemas, refer to the FDA and NIH's Study Schema Examples document available on the IRB website.*

2. Introduction

2.1 Background and Rationale

- *Describe the relevant prior experience and gaps in current knowledge.*
- *Describe any relevant preliminary data.*
- *Provide the scientific or scholarly background for, rationale for, and significance of the research based on the existing literature and how it will add to existing knowledge.*
- *Specify the relevance and usefulness of the objectives.*
- *Specify whether or not this is the first time the study drug, device, or intervention/procedure will be used in humans. If there has been experience with the study drug, device, or intervention/procedure in humans, detail the experience to date.*
- Is there an active control group?

  ☐ **Yes** ☐ **No**

2.2 Risks to Subjects

- *List the reasonably foreseeable risks, discomforts, hazards, and/or inconveniences to the subjects related to their participation in the research, including risk of unintentional loss of confidentiality. Include a description of the probability, magnitude, duration, reversibility, and potential consequences of the risks. Consider physical, psychological, social, legal, and economic risks.*
- *If applicable, indicate which study interventions may have unknown risks.*
- *If applicable, indicate which study interventions may have risks to an embryo or fetus (if a subject is or becomes pregnant) or to a nursing infant of a study subject.*
- *If applicable, describe risks to people other than the participating subject, e.g., risks to family members, friends, others or risks to the community.*
- *If applicable, describe risks to study investigators or staff performing the study procedures due to research with high risk populations (e.g. prisoners, intravenous drug users, patients with major psychiatric issues, etc.).*
  - *Describe the procedures that will be put in place to minimize these risks.*
  - *Describe how these procedures are adequate for the location where study procedures will be performed.*
  - *Contact research administration to clarify whether additional approvals (e.g. Security, Risk Management, etc.) are needed for the performance of this study with high risk populations.*

2.3 Potential Benefits to Subjects

- *Describe the potential benefits that individual subjects may experience from taking part in the research. Include the probability, magnitude, and duration of the potential benefits.*

  Note: Payments and incentives are not considered benefits in the IRB's risk-benefit assessment; payment and incentives should be addressed in the payment section.
- *Indicate if there is no direct benefit.*
- *Specify if there is benefit to the population from which the subject is drawn.*
- *Specify if there is benefit to science, society, and humanity in general.*

2.4 Alternatives

- *Describe alternatives to participating in this research study (e.g. to decide not participate in the study, alternative treatments, no treatment (palliative care), etc.).*
- *If appropriate, indicate that standard clinical care may be an alternative and briefly describe it.*
- *Clarify whether a subject could receive the research procedures/drug/device used in this study in a non-research setting? If so, how.*

3 Objectives

- *Describe the purpose, specific aims, or objectives of the study (i.e. the reason for performing the study in terms of the scientific question to be answered).*
- *Specify which are the primary or secondary aims or objectives of this study as applicable. The primary objective is the main question. Secondary objectives are goals that will provide further information for the study.*

4 Enrollment and Withdrawal

4.1 Inclusion Criteria

- *Describe the criteria that define who will be **included** in the study as a numbered list.*
- *Include age eligibility including upper and lower limit.*
- *Indicate specifically whether you will include any of the following special populations: (You may not include members of the populations listed below as subjects in your research unless you indicate them in your inclusion criteria.)*
    - *Adults unable to consent (cognitively impaired adults)*
    - *Pregnant women*
    - *Pregnant minors*
    - *Minors, i.e., individuals who are not yet adults (neonates, children, teenagers)*
    - *Wards of the state*
    - *Non-Viable neonates*
    - *Neonates of uncertain viability*
    - *Prisoners*

4.2 Exclusion Criteria

- *Describe the criteria that define who will be **excluded** in the study as a numbered list.*
- *Specify whether a study subject may participate in another research study while participating in this research study.*

4.3 Withdrawal of Subjects

- *Describe anticipated circumstances under which subjects will be withdrawn from the research without their consent.*
- *Describe procedures that will be followed when subjects withdraw or are withdrawn from the research, including the possibility of partial withdrawal from study intervention with continued data collection.*
- *Include any necessary safety precautions to be applied to subjects who withdraw or are withdrawn (tapering drug doses, evaluative x-ray, etc.).*

4.4 Recruitment and Retention

4.4.1 Local Recruitment Methods

Describe the following attributes of the recruitment plan for the local Tufts site:

- *When, where, and how potential subjects will be recruited.*

- *Source of subjects (for example, patient population, local community, etc.).*
- *Methods that will be used to identify potential subjects.*
- *Materials that will be used to recruit subjects.*

  Submit a copy of each recruitment-related document with the application. For advertisements, attach the final copy of the print advertisement. When advertisements are audiotaped or videotaped for broadcast, attach the final audio/video. You may submit a script of the proposed audio or video advertisement for IRB review before taping the final version in case revisions are requested. Once recommended changes are made, the final version is to be submitted to the IRB for review and final approval.

  Postings to the Tufts Medical Center Clinical Trials website do not need to be submitted to the IRB for review and approval as long as information in these postings is restricted to the fields listed in the form.

