

**HUMAN RESEARCH PROTOCOL**

**PREFACE**

This protocol template must be used for any Downstate investigator-initiated research submitted on or after **April 1, 2021** to the Downstate IRB for reviewed by the Downstate IRB or whenever required by the Downstate IRB or the Central Methodology Review Committee (CMRC).

*Do not use this protocol template for an industry funded study or a multisite study overseen by a Reviewing (external) IRB when the protocol is provided by the sponsor.*

**It is important to incorporate all sections of the template into your protocol and to do so in the same order. If a particular section is not applicable, include it, but indicate that it is not applicable.**

Please try to limit the total length of the research methods (not including cover pages, table of contents, human research information, and protocol amendment history, or references) to **20 pages**.

When this protocol requires submission to the Central Methodology Review Committee (CMRC), the CMRC will only review the protocol for research methodology. The Downstate IRB will review the entire protocol with an emphasis on the review on the human research protections portions of the research.

Remove this **Preface** before finalizing and submitting the protocol to the CMRC or IRB.

The goal of this template is to assist investigators to write a comprehensive protocol that meets Downstate standards.

This template contains two types of text: instruction/explanatory and example.

**Instruction/explanatory text** are indicated by *italics* and should deleted.

**Example text** is included to further aid in protocol writing and should either be modified to suit the drug, biologic or device (study intervention), design, and conduct of the planned research or deleted. Example text is indicated in [regular font]. Within example text, a need for insertion of specific information is notated by <angle brackets>.

**To update the Table of Contents**, click on the word “Contents” and follow the prompts.

For general, technical, or policy questions, please consult the IRB at IRB@downstate.edu

For research design or statistical questions, please consult a biostatistician in your department or CMRC@downstate.edu

**VERSION 03/16/2021**

**Title:**

**Version:**

**Principal Investigator:**

**PI Contact Information:**

**Department or College:**

**Summary of Changes from Previous Version:**

|  |  |  |
| --- | --- | --- |
| **Affected Section(s)** | **Summary of Revisions Made** | **Rationale** |
|  |  |  |
|  |  |  |

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# Protocol Summary

|  |  |
| --- | --- |
| Scientific Abstract: | *Provide a short description of the protocol, including a brief statement of the study hypothesis. This should be only a few sentences in length.* |
| OBJECTIVES: | Primary Objective: Secondary Objectives |
| ENDPOINTS: | Primary Endpoint:Secondary Endpoints: |
| STUDY POPULATION | *Specify the sample size, gender, age, demographic group, general health status, and geographic location.* |
| STUDY INTERVENTION | *Describe the study intervention. If the study intervention is a drug or biologic, include dose and route of administration. For devices, provide a description of each important component, ingredient, property and the principle of operation of the device.* |
| STUDY DURATION | *Estimated time (in months) from when the study opens to enrollment until completion of data analyses* |
| PARTICIPANT DURATION | *Time (e.g., in months) it will take for each individual participant to complete all participant visits.* |

## Schema

*This section should include a diagram that provides a quick “snapshot” of the study and ideally be limited to 1 page.*

### Study Flow Diagram

*Insert a flow diagram to outline screening and study visits.*

### Timetable

*The schedule of activities must capture the procedures that will be accomplished at each study visit, and all contact, with study participants e.g., telephone contacts. This includes any tests that are used for eligibility, participant randomization or stratification, or decisions on study intervention discontinuation. Only include procedures that contribute to participant eligibility and study objectives and endpoints. Other procedures should be done sparingly and with consideration, as they may add unnecessary complexity and detract from recruitment.*

### Schedule of Activities

*The schedule below is provided as an example and should be modified as appropriate.*

| **Procedures** | ScreeningDay -7 to -1 | Enrollment/BaselineVisit 1, Day 1 | Study Visit 2 Day 7 +/-1 day | Study Visit 3Day 14 +/- 1 day | Study Visit 4Day 21 +/-1 day | Study Visit 5Day 28 +/-1 day | Study Visit 6Day 35 +/-1 day | Study Visit 7Day 42 +/-1 day | Study Visit 8Day 49 +/-1 day | Study Visit 9Day 56 +/-1 day | Study Visit 10Day 63 +/-1 day | Study Visit 11Day 70 +/- 1 day | Study Visit 12Day 77 +/-1day | Final Study Visit 13Day 84 +/-1 day  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Informed consent | X |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Demographics | X |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Medical history | X |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Randomization | X |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Administer study intervention |  | X |  |  | X |  |  | X |  |  | X |  |  |  |
| Concomitant medication review | X | X---------------------------------------------------------------------------------------------X |  |
| Physical exam (including height and weight) | X | X |  |  | X |  |  | X |  |  | X |  |  | X |
| Vital signs | X | X |  |  | X |  |  | X |  |  | X |  |  | X |
| Height | X |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Weight | X | X |  | X |  | X |  | X |  | X |  | X |  | X |
| Performance status | X | X |  | X |  | X |  | X |  | X |  | X |  | X |
| Hematology  | X | X | X | X | X | X | X | X | X | X | X | X | X | X |
| Serum chemistry a | X | X | X | X | X | X | X | X | X | X | X | X | X | X |
| Pregnancy test b | X |  |  |  |  |  |  |  |  |  |  |  |  |  |
| EKG (as indicated) | X |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Adverse event review and evaluation | X | X---------------------------------------------------------------------------------------------X | X |
| Radiologic/Imaging assessment | X |  |  |  | X |  |  |  | X |  |  |  |  | X |
| Other assessments (e.g., immunology assays, pharmacokinetic) | X | X | X | X | X | X | X | X | X | X | X | X | X | X |
| Complete Case Report Forms (CRFs) | X | X | X | X | X | X | X | X | X | X | X | X | X | X |
| a: Albumin, alkaline phosphatase, total bilirubin, bicarbonate, BUN, calcium, chloride, creatinine, glucose, LDH, phosphorus, potassium, total protein, AST, ALT, sodium.b: Serum pregnancy test (women of childbearing potential). |

# Introduction

No text is to be entered in this section; rather it should be included under the relevant subheadings below.

