**Protocol Template for Interventional Clinical Trial Protocol**

**Guidance for Using this Template:**

This protocol template is designed to help research teams develop a clinical trial protocol that includes an investigational intervention. The template may be used in the development of any NYU investigator initiated clinical trial (e.g. Pilot study, Phase I, II, III, IV) involving any sort of interventional investigational product (e.g. drug, device, biologic, vaccine, procedural and/or behavioral etc.). This may be used for a study in which an IND/IDE is involved but its use is not limited to studies involving an IND/IDE (e.g. studies in which there is an IND exemption or clinical trials where an approved investigational product is being used, etc.). Where language specific to a particular type of trial is used this is clearly indicated.

**Directions for Using this Template:**

|  |
| --- |
| * The Study Intervention section (Section 6) of this template includes sub-sections for:   + Study Agent, such as an investigational or approved drug or device (Sections 6.1 - 6.2);   + Behavioral Intervention (Section 6.3) and;   + Procedural Intervention (Section 6.4).   Choose the appropriate section that matches the type of study intervention planned and delete the other sections.   * In the template, instructions for each section are included in *blue italics*. As you complete a section, delete the instructions. * Where sample text is included in standard font, you may include it in your protocol as written or modify as needed for your study. Sample text is set off by the introductory instructional text *{Begin sample text}* and closing instructional text *{End sample text}*. Remove this instructional text if you use the sample text. * Required protocol text is set off by the introductory instructional text *{Begin required text}* and the closing instructional text *{End required text}*. Remove this instructional text while maintaining the required text in the document. * Text enclosed with < > is a placeholder for a specific detail (e.g., <protocol title>); replace as appropriate. * It is not necessary to include text under a major numbered heading (e.g., 1, 2) that is immediately followed by numbered subheadings, (e.g., 2.1, 2.2). That is because certain numbered headings are used only for organizational purposes. Text should be entered under all numbered subheadings. See <Insert text> notations for guidance. * Use the formatting and text styles which already exist in the document, rather than creating your own. * Protocol version control: Primary author controls version number and date, which appear on title page and header of each protocol page. Use 0.1, 0.2, 0.3, etc., for early drafts of the protocol. Once version has been finalized, re-label last draft version 0.x as final version 1.0 for IRB submission. When drafting an amendment to an IRB-approved protocol, use the protocol whole version number with draft numbers in the decimal. For example, version 2.1 is the first draft of an amendment to protocol version 2.0. When the final draft of this amended protocol is ready for IRB review, change the version number to Version 3.0 before IRB submission. * Versioning includes both a version number and version date. When the version number and date change, be sure to update them in the header of each section of the protocol. * Do not change the protocol template footer. * Remove this Tool Summary Sheet before use. |

**Tool Revision History:**

|  |  |  |
| --- | --- | --- |
| **Version Number** | **Version Date** | **Summary of Revisions Made** |
| 1.0 | 28 April 2017 | Original version |
| 1.1 | 03 January 2018 | Section 13.4 posting of a consent on Federal website |
| 1.2 | 18 July 2022 | Section 2.4.2 added, 14.1.1 added |
| 1.3 | 06 January 2023 | Section 2.4.1 revised  Section 5.3.1 – 5.3.5 added |

**<tITLE OF THE PROTOCOL>**

*[Include* ***phase*** *(e.g. pilot proof of concept study, phase I, phase II, etc.),* ***design*** *(e.g. randomized, double blind, placebo controlled, etc.), if the study* ***is multi-center****, the* ***investigational agent (drug, device, biologic, vaccine, procedural and/or behavioral etc.****, and* ***target disease(s****)]*

Example title:

A phase II, randomized, double-blind, placebo-controlled, multi-center study of the effects of XXXX on infarct size in participants with diabetes mellitus presenting with acute myocardial infarction.