  - *For print and media advertisements, specify when, where, how long and frequency of the advertisements that will be published/aired. Confirm also that permission will be obtained for posting/airing them.*

- *When subjects respond to recruitment material, describe the information that will be provided to them about the study and the information that will be collected from subjects (e.g. name, telephone number, etc.) or submit a telephone/email script that will be used.*

  - *If data will be retained for subjects that are determined to be ineligible, specify how privacy and confidentiality of these potential subjects will be maintained. Also, submit the screening log to the IRB for review.*

- *If recruitment material is being mailed or otherwise distributed, describe where/how the distribution list will be obtained.*
- *Specify how and why the listed recruitment methods will be effective in attracting the targeted subject population.*
- *Refer to the Tufts Health Sciences IRB Policy on Direct Advertising Material for Recruitment for additional requirements when recruiting through social media.*

4.4.2 Study-Wide Recruitment Methods

Is this is a multicenter study where subjects will be recruited by methods not under the control of the local Tufts site (e.g., call centers, national advertisements)?

☑ **Yes** ☐ **No**

If **Yes**, describe the following:

- *Methods of recruitment not under the control of the local Tufts site.*
- *When, where, and how potential subjects will be recruited.*
- *Methods that will be used to identify potential subjects.*
- *Materials that will be used to recruit subjects.*

  Submit a copy of each recruitment-related document with the application. For advertisements, attach the final copy of the print advertisement. When advertisements are audiotaped or videotaped for broadcast, attach the final audio/video. You may submit a script of the proposed audio or video advertisement for IRB review before taping the final version in case revisions are requested. Once recommended changes are made, the final version is to be submitted to the IRB for review and final approval.

4.4.3 Payment

Will subjects receive money, gifts, or any other incentive for participating in this study?
This does not include reimbursement for expenses, which is considered in the next section.

☑ **Yes** ☐ **No**

If **Yes**, describe the following*:*

- *Any proposed payment or incentive for subjects (e.g., a specific description of the incentive, its value both in US and local currency [if international], local household income information, provided to whom). State if the payment/incentive value could pose undue influence on the subject's decision to participate.*
- *Payment amount.*
- *How payment will be made (e.g., cash, check, Greenphire ClinCard).*
- *To whom payment will be made (subject, parent [which one], LAR).*
- *Payment schedule:*
  - *When payment will occur.*
  - *The payment schedule to be used, including the payment schedule and amount for subjects who withdraw or are withdrawn from the study.*

4.4.4 Reimbursement

Will subjects be reimbursed for their expenses, such as travel, parking, meals, or any other study related costs?

☑ **Yes** ☐ **No**

If **Yes**, describe the reimbursement plan and procedures, including*:*

- *What qualifies for reimbursement and whether pre-approval is needed.*
- *How subjects will be required to document expenses for reimbursement (e.g., provide receipts).*
- *How and how often subjects will request reimbursement.*
- *How reimbursement will be made (e.g., cash, check, Greenphire ClinCard).*
- *The reimbursement schedule (when will subjects be reimbursed).*

Consider developing a handout to provide to subjects detailing the above information.

5 Study Design

5.1 Study Timelines

- *Describe the duration of an individual subject's participation in the study.*
- *Describe the duration anticipated to enroll all study subjects at the Tufts study site.*
- *Describe the estimated date for investigators to complete this study (complete primary analyses).*
- *Describe the study procedures that will be accomplished at each study visit.*

5.2 Procedures

- Is there a placebo control arm?

  ☑ **Yes** ☐ **No**

  If **Yes**, describe the following:
  - *The scientific, methodological, and medical reasons to use a placebo.*
  - *The care that will be given to subjects who receive placebo. If this is local standard of care, specify that.*
  - *All potential risks to the placebo group and how the risks will be minimized.*

- *Provide a description of all research procedures being performed as follows:*

- *How individuals will be screened for eligibility. Specify screening that will take place prior to informed consent and screening that will take place after informed consent.*
- *Procedures being performed to monitor subjects for safety or to minimize risks.*
- *All drugs and devices used in the research, their regulatory approval status, and the purpose of their use.*
- *The source records that will be used to collect data about subjects. (Attach all surveys, scripts, and data collection forms.)*

- *Describe the following concerning pregnancy testing and birth control:*
  - *Whether pregnancy testing will be conducted on women of reproductive potential? If testing will not be conducted provide the reason.*
  - *What birth control methods **women** of reproductive potential will be instructed to use. If women will not be instructed about acceptable methods of birth control, clarify why.*
  - *What birth control methods **men** of reproductive potential will be instructed to use. If men will not be instructed about acceptable methods of birth control, clarify why.*

- *Specify which procedures, tests, visits, etc. described above are part of usual standard of care at Tufts and which are performed solely for research purposes.*

- *Clarify which tests are routinely performed for clinical care, but are providing data for the research, and which tests are only performed for research purposes.*

5.3 Evaluations

Will you perform any laboratory tests for this study?