## Study Rationale

*State the problem or question (e.g., describe the population, disease, current standard of care, if one exists, and limitations of knowledge or available therapy) and the reason for conducting the research.*

## Background

*As applicable, this section should include:*

* *A summary of findings from nonclinical in vitro or in vivo studies that have potential clinical significance.*
* *A summary of relevant research and any history of human use or exposure to the study intervention, including use in other countries, and clinical pharmacology studies*
* *Discussion of important literature and data that are relevant to the research and that provide background for the research (reference citations should be listed in References)*
* *Applicable clinical, epidemiological, or public health background or context of the research*
* *Importance of the research and any relevant treatment issues or controversies*

# Objectives and Endpoints

| OBJECTIVES | ENDPOINTS | JUSTIFICATION FOR ENDPOINTS |
| --- | --- | --- |
| Primary |  |  |
| The primary objective is the main question. This objective generally drives statistical planning for the study (e.g., calculation of the sample size to provide the appropriate power for statistical testing). | The primary endpoint(s) should be clearly specified and its importance and role in the analysis and interpretation of study results should be defined. The primary endpoint(s) is the basis for concluding that the study met its objective (e.g., “the study wins”).  | Briefly explain why the endpoint(s) were chosen. |
| Secondary |  |  |
| The secondary objective(s) are goals that will provide further information on the use of the intervention. | Secondary endpoints should be clearly specified and may include, for example, endpoints related to efficacy, safety, or both. Secondary endpoints are those that may provide supportive information about the study intervention’s effect on the primary endpoint or demonstrate additional effects on the disease or condition. It is recommended that the list of secondary endpoints be short, because the chance of demonstrating an effect on any secondary endpoint after appropriate correction for multiplicity becomes increasingly small as the number of endpoints increases.  | Briefly explain why the endpoint(s) were chosen. |
| Tertiary/Exploratory  |  |  |
| *Tertiary/exploratory objective(s) serve as a basis for explaining or supporting findings of primary analyses and for suggesting further hypotheses for later research.* | *Exploratory endpoints should be specified.* *Exploratory endpoints may include clinically important events that are expected to occur too infrequently to show a treatment effect or endpoints that for other reasons are thought to be less likely to show an effect but are included to explore new hypotheses.* Endpoints that are not listed in an alpha conserving plan will be considered exploratory. | *Briefly explain why the endpoint(s) were chosen.* |

Study Design

No text is to be entered in this section; rather it should be included under the relevant subheadings below.

## Overall Design

*The scientific integrity of the research and the credibility of the data from the research depend substantially on study design. Include the following as applicable:*

* *A statement of the hypothesis*
* *A description of the type/design of the research to be conducted (e.g., randomized, placebo-controlled, double-blinded, parallel design, open-label, dose escalation, dose-ranging, adaptive, cluster randomized, group sequential, multi-regional, superiority or non-inferiority design)*
* *A description of methods to be used to minimize bias*
* *The number of study groups/arms and study intervention duration*
* *Indicate if single site or multi-site*
* *Name of study intervention(s)*
* *Note if interim analysis is planned*
* *Note if the study includes any stratifications and if so, identify the stratification planned (e.g. sex, race/ethnicity, age, dose).*

## Scientific Rationale for Study Design

*Describe the rationale for the type and selection of control (e.g., placebo, active drug, dose-response, historical) and study design (e.g., non-inferiority as opposed to superiority). Discuss known or potential problems associated with the control group chosen in light of the specific disease and intervention(s) being studied.*

*When applicable, provide a justification for the route of administration, planned maximum dosage, and dosing regimen, including starting dose, of the study intervention(s) and control product(s).*

*When applicable, provide an end of study definition.*

# Study Population

No text is to be entered in this section; rather it should be included under the relevant subheadings below.

## Inclusion Criteria

Example text provided as a guide, customize as needed:

[In order to be eligible to participate in this study, an individual must meet all of the following criteria:

1. Provision of signed and dated informed consent form.
2. Stated willingness to comply with all study procedures and availability for the duration of the study.
3. Male or female, aged <specify range>.
4. In good general health as evidenced by medical history or diagnosed with <specify condition/disease> or exhibiting <specify clinical signs or symptoms or physical/oral examination findings>.
5. <Specify laboratory test> results between <specify range>.
6. Ability to take oral medication and be willing to adhere to the <study intervention> regimen.
7. For females of reproductive potential: use of highly effective contraception for at least 1 month prior to screening and agreement to use such a method during study participation and for an additional <specify duration> weeks after the end of <study intervention> administration.
8. For males of reproductive potential: use of condoms or other methods to ensure effective contraception with partner.
9. Agreement to adhere to Lifestyle Considerations (see section 5.3) throughout study duration]

## Exclusion Criteria

Example text provided as a guide, customize as needed (including adding a statement about equitable selection):

[An individual who meets any of the following criteria will be excluded from participation in this study:

1. Current use of < specify disallowed concomitant medications*>.*
2. Presence of <specific devices (e.g., cardiac pacemaker)>.
3. Pregnancy or lactation.
4. Known allergic reactions to components of the <study intervention>, <specify components/allergens>.
5. Febrile illness within <specify time frame*>*.
6. Treatment with another investigational drug or other intervention within *<*specify time frame*>.*
7. Current smoker or tobacco use within *<*specify timeframe*>.*
8. < Specify any condition(s) or diagnosis, both physical or psychological, or physical exam finding that precludes participation>].

## Lifestyle Considerations

Include content in this section if applicable, otherwise note as not applicable.

*Example text provided as a guide, customize as needed:*

[During this study, participants are asked to:

* Refrain from consumption of red wine, Seville oranges, grapefruit or grapefruit juice, [pomelos, exotic citrus fruits, grapefruit hybrids, or fruit juices] from [X days] before the start of <study intervention> until after the final dose.
* Abstain from caffeine- or xanthine-containing products (e.g., coffee, tea, cola drinks, and chocolate) for [x hours] before the start of each dosing session until after collection of the final pharmacokinetic (PK) and/or pharmacodynamic sample.
* Abstain from alcohol for 24 hours before the start of each dosing session until after collection of the final PK and/or pharmacodynamic sample.
* Participants who use tobacco products will be instructed that use of nicotine-containing products (including nicotine patches) will not be permitted while they are in the clinical unit.
* Abstain from strenuous exercise for [x hours] before each blood collection for clinical laboratory tests. Participants may participate in light recreational activities during studies (e.g., watching television, reading).
* Minimize interactions with household contacts who may be immunocompromised.]

# Screen Failures

Participants who provide consent to participate in the research who do not meet one or more criteria required for participation in the research during the screening procedures, are considered screen failures. Indicate how screen failures will be handled and provide conditions and criteria upon which re-screening is acceptable, when applicable.