|  |  |
| --- | --- |
| **Principal Investigator:** | *Insert the Name of the Sponsor-Investigator*  *Insert Department Name*  *Insert Address*  *Insert Email Address*  *Insert Phone Number* |
| **Additional Investigators:**  *[PI at additional sites, etc. as applicable]* | *Insert the Name of the Investigator*  *Insert Department Name*  *Insert Address*  *Insert Email Address*  *Insert Phone Number* |
| **NYULMC Study Number:** | *Insert Research Navigator Study Number (e.g. 17-01234)* |
| **Funding Sponsor:** *[If applicable]* | *Insert the Name of Primary Funding Sponsor*  *Insert Address*  *Insert Phone Number* |
| **IND/IDE Number:** *[If applicable]* | *Insert IND Number or IDE number if applicable. This number will be assigned by the FDA. If not available write pending.* |
| [**Regulatory Sponsor:**](https://somapps.med.upenn.edu/pennmanual/secure/pm/responsibilities-qualifications-indide-sponsors) *[If applicable]* | *Insert the Name of the entity/individual who holds the IND/IDE*  *Insert Department Name*  *Insert Address*  *Insert Email Address*  *Insert Phone Number* |
| **Study Product:** | *Insert Study product name – Generic, followed by marketed name if applicable* |
| **Study Product Provider:** *[If applicable]* | *Insert the study product provider (e.g. NIH, or company)* |
| **ClinicalTrials.gov Number** | *Include the National Clinical Trial (NCT) Number assigned once the trial is registered on the ClinicalTrials.gov.* |

**Initial version:** [date]

**Amended:** [date]

**Amended:** [date]

# Statement of Compliance

This study will be conducted in accordance with the Code of Federal Regulations on the Protection of Human Subjects (45 CFR Part 46), 21 CFR Parts 50, 56, 312, and 812 as applicable, any other applicable US government research regulations, and institutional research policies and procedures. The International Conference on Harmonisation (“ICH”) Guideline for Good Clinical Practice (“GCP”) (sometimes referred to as “ICH-GCP” or “E6”) will be applied only to the extent that it is compatible with FDA and DHHS regulations. The Principal Investigator will assure that no deviation from, or changes to the protocol will take place without prior agreement from the sponsor and documented approval from the Institutional Review Board (IRB), except where necessary to eliminate an immediate hazard(s) to the trial participants. All personnel involved in the conduct of this study have completed Human Subjects Protection Training.

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*Be sure to update the table of contents when you are finished creating your protocol. You can do this in Microsoft Word by going to the References tab and clicking on “Update Table” in the Table of Contents section.*

# List of Abbreviations

*Create list of any abbreviations that are specific or pertinent to your protocol with their corresponding definitions. Add all disease or study-specific abbreviations/acronyms in this section. Modify this list as needed for your particular study and remove abbreviations that are not used in the document.*

|  |  |
| --- | --- |
| AE | Adverse Event/Adverse Experience |
| CFR | Code of Federal Regulations |
| CRF | Case Report Form |
| CSOC | Clinical Study Oversight Committee |
| DCC | Data Coordinating Center |
| DHHS | Department of Health and Human Services |
| DSMB | Data and Safety Monitoring Board |
| FFR | Federal Financial Report |
| FWA | Federalwide Assurance |
| GCP | Good Clinical Practice |
| HIPAA | Health Insurance Portability and Accountability Act |
| ICF | Informed Consent Form |
| ICH | International Conference on Harmonisation |
| IRB | Institutional Review Board |
| ISM | Independent Safety Monitor |
| MOP | Manual of Procedures |
| N | Number (typically refers to participants) |
| NIH | National Institutes of Health |
| OHRP | Office for Human Research Protections |
| OHSR | Office of Human Subjects Research |
| PI | Principal Investigator |
| QA | Quality Assurance |
| QC | Quality Control |
| SAE | Serious Adverse Event/Serious Adverse Experience |
| SOP | Standard Operating Procedure |
| US | United States |