☑ **Yes** ☐ **No**

If **Yes**, describe the following:

- *List all laboratory tests to be done as part of the study (e.g., hematology, clinical chemistry, urinalysis, pregnancy testing).*

- *Differentiate screening laboratory test(s) from those taken after enrollment.*

  - *List special assays or procedures required to determine study eligibility or assess the effect of the intervention (e.g., immunology assays, pharmacokinetic studies, images, flow cytometry assays, microarray, DNA sequencing). For research laboratory assays, include specific assays, estimated volume and type of specimen needed for each test. For procedures, provide special instructions or precautions.*

- *Include specific test components and estimated volume and type of specimens needed for each test.*

- *Specify laboratory methods to provide for appropriate longitudinal and cross-sectional comparison (e.g., use of consistent laboratory method throughout study, use of single, central laboratory for multi-site studies).*

- *If more than one laboratory will be used to perform study tests, specify which evaluations will be done by each laboratory.*

- *Specify if the laboratory tests that will be performed are in compliance with Clinical Laboratory Improvement Amendments (CLIA) of 1988. If not, explain why.*

- *If samples will be stored for the purpose of this study, describe the preparation, handling, and storage of specimens, including specific time requirements for processing, required temperatures, aliquots of specimens, where they will be stored, how they will be labeled, and what will happen to the samples after the study is over (e.g. will be destroyed).*

5.4 Collection and Storage of Human Biological Specimens (Tissue Banking)

Will biological specimens be stored for **future, unspecified**, research?

☑ **Yes** ☐ **No**

If **Yes**, describe the following:

- *Where specimens will be stored, how long they will be stored, how specimens will be accessed, and who will have access to the specimens.*
- *List the Protected Health Information (PHI) to be stored or associated with each specimen. If PHI will be gathered in the future and associated with the specimen, describe the frequency of gathering such PHI.*
- *Procedures to release specimens, including: the process to request a release, approvals required for release, who can obtain specimens, and the PHI to be provided with specimens.*
- *Risks to subjects and their families associated with this collection and storage for future research use.*
- *Risks to groups or populations associated with this collection and storage for future research use.*
- *The mechanism by which the research subject can withdraw permission to use the stored specimens and associated PHI for future research. Indicate what will happen to the specimens and related research data if permission is withdrawn.*

Refer to the IRB's Policy for Research Involving Collection and Storage of Human Biological Specimens for Future Research to ensure that all relevant information is included in the protocol.

6 Ethics and Protection of Human Subjects

6.1 Informed Consent Process

Will subjects be required to provide informed consent?

☑ **Yes** ☐ **No**

If **Yes**, describe the following:

- *Where the consent process will take place (e.g. a private clinic room.)*
- *Anticipated amount of time a potential subject will have to make a decision about participation in the study.*
- *Processes to ensure ongoing consent throughout the study.*
- *State if you will follow "SOP: Informed Consent Process for Research (HRP-090)". If not, describe:*
    - *Role of each research team member involved in the consent process.*
    - *Steps that will be taken to minimize the possibility of coercion or undue influence.*
    - *Steps that will be taken to ensure subjects' understanding.*
- *Non-English Speaking Subjects*
    - *Describe the consent procedures that will be used to enroll non-English speakers (for example, the use of IRB approved Short Forms per the IRB's Short Form policy). If IRB approved Short Forms will not be used, describe who will conduct the consent interview, use of interpreters, use of IRB approved translated documents, etc.*
    - *If non-English speakers are being excluded, provide the ethical and scientific justification, including whether this would be equitable. For example, if non-English speakers are eligible for the study and could potentially benefit from participation, it would not be equitable to exclude them.*

  Refer to the IRB Short Form Policy on the IRB website for information on enrolling non-English speakers.
- *Process to Document Consent in Writing*
    - *State if you will follow "SOP: Written Documentation of Consent (HRP-091)". If not, describe how consent will be documented in writing.*

- *If you will obtain consent, but will not document consent in writing, attach a consent script and confirm the following (you may use Tufts IRB ICF templates to create the consent document or script):*
  - *The only record linking the subject and the research would be the consent document.*
  - *The principal risk of a signed consent document would be the potential harm resulting from a breach of confidentiality.*
  - *Each subject will be asked if they want documentation linking them with the research, and their wishes will govern.*
    Note: If your research presents no more than minimal risk of harm to subjects and involves no procedures for which written documentation of consent is normally required outside of the research context, the IRB will generally waive the requirement to obtain written documentation of consent.

- *If consent will **not** be obtained in-person (i.e., it will be obtained remotely) then a signed copy of the ICF can be faxed or scanned then emailed to the study team. If you plan to obtain consent remotely, describe the following:*
  - *A compelling rationale for remote consent.*
  - *Justification for why this is appropriate for the study population.*
  - *How participants will be provided with an opportunity to ask questions about the study and how the PI/study team will confirm understanding, including the assent of minors, if applicable.*
  - *A description of the process of obtaining consent remotely.*

  Note: Best practice is to have subjects mail back the original signed ICF to the study team.

6.2 Waiver or Alteration of Consent Process

This applies for studies where informed consent will not be obtained, required information will not be disclosed, or the research involves deception.

- Is a waiver or alteration of the consent process being requested for this study?

  ☑ **Yes** ☐ **No**

  If **Yes**, describe the following:
  - *Provide the rationale for the waiver.*
  - *How the waiver or consent alteration will **NOT** adversely affect the rights and welfare of subjects.*
  - *How the research could **NOT** practicably be carried out without the waiver or alteration.*
  - *How, subjects will be provided with additional pertinent information after participation. If subjects will not be provided this information after participation, explain why.*

- Is a waiver of the consent process being requested for parents for research involving children?

  ☑ **Yes** ☐ **No**

  If **Yes**, describe the following:
  - *The rationale for this waiver.*
  - *How the research could **NOT** practicably be carried out without the waiver or alteration.*
  - *How this waiver is an appropriate substitute to parental consent for protecting the children who will participate as subjects in the research.*
  - *Confirm that the waiver is consistent with Federal, State, and local laws.*

- Is a waiver of the consent process for planned emergency research being requested?