# Study Intervention

*Describe the study intervention, any dosing of drugs, planned routes of drug administration.*

*Describe measures to minimize bias, including randomization and blinding.*

*Describe any concomitant therapy and rescue medications.*

# Study Assessments and Procedures

*List and describe all study procedures and evaluations to be done as part of the study to support the determination of efficacy, as per the primary and secondary objectives outlined in this protocol.*

*List and describe all study procedures and evaluations to be done as part of the study to monitor safety and support the understanding of the study intervention’s safety or that are done for other purposes (e.g., screening, eligibility, enrollment).*

*This section may include a list and description of the following procedures/evaluations, as applicable:*

* ***Physical examination*** *(e.g., height and weight, organ systems, motor or vision assessment, or other functional abilities). If appropriate, discuss what constitutes a targeted physical examination.*
* ***Radiographic or other imaging assessments****. State the specific imaging required and, as appropriate, provide description of what is needed to perform the specialized imaging. Details describing how to perform the imaging in a standard fashion and equipment specifications may be described in the study’s Manual of Procedures (MOP) or a separate Standard Operating Procedures (SOP).*
* ***Biological specimen collection and laboratory evaluations****. 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, specify which evaluations will be done by each laboratory. In addition, compliance with Clinical Laboratory Improvement Amendments (CLIA) of 1988 should be addressed. If such compliance is not required, a brief discussion should be included explaining why this is the case. In addition, discussion should include whether any laboratory tests (e.g., diagnostics) that will be used are being developed concurrently or are commercially available. Special instructions for the preparation, handling, storage, and shipment of specimens should be briefly explained in this section with detailed discussion in the study’s MOP.*
* ***Special assays or procedures required*** *(e.g., immunology assays, pharmacokinetic studies, flow cytometry assays, microarray, DNA sequencing). For research laboratory assays, include specific assays, estimated volume and type of specimen needed for each test. If more than one laboratory will be used, specify which assays will be done by each laboratory. Special instructions for the preparation, handling, storage, and shipment of specimens should be briefly explained in this section with detailed discussion in the study’s MOP.*
* ***Administration of questionnaires or other instruments*** *for patient-reported outcomes, such as a daily diary.*
* ***Procedures that will be completed during the study as part of regular standard of clinical care****.*

# Statistical Considerations

No text is to be entered in this section; rather it should be included under the relevant subheadings below.

## Statistical Hypotheses

*State the formal and testable null and alternative hypotheses for primary and key secondary endpoints, specifying the type of comparison (e.g., superiority, equivalence or non-inferiority, dose response) and time period for which each endpoint will be analyzed.*

* Primary Efficacy Endpoint(s):
* Secondary Efficacy Endpoint(s):

## Sample Size Determination

*Include number of participants to recruit, screen, and enroll to have adequate power to test the key hypotheses for the study. Provide all information needed to validate your calculations and judge the feasibility of enrolling and following the necessary number of participants.*

*Further, present calculations from a suitable range of assumptions to gauge the robustness of the proposed sample size.*

*Discuss whether the sample size provides sufficient power for addressing secondary endpoints or exploratory analyses (e.g., subgroup analyses or moderator analyses involving an interaction term).*

## Populations for Analyses

*Clearly identify and describe the analysis datasets (e.g., which participants will be included in each).*

## Statistical Analyses

*Include a description of the planned statistical methods, including any of the following as applicable to the study:*

* *General approach*
* *Analysis of the primary efficacy endpoints*
* *Analysis of secondary endpoints*
* *Safety analyses*
* *Baseline descriptive statistics*
* *Planned interim analyses*
* *Sub-group analyses*
* *Tabulation of individual participant data*
* *Exploratory analyses*

# Other Scientific or METHODOLOGY Considerations

*Provide any additional information related as needed or indicate this is not applicable.*

# Human Research Protections

No text is to be entered in this section; rather it should be included under the relevant subheadings below.

## Risk/Benefits Assessment

*No text is to be entered in this section; rather it should be included under the relevant subheadings below.*

*The following subsections should include a discussion of known risks and benefits, if any, to human participants.*

### Known Potential Risks

*Include a discussion of known potential risks from either clinical or nonclinical studies. If a package insert or device labeling from a licensed or approved product is available, it should be used as the primary source of risk information. If the product is investigational, the Investigational Brochure (IB) should be the primary source of the risk information. In addition, relevant published literature can also provide relevant risk information. If the risk profile cannot be described from the package insert, device labeling, or the IB, the risk information discussion will result from published literature and should be included and referenced appropriately.*

*Describe any physical, psychological, social, legal, economic, or any other risks to participants by participating in the study that the Principal Investigator (PI) foresees, addressing each of the following:*

* *Immediate risks*
* *Long-range risks*
* *If risk is related to proposed procedures included in the protocol, describe alternative procedures that have been considered and explain why alternative procedures are not included*

<Insert text>

### Known Potential Benefits

*Include a discussion of known potential benefits from either clinical or nonclinical studies. If a package insert or device labeling from a licensed or approved product is available, it should be used as the primary source of potential benefit information. If the product is investigational, the IB should be the primary source of the potential benefit information. In addition, relevant published literature can also provide potential relevant benefit information. If the potential benefit cannot be described from the package insert, device labeling, or the IB, the potential benefit information discussion will result from published literature and should be included and referenced appropriately.*

*Describe any physical, psychological, social, legal, or any other potential benefits to individual participants or society in general, as a result of participating in the study, addressing each of the following:*

* *Immediate potential benefits*
* *Long-range potential benefits*

*Note that payment to participants, whether as an inducement to participate or as compensation for time and inconvenience, is not considered a “benefit.” Provision of incidental care is also not to be considered a benefit.*

<Insert text>

### Assessment of Potential Risks and Benefits

Include an assessment of known potential risks and benefits, addressing each of the following:

* *Rationale for the necessity of exposing participants to risks and a summary of the ways that risks to participants were minimized in the study design*
* *Justification as to why the risks of participation in the study outweigh the value of the information to be gained*

<Insert text>

## Strategies for Recruitment and Retention

Identify general strategies for participant recruitment and retention. Consider inclusion of the information below either in this section:

* *Target study sample size by gender, race and ethnicity, and age; identify anticipated number to be screened including women and minorities in order to reach the target enrollment* (should be consistent with information contained inSample Size Determination)
* Anticipated accrual rate
* Anticipated number of sites and participants to be enrolled from the U.S. and outside the U.S.
* Source of participants *(e.g., inpatient hospital setting, outpatient clinics, student health service, or general public)*
* Recruitment venues
* How potential participants will be identified and approached
* Types of recruitment strategies planned (e.g. patient advocacy groups, national newspaper, local flyers; social media, specific names of where advertisements may be planned are not needed)
* If the study requires long-term participation, describe procedures that will be used to enhance participant retention (e.g., multiple methods for contacting participants, visit reminders, incentives for visit attendance).
* Specific strategies that will be used to recruit and retain historically under-represented populations. Include the number of women and minorities expected to be recruited, or provide justification on those rare occasions where women and/or minorities will not be recruited.

In addition, this section should address:

* If appropriate, include justification for inclusion of vulnerable participants and recruitment strategy. Vulnerable participants include, but are not limited to pregnant women, those who lack consent capacity, including the mentally ill, prisoners, cognitively impaired participants, children, and employee volunteers. Include safeguards for protecting vulnerable populations.
* Include procedures to minimize undue influence or coercion of students, residents, fellows, employees, or volunteers as research participants.
* *If participants will be compensated or provided any incentives* (e.g. vouchers, gift cards,) *for study participation, describe amount, form and timing of such compensation in relation to study activities (include financial and non-financial incentives). Describe who will receive incentives (if not the participant). For example, if minors, state whether the minor or the parent/guardian will receive the incentive. If incapacitated adults, state if payment will be provided to the participant or to a legally authorized representative or guardian.*

<Insert text>

## Informed Consent Process and Documentation

*Describe how informed consent will be administered. Describe any proposed waivers or alterations to informed consent. Describe any special circumstances regarding obtaining consent. Describe plans for obtaining consent from speakers of language other than English. Describe procedures for obtaining surrogate consent for those unable to consent on their own behalf. This section should be consistent with, Strategies for Recruitment and Retention when describing consent plans and special considerations for children or other vulnerable participants. Address re-consent processes for children who become adults or emancipated during a study.*

*Example text provided as a guide, customize as needed:*

[Informed consent is a process that is initiated prior to the individual’s agreeing to participate in the study and continues throughout the individual’s study participation. Consent forms will be Institutional Review Board (IRB)-approved and the participant will be asked to read and review the document. The investigator will explain the research study to the participant and answer any questions that may arise. A verbal explanation will be provided in terms suited to the participant’s comprehension of the purposes, procedures, and potential risks of the study and of their rights as research participants. Participants will have the opportunity to carefully review the written consent form and ask questions prior to signing. The participants should have the opportunity to discuss the study with their family or surrogates or think about it prior to agreeing to participate. The participant will sign the informed consent document prior to any procedures being done specifically for the study. Participants must be informed that participation is voluntary and that they may withdraw from the study at any time, without prejudice. A copy of the informed consent document will be given to the participants for their records. The informed consent process will be conducted and documented in the source document (including the date), and the form signed, before the participant undergoes any study-specific procedures. The rights and welfare of the participants will be protected by emphasizing to them that the quality of their medical care will not be adversely affected if they decline to participate in this study.]

<Insert text>

*Include statements describing whether other consent forms are required for the study, such as Pregnant Partner Authorization, SUNY RF Consent Addendum, etc.*

*Described how assent will be obtained and documented when applicable for research with children.*

## Confidentiality and Privacy

*This section will describe protections for maintaining confidentiality of participant data, including, but not limited to forms, records and samples and participant privacy.*

*Include procedures for maintaining participant confidentiality, privacy protections, any special data security requirements, and record retention requirements. Describe who would have access to records, including the investigator and other study staff, the clinical monitor, IND/IDE sponsor, representatives from the IRB, regulatory agencies, and representatives of the pharmaceutical company supplying product to be tested. In addition, consider inclusion of the following information:*

* Describe whether identifiers will be attached to data/samples, or whether data will be coded or unlinked.
* If unlinked or coded, and additional information (e.g., age, ethnicity, sex, diagnosis) is available, discuss whether this might make specific individuals or families identifiable.
* If research data/samples will be coded, describe how access to the “key” for the code will be limited. Include description of security measures (password-protected database, locked drawer, other). List names or positions of persons with access to the key.
* *Include a discussion of the circumstances in which data or samples will be shared with other researchers.*
* *Include a discussion of plans to publish participant’s family pedigrees, with a description of measures to minimize the chance of identifying specific families.*
* *Describe any situations in which personally identifiable information will be released to third parties.*
* *State who has access to records, data, and samples. Consider if monitors or auditors outside of study investigators will need access.*
* *Discuss any additional features to protect confidentiality (e.g., use of a certificate of confidentiality).*
* *Approaches to ensure privacy of study participants*

*For some studies, a Certificate of Confidentiality (CoC) may be necessary. Example text provided as a guide, customization will be required to address all aspects that should be included in this section:*

[Participant confidentiality and privacy is strictly held in trust by the participating investigators, their staff, and the sponsor(s) and their interventions. This confidentiality is extended to cover testing of biological samples and genetic tests in addition to the clinical information relating to participants. Therefore, the study protocol, documentation, data, and all other information generated will be held in strict confidence. No information concerning the study or the data will be released to any unauthorized third party without prior written approval of the sponsor.

All research activities will be conducted in as private a setting as possible.

The study monitor, other authorized representatives of the sponsor, representatives of the Institutional Review Board (IRB), regulatory agencies or pharmaceutical company supplying study product may inspect all documents and records required to be maintained by the investigator, including but not limited to, medical records (office, clinic, or hospital) and pharmacy records for the participants in this study. The clinical study site will permit access to such records.

The study participant’s contact information will be securely stored at each clinical site for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as dictated by the reviewing IRB, Institutional policies, or sponsor requirements.

Study participant research data, which is for purposes of statistical analysis and scientific reporting, will be transmitted to and stored at the <specify name of Data Coordinating Center or other location>. This will not include the participant’s contact or identifying information. Rather, individual participants and their research data will be identified by a unique study identification number. The study data entry and study management systems used by clinical sites and by <specify name of Data Coordinating Center or other location > research staff will be secured and password protected. At the end of the study, all study databases will be de-identified and archived at the <specify name of Data Coordinating Center or other location >.

Certificate of Confidentiality (if applicable)

To further protect the privacy of study participants, a Certificate of Confidentiality will be issued by the National Institutes of Health (NIH). This certificate protects identifiable research information from forced disclosure. It allows the investigator and others who have access to research records to refuse to disclose identifying information on research participation in any civil, criminal, administrative, legislative, or other proceeding, whether at the federal, state, or local level. By protecting researchers and institutions from being compelled to disclose information that would identify research participants, Certificates of Confidentiality help achieve the research objectives and promote participation in studies by helping assure confidentiality and privacy to participants.]

<Insert text>

## Data Security

Describe the data security protections for this study. Refer to the IRB guidance on Data Security for more details.

## Data and Specimen Sharing

Describe any data or specimen sharing. If future funding is anticipated from the NIH, be sure the plans are consistent with NIH requirements.

## Future Use of Stored Specimens or Data

*If intended specimens or residual specimens are retained after the study is complete, include the provisions for consent and the options that are available for the participant to agree to the future use of his/her specimens, images, audio or video recordings. Specify the location(s), if other than the clinical site, where specimens or other data will be maintained, how long specimens or other data will be stored, if the site's IRB will review future studies, and protections of confidentiality for any future studies with the stored specimens or data (e.g., specimens will be coded, bar-coded, de-identified, identifying information will be redacted from audio recording transcripts). Include a statement that genetic testing will or will not be performed.*

*See also Sections for Confidentiality and Privacy and Data Handling and Record Keeping, for further information on future use of study records.*

*Example text provided as a guide, customize as needed:*

[Data collected for this study will be analyzed and stored at the <specify name of Data Coordinating Center >. After the study is completed, the de-identified, archived data will be transmitted to and stored at the <specify name of Data Repository>, for use by other researchers including those outside of the study. Permission to transmit data to the <specify name of Data Repository> will be included in the informed consent.