  ☑ **Yes** ☐ **No**

  If **Yes**, describe the following:
  - *How the subjects are in a life-threatening situation.*
  - *How available treatments are unproven or unsatisfactory.*
  - *How the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.*

- *The appropriate animal and other preclinical studies that have been conducted, and the information derived from those studies and related evidence that supports the potential for the study drug, device, or procedure to provide a direct benefit to the individual subject.*
- *How the research could not practicably be carried out without the waiver.*
- *How obtaining informed consent is not feasible because:*
  - *Subjects will not be able to give their informed consent as a result of their medical condition (specify why):*
  - *The study drug, device, or procedure must be administered before consent from the subjects' legally authorized representatives can be obtained (specify why):*
  - *There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the research (specify why):*
- *The length of the potential therapeutic window based on scientific evidence.*
- *Specify that the research team will attempt to contact a legally authorized representative for each subject within that window of time and, if feasible, ask for consent within that window rather than proceeding without consent. Note that at continuing review, you will need to report to the IRB the efforts made to contact legally authorized representatives or subject's family member if a legally authorized representative is not available.*
- *If the subject dies before a legally authorized representative or family member can be contacted, specify that information about the research will be provided to the subject's legally authorized representative or family member, if feasible.*
- *If a legally authorized representative or family member is told about the research and the subject's condition improves, specify that the subject will also to be informed as soon as feasible.*
- *The consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the research will be conducted and from which the subjects will be drawn.*
- *The public disclosure to the communities in which the research will be conducted and from which the subjects will be drawn, prior to initiation of the research, of the plans for the investigation and its risks and expected benefits.*
- *The public disclosure following completion of the research to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results.*
- *The procedures to inform, at the earliest feasible opportunity, each subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, of the subject's inclusion in the research, the details of the investigation and other information contained in the ICF, and that he or she may discontinue the subject's participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.*

6.3 International Research

- *Refer to the IRB's International Checklist and International Guidance to ensure that all relevant information described in those documents is included in this protocol.*

6.4 Confidentiality

- *Describe the procedures in place to maintain confidentiality as follows:*
  - *Where and how data or specimens will be stored.*
    - *Specifically, state where the study records, including both electronic and/or paper study documents including signed ICFs/assent forms, will be retained (stored) during the study (state the location for original document plus any copies that are made, e.g., if a copy of the ICF will be retained in the subject's medical record).*
  - *How long the data or specimens will be stored.*
  - *Who will have access to the data or specimens.*
  - *Who is responsible for receipt or transmission of the data or specimens locally?*
  - *How data and specimens will be transported.*

  - *Whether data will be coded.*
    - *If so, specify if there is a key to the code that matches the subjects' study identification number with their name and who will have access to it*
  - *Whether videotapes and/or photographs of subjects will be capable of identifying the study subject. If so, indicate who will have access to (be able to view) these items and how long the videotapes or photographs will be retained for the study and what the plan is for their destruction.*
  - *If identifiable screening data will be retained for the study, clarify why, and who will have access to it. Submit the screening log.*
  - *Clarify whether confidential genetic information will be collected from subjects. Data and specimens should be stored in a secure location only accessible by the research team. The PI must ensure that study documents are stored in a manner that protects the privacy of subjects and the confidentiality of study data.*
- *Indicate whether a Certificate of Confidentiality will be obtained. A Certificate of Confidentiality should be obtained for research involving collection of information that, if disclosed, could have adverse consequences for subjects or damage their financial standing, employability, insurability, or reputation. For more information, refer to NIH's Certificates of Confidentiality Kiosk.*

6.5 Provisions to Protect the Privacy Interests of Subjects

- *Describe the steps that will be taken to protect subjects' privacy interests. "Privacy interest" refers to a person's desire to place limits on with whom they interact or to whom they provide personal information.*
- *Describe the steps that will be taken to make the subjects feel at ease with the research situation in terms of the questions being asked and the procedures being performed. "At ease" does not refer to physical discomfort, but the sense of intrusiveness a subject may or may not experience in response to questions, examinations, and procedures.*
- *Under what circumstances will the research team access sources of information about the subjects.*

6.6 Provisions to Monitor the Study to Ensure the Safety of Subjects

- *Describe the plan to periodically evaluate the data regarding both harms and benefits to assess subject safety as follows:*
  - *The data that will be reviewed, including safety data, untoward events, and efficacy data.*
  - *Who will review the data.*
  - *How the safety information will be obtained and documented (e.g., case report forms, by telephone calls with participants, printouts of laboratory results, etc.).*
  - *The frequency of data collection, including when safety data collection starts.*
  - *The frequency or periodicity of review of cumulative data.*
  - *The statistical tests for analyzing the safety data to determine whether harm is occurring.*
  - *Any conditions that trigger an immediate suspension of the research or other action for the research.*
  - *The plan might include establishing a data monitoring committee which addresses all the above.*
- *Describe the entity responsible for monitoring the data, and their respective roles (e.g., the investigators, the research sponsor, a coordinating or statistical center, an independent medical monitor, a Data and Safety Monitoring Board (DSMB) /Data Monitoring Committee (DMC), and/or some other entity, and the timeframe for reporting events to this entity.*
  - *Submit a copy of the DSMB/DMC Charter if the study is monitored by a DSMB/DMC.*