With the participant’s approval and as approved by local Institutional Review Boards (IRBs), de-identified biological samples will be stored at the <specify name of Biosample Repository> with the same goal as the sharing of data with the <specify name of Data Repository>. These samples could be used to research the causes of <specify condition(s)>, its complications and other conditions for which individuals with < specify condition(s)> are at increased risk, and to improve treatment. The <specify name of Repository> will also be provided with a code-link that will allow linking the biological specimens with the phenotypic data from each participant, maintaining the blinding of the identity of the participant.

During the conduct of the study, an individual participant can choose to withdraw consent to have biological specimens stored for future research. However, withdrawal of consent with regard to biosample storage may not be possible after the study is completed.

When the study is completed, access to study data and/or samples will be provided through the <specify name of Repository>.]

<Insert text>

## Safety Oversight

*Appropriate safety oversight should be used for each study. This could include a Safety Monitoring Committee (SMC)[[1]](#footnote-2), Data Safety Monitoring Board (DSMB)[[2]](#footnote-3), Safety Assessment Committee[[3]](#footnote-4), and/or an Independent Safety Monitor (ISM)[[4]](#footnote-5). Independent oversight is an important component to ensure human research protections and data integrity and should be considered for each study. In this section, the type of safety oversight should be clearly identified along with any known responsibilities for the oversight of safety and data integrity in the study. Describe the composition of the SMC or DSMB, frequency of interim data review, final data analysis and method of reviews. A separate DSMB Charter will provide further detail of DSMB membership, responsibilities and administration of the DSMB.*

*Example text provided for a DSMB, as a guide, customize as needed:*

[Safety oversight will be under the direction of a Data and Safety Monitoring Board (DSMB) composed of individuals with the appropriate expertise, including <list expertise>. Members of the DSMB should be independent from the study conduct and free of conflict of interest, or measures should be in place to minimize perceived conflict of interest. The DSMB will meet at least semiannually to assess safety and efficacy data on each arm of the study. The DMSB will operate under the rules of an approved charter that will be written and reviewed at the organizational meeting of the DSMB. At this time, each data element that the DSMB needs to assess will be clearly defined. The DSMB will provide its input to <specify the study sponsor/National Institutes of Health staff/other>.]

<Insert text>

## Safety Assessments

*List and describe all study procedures and evaluations to be done as part of the study to monitor safety and support the understanding of the study intervention’s safety or that are done for other purposes (e.g., screening, eligibility, enrollment).*

*Discuss the sequence of events that should occur during the screening process and any decision points regarding participant eligibility. Include the time frame prior to enrollment within which screening procedures/ evaluations must be performed (e.g., within 28 days prior to enrollment). If a separate screening protocol is developed, describe how the screening protocol will be used to identify participants for this study. In addition, discuss any special conditions that must be achieved during the enrollment and/or initial administration of study intervention.*

*This section may include a list and description of the following procedures/evaluations, as applicable:*

* ***Physical examination*** *(e.g., height and weight, organ systems, motor or vision assessment, or other functional abilities). If appropriate, discuss what constitutes a targeted physical examination.*
* ***Vital signs*** *(e.g., temperature, pulse, respirations, blood pressure). Carefully consider which vital signs (if any) should be measured to ensure that only essential data are collected. Include any specific instructions with respect to the collection and interpretation of vital signs.*
* ***Electrocardiograms (EKGs)****: specify if the EKG is for screening purposes only. Include any specific instructions for the collection and interpretation of the EKG (e.g., time points relative to dosing with study intervention or other evaluations). If EKGs will be analyzed at a central laboratory, instructions for the collection (e.g., equipment), transmission and archiving of the EKG data should be summarized in this protocol, and further outlined in the MOP. If the EKG will be read locally, indicate how these will be handled and in what format (e.g., digital or paper), as well as instructions with respect to local review.*
* ***Radiographic or other imaging assessments.*** *State the specific imaging required and, as appropriate, provide description of what is needed to perform the specialized imaging. Details describing how to perform the imaging in a standard fashion and equipment specifications may be described in the study’s MOP or a separate SOP.*
* ***Biological specimen collection and laboratory evaluations****. 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, specify which evaluations will be done by each laboratory. In addition, compliance with Clinical Laboratory Improvement Amendments (CLIA) of 1988 should be addressed. If such compliance is not required, a brief discussion should be included explaining why this is the case. In addition, discussion should include whether any laboratory tests (e.g., diagnostics) that will be used are being developed concurrently or are commercially available. Special instructions for the preparation, handling, storage, and shipment of specimens may be briefly explained in this section; detailed discussion should be included in the study’s MOP.*
* ***Special assays or procedures required*** *(e.g., immunology assays, pharmacokinetic studies, flow cytometry assays, microarray, DNA sequencing). For research laboratory assays, include specific assays, estimated volume and type of specimen needed for each test. If more than one laboratory will be used, specify which assays will be done by each laboratory. Special instructions for the preparation, handling, storage, and shipment of specimens should be briefly explained in this section with detailed discussion in the study’s MOP.*
* ***Counseling procedures, including any dietary or activity considerations*** *that need to be adhered to during study participation.*
* ***Assessment of study intervention adherence*** *or see Study Intervention Compliance, section 6.4*
* ***Administration of questionnaires or other instruments*** *for patient-reported outcomes, such as a daily diary.*
* ***Assessment of adverse events.*** *Describe provisions for follow-up of ongoing AEs/SAEs.*

*Include in this section a discussion of the results of any study specific procedures that will be provided to participant (e.g., radiographic or other imaging or laboratory evaluations).*

*As previously noted, if an individual’s medical chart or results of diagnostic tests performed as part of an individual’s regular medical care are going to be used for screening or as a part of collection of study data, Health Insurance Portability and Accountability Act (HIPAA) rules, other relevant federal or state laws, and local institutional requirements should be followed, as applicable. If this is the case, this section should note which information is to be obtained through review of existing data.*

<Insert text>

## Clinical Monitoring

*Site monitoring is conducted to ensure that the rights and well-being of study participants are protected, that the reported study data are accurate, complete, and verifiable, and that the conduct of the study is in compliance with the currently approved protocol/amendment(s), with ICH GCP, and with applicable regulatory requirement(s).*

*This section should give a general description of how monitoring of the conduct and progress of the clinical investigation will be conducted (i.e., who will conduct the monitoring, the type, frequency, and extent of monitoring, who will be provided reports of monitoring, if independent audits of the monitoring will be conducted). This section may refer to a separate detailed clinical monitoring plan.*

*A separate clinical monitoring plan (CMP) should describe in detail who will conduct the monitoring, at what frequency monitoring will be done, at what level of detail monitoring will be performed, and the distribution of monitoring reports.* *A CMP ordinarily should focus on preventing or mitigating important and likely risks, identified by a risk assessment, to critical data and processes. The types (e.g., on-site, centralized), frequency (e.g., early, for initial assessment and training versus throughout the study), and extent (e.g., comprehensive (100% data verification) versus targeted or random review of certain data (less than 100% data verification)) of monitoring activities will depend on a range of factors, considered during the risk assessment, including the complexity of the study design, types of study endpoints, clinical complexity of the study population, geography, relative experience of the PI and of the sponsor with the PI, electronic data capture, relative safety of the study intervention, stage of the study, and quantity of data.*

*If a separate CMP is not used, include all the details noted above in this section of the protocol.*

*Example text when a* ***separate CMP is being used is provided as a guide, customize as needed****:*

[Clinical site monitoring is conducted to ensure that the rights and well-being of study participants are protected, that the reported study data are accurate, complete, and verifiable, and that the conduct of the study is in compliance with the currently approved protocol/amendment(s), with International Conference on Harmonisation Good Clinical Practice (ICH GCP), and with applicable regulatory requirement(s).

* Monitoring for this study will be performed by <insert text>.
* *<*Insert brief description of type of monitoring (e.g., on-site, centralized), frequency (e.g., early, for initial assessment and training versus throughout the study), and extent (e.g., comprehensive (100% data verification) versus targeted or random review of certain data (less than 100% data verification or targeted data verification of endpoint, safety and other key data variables)>.
* <Insert text> will be provided copies of monitoring reports within <x> days of visit.
* Details of clinical site monitoring are documented in a Clinical Monitoring Plan (CMP). The CMP describes in detail who will conduct the monitoring, at what frequency monitoring will be done, at what level of detail monitoring will be performed, and the distribution of monitoring reports.
* Independent audits <will/will not> be conducted by <insert text> to ensure monitoring practices are performed consistently across all participating sites and that monitors are following the CMP.]

OR

*Example text when a* ***separate CMP is not being used is provided as a guide, customize as needed****:*

[Clinical site monitoring is conducted to ensure that the rights and well-being of study participants are protected, that the reported study data are accurate, complete, and verifiable, and that the conduct of the study is in compliance with the currently approved protocol/amendment(s), with International Conference on Harmonisation Good Clinical Practice (ICH GCP), and with applicable regulatory requirement(s).

* <Insert detailed description of who will conduct the monitoring, the type of monitoring (e.g., on-site, centralized), frequency (e.g., early, for initial assessment and training versus throughout the study), and extent (e.g., comprehensive (100% data verification) versus targeted or random review of certain data (less than 100% data verification or targeted data verification of endpoint, safety and other key data variables)), and the distribution of monitoring reports>
* Independent audits <will/will not> be conducted by <insert text> to ensure monitoring practices are performed consistently across all participating sites.]

<Insert text>

## Quality Assurance and Quality Control

*This section will briefly describe the plans for quality management, the system for assessing the quality of processes within a system. Quality management encompasses quality assurance (QA)[[5]](#footnote-6) and quality control (QC)[[6]](#footnote-7).*

*Each site, both clinical and laboratory, should have SOPs for quality management that describe:*

* *How data and biological specimens (when applicable) will be evaluated for compliance with the protocol, ethical standards, regulatory compliance, and accuracy in relation to source documents.*
* *The documents to be reviewed (e.g., CRFs, clinic notes, product accountability records, specimen tracking logs, questionnaires, audio or video recordings), who is responsible, and the frequency for reviews.*
* *Who will be responsible for addressing QA issues (e.g., correcting procedures that are not in compliance with protocol) and QC issues (e.g., correcting errors in data entry).*
* *Staff training methods and how such training will be tracked.*
* *If applicable, calibration exercises conducted prior to and during the study to train examiners and maintain acceptable intra- and inter-examiner agreement.*

*Regular monitoring and an independent audit, if conducted, must be performed according to ICH GCP. See also* ***Section 10.1.7, Clinical Monitoring****.*

*Example text provided as a guide, customize as needed:*

[Each clinical site will perform internal quality management of study conduct, data and biological specimen collection, documentation and completion. An individualized quality management plan will be developed to describe a site’s quality management.]

Quality control (QC) procedures will be implemented beginning with the data entry system and data QC checks that will be run on the database will be generated. Any missing data or data anomalies will be communicated to the site(s) for clarification/resolution.

Following written Standard Operating Procedures (SOPs), the monitors will verify that the research is conducted and data are generated and biological specimens are collected, documented (recorded), and reported in compliance with the protocol, International Conference on Harmonisation Good Clinical Practice (ICH GCP), and applicable regulatory requirements (e.g., Good Laboratory Practices (GLP), Good Manufacturing Practices (GMP)).

The investigational site will provide direct access to all study related sites, source data/documents, and reports for the purpose of monitoring and auditing by the sponsor, and inspection by local and regulatory authorities.]

<Insert text>

## Data Handling and Record Keeping

*No text is to be entered in this section; rather it should be included under the relevant subheadings below.*

*The following subsections should include a description of the data handling and record keeping for the conduct of the researchl.*

### Data Collection and Management Responsibilities

*Provide details regarding the type(s) of data capture that will be used for the study and any relevant data standards or common data elements that are being utilized as a part of the study. Specify whether it will be paper or electronic, distributed or central, batched or ongoing processing, and any related requirements.*

*Source data are all information, original records of clinical findings, observations, or other activities in the research necessary for the reconstruction and evaluation of the study. Electronic source data are data initially recorded in electronic form. Examples of source data include, but are not limited to, hospital records, clinical and office charts, laboratory notes, memoranda, participants’ memory aids or evaluation checklists, pharmacy dispensing records, audio recordings of counseling sessions, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate and complete, microfiches, photographic negatives, microfilm or magnetic media, x-rays, and participant files and records kept at the pharmacy, at the laboratories, and medico-technical departments involved in the research.*

*Describe responsibilities for data handling and record keeping as they specifically relate to the IND/IDE sponsor (if applicable), the award site, clinical site(s), laboratory(ies), and Data Coordinating Center. Information should include the role in data collection, review of data, study materials, and reports, as well as retention of source documents, files, and records. Describe coding dictionaries to be used and reconciliation processes (if applicable).*

*If data are to be generated in one location and transferred to another group, describe the responsibilities of each party.*

*Example text provided as a guide, customize as needed:*

[Data collection is the responsibility of the research staff at the site under the supervision of the site investigator. The investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported.