6.7 Compensation for Research-Related Injury

Does the research involve greater than minimal risk to subjects? *(or if minimal risk, is there potential risk of research-related injury?)*:

☑ **Yes** ☐ **No**

If **Yes**, describe the available compensation in the event of research related injury including*:*

- *What this compensation will be (e.g. free medical care, payment for treatment, compensation for lost wages, dependent care, etc.).*
- *Who will provide this compensation (e.g. sponsor, institution, etc.).*
- *What will count as a qualified harm (e.g., physical, psychological, economic, social, or other injury).*
- *Whether only injuries "related" to study participation will be covered. If yes, clarify how it will be determined what injuries are considered related, and who will decide this.*
- *Will the study distinguish between injury (short-term, resolvable) and impairment (often longer-term, potentially manageable, but not resolvable) and if so, why.*
- *The process subjects must follow to obtain this compensation.If no funds are set aside for research-related injury and subjects and/or their insurance will have to pay for the treatment of such injuries, include a statement such as: "No funds have been set aside for research-related injury. You or your insurance carrier will be required to pay for medical care associated with your research-related injury."*

6.8 Economic Burden to Subjects

Does the research involve any costs to subjects?

☑ **Yes** ☐ **No**

If **Yes**, describe the following*:*

- *Costs that subjects might be responsible for due to participation in the research.*
- *If a subject's health insurance denies payment for the research procedures/drugs/devices, describe the mechanism for providing the procedures/drugs/devices free of charge, if one exists.*

6.10 Vulnerable Populations

If the research involves individuals who are vulnerable to coercion or undue influence, describe the rationale for their inclusion and the additional safeguards included to protect their rights and welfare.

Will pregnant women be enrolled?

☑ **Yes** ☐ **No**

If **Yes**, describe the following:

- *Any preclinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, that have been conducted that provide data for assessing potential risks to pregnant women and fetuses.*
- *Whether the risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus or if there is no prospect of benefit to the fetus, the risk to the fetus is NOT greater than Minimal Risk, and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means.*
- *The biomedical knowledge that is expected to result from this research for this population.*
- *How any risk of this research is the least possible for achieving the objectives of the research.*
- *How mothers providing consent are informed of the reasonably foreseeable impact of the research on the fetus or neonate.*
- *Specify that no inducements, monetary or otherwise, will be offered to terminate a pregnancy and that in the case of a fetus, the fetus is not the subject of a planned abortion.*
- *Specify that individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy or in determining the viability of a neonate.*

Will the research involve neonates of uncertain viability or non-viable neonates?

☑ **Yes** ☐ **No**

If **Yes**, describe the following:

- *Any preclinical and clinical studies that have been conducted that provide data for assessing potential risks to neonates.*
- *The important biomedical knowledge that will be developed from this research and why it cannot be obtained by other means.*
- *Whether there will be added risk to the neonate resulting from the research.*
- *How individuals providing consent are informed of the reasonably foreseeable impact of the research on the neonate.*
- *Specify that no person shall perform or offer to perform an abortion where part or all of the consideration for said performance is that the fetal remains may be used for experimentation or other kind of research or study.*
- *Specify that no person shall knowingly sell, transfer, distribute or give away any fetus or neonate for a use which is in violation of Massachusetts General Laws Chapter 112 Section 12J.*
- *Specify that individuals engaged in the research will have no part in determining the viability of a neonate.*
- *For non-viable neonates, specify that the vital functions of the neonate will not be artificially maintained and that the research will not terminate the heartbeat or respiration of the neonate.*
- *For neonates of uncertain viability, whether the research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective.*

Will subjects who are not yet adults (neonates, children, teenagers) be enrolled?

☑ **Yes** ☐ **No**

If **Yes**, describe the following:

- *Specify that you will follow "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)" to determine whether a prospective subject has or has not attained the legal age for consent to treatments or procedures involved in the research under the applicable law of the jurisdiction in which the research will be conducted. (e.g., individuals under the age of 18 years). If this SOP will not be followed, describe how this (attainment of legal age for consent or not) will be determined.*
- *How permission to participate in the study will be obtained from the parents or legal guardians.*
- *The assent process of children as follows:*
  - *Any waiting period available between informing the prospective subject and obtaining the assent.*
  - *Any process to ensure ongoing assent.*
  - *Research team members involved in the assent process.*
  - *How long children will have to consider study participation.*
  - *Steps that will be taken to minimize the possibility of coercion or undue influence.*
  - *Steps that will be taken to ensure the subjects' understanding.*
  - *If assent will not be obtained from children, specify why.*
    - *If children reach 18 years of age while in the study describe the following:*
  - *The plan to obtain written informed consent from the subject at age 18 years.*
  - *Who will be responsible for managing the plan.*
  - *Where the consent discussion will take place.*
  - *What will happen if the subject cannot be located to provide consent at age 18 years.*

Will minors who are:

i) married, widowed, divorced; or
ii) the parent of a child; or
iii) a member of any of the armed forces; or
iv) pregnant or believes herself to be pregnant; or
v) living separate and apart from his/her parent or legal guardian, and is managing his/her own financial affairs

be approached for study participation for either themselves or their child?

☑ **Yes** ☐ **No**

If **Yes**, describe the following:

- *How it will be determined that this population has the capacity to execute informed consent for this study. Please note that the circumstance of parenthood, pregnancy, etc. may not equate with a fully adult ability to appreciate the risks, benefits, and alternatives for indicated care. Thus, sound and sensitive clinical judgment that is attentive to both the minor's rights* and *the minor's actual competence and needs is to be brought to bear, and is to include a determination as to whether involvement of family or other adults familiar to the minor is necessary and appropriate.*
- *How informed consent will be executed with this population in a way that allows for independent and thoughtful decision-making.*
- *Any additional steps or procedures that will be used when performing informed consent with this population.*

  Refer to Massachusetts state law (MGL Chapter 112, Section 12F) for more information about this population. Please note, the statute applies to clinical care and should be applied to research only as applicable.

Will wards of the state and/or children at risk of becoming wards of the state be enrolled (this includes foster children or any child that is in state custody)?

☑ **Yes** ☐ **No**

If **Yes**, describe the following:

- If **Yes**, describe the following:
- *Justification for recruiting and enrolling this population*
- *Any additional details about the recruitment methods to be used. If the same recruitment methods previously described in the protocol will be used, then state that.*
- *Any additional details about the informed consent process to be used. If the same informed consent process for enrolling minors previously described in the protocol will be used, then state that.*
- *How it will be ensured that the appropriate person(s) grants permission for each ward to participate in the research.*
- *How the research team will know if there has been a change in guardianship status during the course of the research and how permission will be obtained from the new guardian in the case that there has been a change in guardianship status.*
- *Submit documentation of review by the Department of Children and Families (DCF) to the IRB.*
- *If the study is greater than minimal risk, describe the following:*
  - *Whether the research is related to their status as wards OR if the research is conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.*
  - *How an advocate will be appointed for each child who is a ward, in addition to any other individual acting on behalf of the child as guardian or in loco parentis.*
  - *The background and experience of the advocate to act in the best interests of the child for the duration of the child's participation in the research.*
  - *Specify that the advocate will not be associated in any way (except in the role as advocate or member of the IRB) with the research, the investigator(s), or the guardian organization.*
- *Refer to the IRB's Wards of the State policy for additional information on enrolling wards of the state.*

Will cognitively impaired adults (adults with impaired-decision making capacity) or adults who may lose the capacity to consent be enrolled?

☑ **Yes** ☐ **No**

If **Yes**, describe the following:

- *Whether the research holds out a prospect of direct benefit to the individual subject that is unavailable outside the research context.*
- *Why the objectives of the study cannot be met by means of study of subjects who can give consent personally.*
- *Whether this study is prohibited by law.*
- *The process to determine whether the individual is capable of consent.*
- *Who will determine if the subject is able to provide informed consent.*
- *How it will be determined whether the subject is able to provide informed consent:*
- *When and how often (even after obtaining informed consent) it will be determined whether the subject is able to provide informed consent.*
- *List the individuals from whom permission will be obtained if the subject cannot provide informed consent. Prioritize the list (e.g., durable power of attorney for health care, court appointed guardian for health care decisions, spouse, and adult child.)*
    - *For research conducted in this state, review "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)" to be aware of which individuals in the state meet the definition of "legally authorized representative."*
    - *For research conducted outside of the state, provide information that describes which individuals are authorized under applicable law to consent on behalf of a prospective subject to their participation in the procedure(s) involved in this research. One method of obtaining this information is to have a legal counsel or authority review your protocol regarding the definition of "legally authorized representative" in "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)."*
- *If it is possible that subjects may regain capacity to provide informed consent during the study, describe how frequently this will be assessed and state that subjects will be consented to the study in the event that they regain capacity to provide informed consent.*
- *Describe the process for assent of the subjects as follows:*
    - *Whether assent will be required of all, some, or none of the subjects. If some, specify which subjects will be required to assent and which will not.*
    - *If assent will not be obtained from some or all subjects, an explanation of why not.*
    - *Whether assent of the subjects will be documented and the process to document assent. The IRB allows the person obtaining assent to document assent on the consent document and does not routinely require assent documents and does not routinely require subjects to sign assent documents.*
- *Provide a description of how the patient will be informed of the potential risks and benefits of the study and any procedures associated with its use.*
- *Specify that subjects will be withdrawn if they appear to be unduly distressed at any time during the study.*

Will prisoners be enrolled?

☑ **Yes** ☐ **No**

If **Yes**, describe the following:

- *Any possible advantages accruing to the Prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired.*
- *Whether the risks involved in the research are commensurate with risks that would be accepted by non-Prisoner volunteers.*
- *Procedures for the selection of subjects within the prison which are fair to all Prisoners and immune from arbitrary intervention by prison authorities or Prisoners. Unless the Principal Investigator provides to the Board justification in writing for following some other procedures, control subjects must be selected randomly from the group of available Prisoners who meet the characteristics needed for that particular research project.*

- *Assurance exists that parole boards will not take into account a Prisoner's participation in the research in making decisions regarding parole, and each Prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole.*
- *Will follow-up examination or care of subjects after the end of their participation be required? If yes, describe the provision for such examination or care, taking into account the varying lengths of individual Prisoners' sentences, and for informing subjects of this fact.*

Will students and/or employees be enrolled in this research?