All source documents should be completed in a neat, legible manner to ensure accurate interpretation of data.

Hardcopies of the study visit worksheets will be provided for use as source document worksheets for recording data for each participant enrolled in the study. Data recorded in the electronic case report form (eCRF) derived from source documents should be consistent with the data recorded on the source documents.

Clinical data (including adverse events (AEs), concomitant medications, and expected adverse reactions data) and clinical laboratory data will be entered into <specify name of data capture system>, a 21 CFR Part 11-compliant data capture system provided by the <specify Data Coordinating Center>. The data system includes password protection and internal quality checks, such as automatic range checks, to identify data that appear inconsistent, incomplete, or inaccurate. Clinical data will be entered directly from the source documents.]

<Insert text>

### Study Records Retention

*Specify the length of time for the investigator to maintain all records pertaining to this study. The investigator should use the most conservative rule for document retention – i.e., retention should follow the rule that has the longest period.*

*Indicate whether permission is required (and from whom) prior to destruction of records. If under an IND/IDE, records should not be destroyed without the IND/IDE sponsor’s agreement. Pharmaceutical companies who supply unapproved products should be consulted.*

*Study intervention records may be described here if not addressed elsewhere in the protocol.*

*Downstate faculty should consult with FDA regulations, State Retention Policies, Downstate guidance and their departmental policies for additional information. Research records and specimens must be securely stored in accordance with the research procedures,*

*IRB approved documents, and Downstate policies. Research records and specimens may not be destroyed unless in conformity with Downstate policies, and when applicable other requirements of sponsors or external research sites. In general, research retention periods are described below, but may differ depending on the details of the study. Some of the minimum retention periods are provided below:*

* *Records relating to a specific research activity, including research records collected by investigators must be maintained for at least three years after completion of the research. This minimum retention period applies whether or not any research participants were enrolled in the study.*
* *If the research is FDA regulated, records should be retained for at least two years after approval of the investigational agent by FDA; if it is not approved, records should be retained at least two years after the study is terminated and FDA is notified. However, the FDA requirements for record retention differ and the individual pharmaceutical or device manufacturing companies sponsoring the research may have their own policies on record retention to which the investigators may be subject. Consult with the sponsor before destroying any records.*
* *Research participants' signed HIPAA Research Authorization forms must be kept for a minimum of six years after such authorization last was in effect.*
* *Records concerning controlled substance research must be maintained for five years after completion of the study.*
* *When research takes place an external site, the PI must follow the longer specified retention period of either the external site or Downstate.*

*Example text provided as a guide, customize as needed:*

[Study documents should be retained for a minimum of 10 years after the study closure or after the last approval of an FDA marketing application. No records will be destroyed without a Downstate Records Management Certificate of Destruction.]

<Insert text>

## Discontinuation of the Study or a Study Participant

### Discontinuation of Study Intervention

Describe the criteria for discontinuing the study intervention (e.g., halting rules), including any monitoring test(s) and associated clinical decision point(s). Include reasons for temporary discontinuation of the study intervention (e.g., type and quantity of adverse events), clearly stating the length of time, if applicable, and describe the data to be collected at the time of study intervention discontinuation and approaches for restarting administration of or rechallenging with study intervention.

Describe efforts that will be made to continue follow-up of participants who discontinue the study intervention, but remain in the study for follow-up, especially for safety and efficacy study endpoints (if applicable). Reasonable efforts must be made to undertake protocol-specified safety follow-up procedures to capture adverse events (AE), serious adverse events (SAE), and unanticipated problems (UPs).

Example text provided as a guide, customize as needed:

[Discontinuation from <study intervention> does not mean discontinuation from the study, and remaining study procedures should be completed as indicated by the study protocol. If a clinically significant finding is identified (including, but not limited to changes from baseline) after enrollment, the investigator or qualified designee will determine if any change in participant management is needed. Any new clinically relevant finding will be reported as an adverse event (AE).

The data to be collected at the time of study intervention discontinuation will include the following:

* <Describe the procedures and data to be collected, as well as any follow-up evaluations>]

<Insert text>

### Participant Discontinuation/Withdrawal from the Study

Provide a list of reasons participation may be discontinued. It may be appropriate to provide distinct discontinuation criteria for participants and cohorts. If so, both sets of criteria should be listed separately and the distinction between the two must be stated clearly. Also, note that participants may withdraw voluntarily from the study or discontinue the study intervention at any time. But, investigators should seek to minimize participant discontinuation/withdrawal from study except for safety reasons.

In studies of implantable devices, a discussion should be included of any pertinent information that will be provided to withdrawn or discontinued participants (e.g., whether and how the device can be removed, how to replace batteries, how to obtain replacement parts, who to contact). In addition, it is important to capture the reason for withdrawal or discontinuation, as this may impact inclusion of participant data in the analysis of results.

This section should include a discussion of replacement of participants who withdraw or discontinue early, if replacement is allowed. This section should not include a discussion of how these participants will be handled in the analysis of study data. This should be captured in the Section for Statistical Analyses.

Example text provided as a guide, customize as needed:

[Participants are free to withdraw from participation in the study at any time upon request.

An investigator may discontinue or withdraw a participant from the study for the following reasons:

* Pregnancy
* Significant study intervention non-compliance
* If any clinical adverse event (AE), laboratory abnormality, or other medical condition or situation occurs such that continued participation in the study would not be in the best interest of the participant
* Disease progression which requires discontinuation of the study intervention
* If the participant meets an exclusion criterion (either newly developed or not previously recognized) that precludes further study participation
* Participant unable to receive <study intervention> for [x] days/weeks.]

The reason for participant discontinuation or withdrawal from the study will be recorded on the <specify> Case Report Form (CRF). Participants who sign the informed consent form and are randomized but do not receive the study intervention may be replaced. Participants who sign the informed consent form, and are randomized and receive the study intervention, and subsequently withdraw, or are withdrawn or discontinued from the study, <will> *or* <will not> be replaced.]

<Insert text>

### Lost to Follow-Up

The protocol should describe the nature and duration of study follow-up. Validity of the study is a potential issue when participants are lost to follow-up, as information that is important to the endpoint evaluation is then lost. Participants are considered lost to follow-up when they stop reporting to scheduled study visits and cannot be reached to complete all protocol-required study procedures. Describe the plans to minimize loss to follow-up and missing data.

Example text provided as a guide, customize as needed:

[A participant will be considered lost to follow-up if he or she fails to return for <specify number of visits> scheduled visits and is unable to be contacted by the study site staff.