☑ **Yes** ☐ **No**

If **Yes**, describe the following:

- *Justification for specifically recruiting and enrolling students and/or employees into the study.*
- *How potential coercion will be eliminated.*
- *Recruitment methods to be applied specifically to students or employees. If the same recruitment methods previously described in the protocol will be used, then state that.*
- *Additional safeguards included to protect the rights and welfare of students and employees.*
- *Protections to ensure that a subject's participation or early withdrawal from the study will not affect his/her status as a student or employee.*
- *Submit a letter from the appropriate institutional official (e.g., Department Chair, Vice-President) who oversees the students and/or employees attesting to the fact that the employee's or student's participation in the research is acceptable and that coercion has been minimized.*

7 Adverse Event Monitoring

7.1 Definitions

- *Define adverse events (AEs), serious adverse events (SAEs), and unanticipated problems for your study.*

7.2 Reporting Procedures

- *Describe the protocol-specific reporting procedures, including who will be responsible for each step (e.g., PI, Data Coordinating Center, Medical Monitor), which forms should be completed, timeframes for reporting, how reports will be distributed, and what follow-up is required.*
- *Include specific details of reporting procedures for:*
  - *Deaths, life-threatening events, pregnancies*
  - *Other SAEs*
  - *Other AEs*
  - *Other UPs*
- *Ensure that the reporting procedures meet the reporting requirements of the FDA, NIH, OHRP, sponsor, study leadership and any other regulatory body that applies to the study, as applicable.*

7.3 Reportable New Information

- *Indicate also, that reportable new information will be reported to the IRB per the Tufts Health Sciences IRB's Reportable New Information policy. If your reporting plan to the IRB differs from the IRB's policies, please describe it in detail.*

8 Statistical Considerations

8.1 Study Endpoints

- *Describe the primary and secondary study endpoints.*
- *Describe any primary or secondary safety endpoints.*

8.2 Statistical Analysis

- *Describe the statistical analyses that will be performed for this study*
- *Provide a power analysis.*

8.3 Number of Subjects

- *If this is a multicenter study, specify the number of subjects to be enrolled in total across all sites.*
- *Specify the number of subjects to be enrolled at the Tufts site. Subjects who sign an ICF are considered "enrolled". For studies that have a separate screening ICF, this number is the number of subjects who sign a screening ICF.*
    - *Provide the rationale for enrolling this number of subjects at the Tufts site.*
    - *Estimate the number of subjects expected to be enrolled at the Tufts site (i.e. sign the screening or study ICF) as well as the number needed to complete the study at the Tufts site.*
    - *If a large number of withdrawals and/or dropouts is expected, explain why.*

8.4 Data Management

- *Describe the data analysis plan, including descriptions of the data.*
- *Provide a power analysis.*
- *Describe the steps that will be taken to secure the data (e.g., training, authorization of access, password protection, encryption, physical controls, certificates of confidentiality, and separation of identifiers and data) during storage, use, and transmission.*
- *Describe any procedures that will be used for quality control of collected data.*
- *Describe how data and specimens will be handled study-wide:*
    - *What information will be included in that data or associated with the specimens.*
    - *Where and how data or specimens will be stored.*
    - *How long the data or specimens will be stored.*
    - *Specify who will have access to the data or specimens.*
    - *Specify who is responsible for receipt or transmission of the data or specimens.*
    - *Specify how data and specimens will be transported.*
    - *Specify the plan for study data retention and storage (accounting for research team turnover).*

8.5 Randomization

Will subjects be randomized?

☑ **Yes** ☐ **No**

If **Yes** describe the following:

- *The randomization procedures, including the ratio of subjects randomized to each study arm.*
- *The blinding procedures if the study will be blinded.*

9 Drugs or Devices

Will the research involve drugs?

☑ **Yes** ☐ **No**

Will the research involve devices?

☑ **Yes** ☐ **No**

If **Yes** to either, describe the following:

- *Who on the research team, in addition to the Principal Investigator, will be accountable for drug(s)/device(s).*
- *Who will interface with the pharmacy (drugs) or sponsor (devices).*

- *If pre-printed orders will be created to obtain study drug(s) from the pharmacy, describe the procedures for reviewing and verifying the accuracy of the pre-printed orders prior to their being implemented.*
- *If computerized order sets are created and/or infusion devices need to be programmed to administer an investigational drug, indicate the mechanism to pre-review and verify their accuracy, including who will be involved in this process from the research team, pharmacy, and nursing.*
- *Specify if the study drug, device, or procedure (including beneficial health care procedures) will be available to subjects after participation in the study.*
- *Specify if there are any medications or other substances that should not be taken while participating in the study. Attach a list of these to the ICF or create a subject handout.*
- *Submit any handouts or instructions sheets that will be given to subjects on how to administer study drug(s) or use study device(s).*
- *If the study drug(s) have an IND or the device(s) have an IDE or a claim of abbreviated IDE (non-significant risk device), identify the holder of the IND/IDE/Abbreviated IDE.*

10 Study Administration

10.1 Setting

- *Describe the sites or locations where your research team will conduct the research.*
- *If the research will take place at an international site, refer to the International Guidance and International Checklist.*
- *Describe the following:*
  - *Where research procedures will be performed.*
  - *The composition and involvement of any community advisory board.*
  - *If a hospital stay will be required solely for research and if so, the expected duration of the hospital stay.*
  - *If inpatients will be enrolled, clarify if study participation will require an increase in the length of hospital stay, and if so, for how long.*
  - *For research conducted outside of Tufts and its affiliates:*
    - *Describe the site-specific regulations/customs affecting the research*
    - *Describe the site-specific local scientific review and ethical review structure and procedures.*
    - *Describe how the study team is/will become knowledgeable of the local study site's culture, customs, regulations, and society.*

10.2 Registration

- *Describe the steps the research team will take to ensure that a subject is appropriately enrolled or registered in the study prior to receiving any study intervention (e.g. describe and submit any protocol eligibility checklist that will be used, specify who on the research team will confirm eligibility and that consent was documented, etc.).*

10.3 Resources Available

- *Specify the role and tasks delegated to each research team member.*
- *Describe the qualifications (e.g., training, experience) of the PI and research team to perform their roles. Provide enough information for the IRB to determine the PI and research team are qualified to conduct the proposed research.*

- *Specify the coverage plan to address any issues (including subject safety issues) that occur while the PI is away and/or unavailable. The research team member designated to serve as the acting PI in the PI's absence should have similar training and expertise as the PI.*
- *Describe other resources available to conduct the research, for example:*
    - *Feasibility of recruiting the required number of suitable subjects within the proposed recruitment period. For example, how many potential subjects do you have access to? What percentage of those potential subjects do you anticipate recruiting?*
    - *Confirm that the amount of time you will spend on the research is adequate to conduct and complete the research*
    - *Facilities*
    - *Availability of medical or psychological resources that subjects might need*
    - *Process to ensure the research team members have adequate oversight and are adequately trained regarding the protocol, study procedures, and their roles and responsibilities.*

10.4 IRB Review

- *Specify that an appropriate IRB registered with the OHRP, will review and approve this study.*
- *Specify that any amendments to the protocol or informed consent documents will be reviewed and approved by the IRB prior to use, unless required to eliminate an apparent immediate hazard to subjects.*

10.5 Multi-Site Research

Is this a multi-site study where Tufts is the sponsor, primary grant recipient, or coordinating site?:

☑ **Yes** ☐ **No**

If **Yes**:

- *Describe the processes to ensure pertinent and timely communication among sites, including:*
    - *When and how sites will be provided with the current version of the protocol, informed consent form, and other study documents.*
    - *That all required approvals will be obtained at each site (including approval by the site's IRB of record).*
    - *How all modifications will be communicated to sites, and will be reviewed and approved (including approval by the site's IRB of record) before the modification is implemented.*
    - *That all participating sites will safeguard data as required by local information security policies.*
    - *Assurance that all local site investigators will conduct the study appropriately.*
    - *That all non-compliance with the study protocol or other reportable new information will be reported in accordance with local policy.*
- *Describe the method for communicating the following information to participating sites:*
    - *Problems*
    - *Interim results*
    - *Study closure*
    - *Amendments*
    - *Research related communications*
- *Specify which site is the Data Coordinating Center.*
- *Specify if Tufts' data will be shared outside of Tufts (e.g., with other investigators, sponsor, etc.) and how data will be shared.*
- *Describe any collaborations not described above, such as:*

- *Tufts investigators with multiple affiliations that would engage other institutions in research (e.g., Tufts making direct payment to another institution for the research, the research is being conducted on behalf of another institution).*
- *Tufts Health Sciences IRB review and oversight of additional locations. Complete a Form 10 (IAA/IIA) to request Tufts Health Sciences IRB serve as the IRB of record for other sites. Refer to the Tufts Health Sciences IRB website for more information about requests to cede/assume IRB review.*

10.6 Community-Based Participatory Research

Note: "Community-based Participatory Research" is a collaborative approach to research that equitably involves all partners in the research process and recognizes the unique strengths that each brings. Community-based Participatory Research begins with a research topic of importance to the community, has the aim of combining knowledge with action and achieving social change to improve health outcomes and eliminate health disparities.

Will this study involve community-based participatory research?

☑ **Yes** ☐ **No**

If Yes, describe the following

- *Communities that will be involved in this research.*
- *Involvement of the community in the design, protocol development, informed consent process, access to data and samples, and conduct of the research.*
- *Plans on dissemination and publication of study results which are in agreement with the community.*

10.7 Sharing Results with Subjects

Will results (overall study results or individual subject results, such as results of investigational diagnostic tests, genetic tests, or incidental findings) be shared with subjects or others (e.g., the subject's primary care physician or the subject's treating physician)?

☑ **Yes** ☐ **No**

If **Yes**, describe the following:

- *Rationale for sharing these results.*
- *How results will be shared.*
- *For individual subject results, specify if subjects have the option to opt-in or opt-out of receiving these results or allowing these results to be shared with others.*
- *Any referral policies (i.e. for confirmation of any individual subject results).*
- *Whether testing of research specimens is being conducted in a laboratory certified (CLIA-approved) to conduct diagnostic testing. If patient-specific research results are reported from the laboratory and those results will or could be used for the diagnosis, prevention, or treatment of any disease or impairment, or the assessment of the health of human beings, the laboratory must be CLIA certified.*
    - *If the research tests are experimental or of unknown or unproven clinical significance and the results will be provided to the source individual or physician or placed in the source individual's medical record, provide the rationale for this.*

11 References

- *Provide a list of references for all citations included in the protocol.*