The following actions must be taken if a participant fails to return to the clinic for a required study visit:

* The site will attempt to contact the participant and reschedule the missed visit <specify time frame> and counsel the participant on the importance of maintaining the assigned visit schedule and ascertain if the participant wishes to and/or should continue in the study.
* Before a participant is deemed lost to follow-up, the investigator or designee will make every effort to regain contact with the participant (where possible, 3 telephone calls and, if necessary, a certified letter to the participant’s last known mailing address or local equivalent methods). These contact attempts should be documented in the participant’s medical record or study file.
* Should the participant continue to be unreachable, he or she will be considered to have withdrawn from the study with a primary reason of lost to follow-up.]

<Insert text>

### Discontinuation and Closure

*List possible reasons for termination or temporary suspension of the study (e.g., study closure based on PI decision, sponsor/funder decision, regulatory or other oversight bodies; review of serious, unexpected, and related AEs; noncompliance; futility). For any study that is prematurely terminated or temporarily suspended, the PI will promptly inform study participants, the IRB, and sponsor and provide the reason(s) for the termination or temporary suspension.*

*When a study is prematurely terminated, refer to the previous applicable sections**for handling of enrolled study participants.*

*Example text provided as a guide, customize as needed:*

[This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to <study participants, investigator, the Investigational New Drug (IND) or Investigational Device Exemption (IDE) sponsor and regulatory authorities>. If the study is prematurely terminated or suspended, the Principal Investigator (PI) will promptly inform study participants, the Institutional Review Board (IRB), and sponsor and will provide the reason(s) for the termination or suspension. Study participants will be contacted, as applicable, and be informed of changes to study visit schedule.

Circumstances that may warrant termination or suspension include, but are not limited to:

* Determination of unexpected, significant, or unacceptable risk to participants
* Demonstration of efficacy that would warrant stopping
* Insufficient compliance to protocol requirements
* Data that are not sufficiently complete and/or evaluable
* Determination that the primary endpoint has been met
* Determination of futility

Study may resume once concerns about safety, protocol compliance, and data quality are addressed, and satisfy the sponsor, IRB and/or Food and Drug Administration (FDA).]

<Insert text>

## Reportable Events

As required by Policy IRB-01, all reportable events will be reported to the IRB within the specified deadlines.

## Publication Plans

*The publication and authorship policies should be described in this section. For example, for a study with multiple investigators, this section might state that an Executive Committee will be responsible for developing publication procedures and resolving authorship issues.*

<Insert text>

## Conflict of Interests

*This section should include a description of how the study will manage actual or perceived conflicts of interest. The PI is responsible for stating whether or not he or she has a conflict of interest with respect to the research study. All conflicts should be disclosed to the IRB and sponsor.*

*Example text* *provided as a guide, customize as needed:*

[The independence of this study from any actual or perceived influence, such as by the pharmaceutical industry, is critical. Therefore, any actual conflict of interest of persons who have a role in the design, conduct, analysis, publication, or any aspect of this study will be disclosed and managed. Furthermore, persons who have a perceived conflict of interest will be required to have such conflicts managed in a way that is appropriate to their participation in the design and conduct of this study.

<Insert text>

## Additional Human Research Considerations

*This section should include a description of any additional considerations not currently covered in this protocol template, such as particular institutional or IRB-related requirements.*

<Insert text>

# Protocol Amendment History

*The table below is intended to capture changes of IRB-approved versions of the protocol, including a description of the change and rationale. A Summary of Changes table for the current amendment is located in the Protocol Title Page.*

|  |  |  |  |
| --- | --- | --- | --- |
| **Version** | **Date** | **Description of Change**  | **Brief Rationale** |
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# References/Biography

*Include a list of relevant literature and citations for all publications referenced in the text of the protocol. Use a consistent, standard, modern format, which might be dependent upon the required format for the anticipated journal for publication (e.g., N Engl J Med, JAMA, etc.). The preferred format is International Committee of Medical Journal Editors (ICMJE). Include citations to product information such as manufacturer’s IB, package insert, and device labeling.*

1. A Safety Monitoring Committee (SMC) is a small group of experts with at least two members who are independent of the protocol who review data from a particular study. Generally, independent investigators and biostatisticians should be included. The primary responsibility of the SMC is to monitor participant safety. The SMC considers study-specific data as well as relevant background information about the disease, intervention, and target population under study. [↑](#footnote-ref-2)
2. A Data and Safety Monitoring Board (DSMB) is an independent group of experts that advises funding IC(s) and the study investigators. The members of the DSMB provide their expertise and recommendations. The primary responsibilities of the DSMB are to 1) periodically review and evaluate the accumulated study data for participant safety, study conduct and progress, and, when appropriate, efficacy, and 2) make recommendations concerning the continuation, modification, or termination of the study. The DSMB considers study-specific data as well as relevant background knowledge about the disease, intervention, or target population under study. [↑](#footnote-ref-3)
3. As noted on page 4 of the FDA Draft Guidance for Industry: Safety Assessment for IND Safety Reporting, “A group of individuals chosen by the sponsor to review safety information in a development program (i.e., across studys, INDs, and other sources) for IND safety reporting purposes...The safety assessment committee should oversee the evolving safety profile of the investigational drug by evaluating, at appropriate intervals, the cumulative serious adverse events from all of the studys in the development program, as well as other available important safety information (e.g., findings from epidemiological studies and from animal or in vitro testing) and performing unblended comparisons of event rates in investigational and control groups, as needed, so the sponsor may meet its obligations under § 312.32(b) and (c). The safety assessment committee’s primary role should be to review important safety information on a regular basis, with additional reviews as needed, and make a recommendation to the sponsor to help the sponsor determine whether an event or group of events meets the criteria for IND safety reporting. The safety assessment committee, possibly together with other parties (e.g., steering committees, data monitoring committees [DMCs]), can also participate in decisions about whether the conduct of the study should be revised (e.g., change ineligibility criteria, revision of informed consent). [↑](#footnote-ref-4)
4. An Independent Safety Monitor (ISM) is a physician, nurse, or other individual with relevant expertise whose primary responsibility is to provide independent safety monitoring in a timely fashion. This is accomplished by review of adverse events, immediately after they occur or are reported, with follow-up through resolution. The ISM evaluates individual and cumulative participant data when making recommendations regarding the safe continuation of the study. [↑](#footnote-ref-5)
5. All those planned and systematic actions that are established to ensure that the study is performed and the data are generated, documented (recorded), and reported in compliance with ICH GCP and the applicable regulatory requirement(s) (ICH E6 Section 1.46). [↑](#footnote-ref-6)
6. The operational techniques and activities undertaken within the quality assurance system to verify that the requirements for quality of the study-related activities have been fulfilled (ICH E6 Section 1.47). [↑](#footnote-ref-7)