# Protocol Summary

|  |  |
| --- | --- |
| Title | *Full title of protocol* |
| Short Title | *Shortened title, if one is typically used by you or your Center/Dept.* |
| Brief Summary | *Provide a brief overview of the study design, including sample size, study groups, schedule of interventions, schedule for specimen or data collection, and analyses to be performed.*  *This summary should be only a few sentences in length. A detailed schematic describing all visits and assessments (schedule of events) should be included in the Schematic of Study Design.* |
| Phase | *Clinical study phase (e.g. Phase 1, 2, 3 or 4)* |
| Objectives | *Insert objectives that are the same as the objectives contained in the body of the protocol. Include the primary objective and important secondary objectives.* |
| Methodology | *Design attributes such as single blind, double blind or open label; Randomized, placebo or active placebo control; cross-over design, etc.* |
| Endpoint | *Insert endpoints that are the same as the endpoints contained in the body of the protocol. Include the primary endpoint and important secondary endpoints.* |
| Study Duration | *Estimated time from when the study opens to enrollment until completion of data analysis.* |
| Participant Duration | *Time it will take for each individual participant to complete all participant visits.* |
| Duration of IP administration | *Total duration of investigational product administration (including any open-label lead-in, if applicable).* |
| Population | *Specify sample size, gender, age, demographic group, general health status, and geographic location.* |
| Study Sites | *Insert a list of participating sites. If greater than 3 sites, indicate number of sites and refer to Section 1, Key Roles for a complete list of participating sites.* |
| Number of participants | *Number of participants projected for the entire study (e.g. 100 participants expected to be enrolled across 2 sites)* |
| Description of Study Agent/Procedure | *Describe the agent/intervention. If agent/intervention is a drug or biologic, include dose and route of administration. For other agents (e.g. device, procedural), provide brief description.* |
| Reference Therapy | *Note if there is a standard reference therapy against which the investigational product is being compared, or if the reference is a placebo* |
| Key Procedures | *Procedures that are required for the study (e.g. harvesting of tumor, vaccine, tumor biopsy and blood draws)* |
| Statistical Analysis | *A very brief description of the main elements of the statistical methodology to be used in the study. Limit this section to discussion of the analysis of the primary endpoint and perhaps the main secondary endpoint.* |

# Schematic of Study Design

*This section should include a diagram that provides a quick “snapshot” of the study and ideally be limited to one page. Below are examples of schematics that show the level of detail needed to convey an overview of study design. Depending on the nature of your study, one example may be more appropriate than another. Regardless, the examples included here are intended to guide the development of a schematic that is appropriate to the planned study design and will need to be customized for the protocol. If you utilize Example 1, complete the tables with study-specific information and adapt the table(s) to illustrate your study design. If you utilize Example 2 or 3, revise with study-specific information and adapt the diagram to illustrate your study design (e.g., changing method of assignment to study group, adding study arms, visits, etc.). The time point(s) indicated in the schematic should correspond to the time point(s) in Section 7.3, Study Schedule, e.g., Visit 1, Day 0; Visit 2, Day 30 ± 7; etc.*

***Example #1: Table format*** *(e.g., dose escalation)*

|  |  |  |  |
| --- | --- | --- | --- |
| Cohort A | ARM 1 | Sample Size | Intervention 1 |
| Cohort A | ARM 2 | Sample Size | Intervention 2 |

*Include instructions for progressing to next phase (if applicable):*

*Interim Analysis*

|  |  |  |  |
| --- | --- | --- | --- |
| Cohort B | ARM 1 | Sample Size | Intervention 1 |
| Cohort B | ARM 2 | Sample Size | Intervention 2 |

***Example #2: Flow diagram*** *(e.g., randomized controlled trial)*

Total N: Obtain informed consent. Screen potential subjects by inclusion and exclusion criteria; obtain history, document.

Randomize

Perform baseline assessments. <list specimens to be collected, examinations or imaging or laboratory assays to be performed, questionnaires to be completed OR refer to **Section 19, Schedule of Events Table**> Administer initial study intervention.

Repeat study intervention (if applicable)

Follow-up assessments of study end points and safety <list specimens to be collected, examinations or imaging or laboratory assays to be performed, questionnaires to be completed OR refer to **Section 19, Schedule of Events Table**>

Follow-up assessments of study end points and safety <list specimens to be collected, examinations or imaging or laboratory assays to be performed, questionnaires to be completed OR refer to **Section 19, Schedule of Events Table**>

Final Assessments   
<list analyses to be performed OR refer to **Section 19, Schedule of Events Table**>

Visit 1

Time Point

Prior to

Enrollment

Visit 2

Time Point

Visit 3

Time Point

Visit 4

Time Point

Visit X

Time Point

***Example #3: Process diagram*** *(e.g., randomized controlled trial)*

***Week/Day (Insert time) Screening***

* *Total n=x*
* *Obtain informed consent*
* *Screen potential subjects by inclusion and exclusion criteria*
* *Obtain history, document*

***Week/Day (Insert time) Randomization***

* *Treatment Group 1 (n=y)*
* *Placebo (n=z)*

***Week/Day (Insert time) Baseline assessments/ Study Intervention***

* *<List specimens to be collected, examinations or imaging or laboratory assays to be performed, questionnaires to be completed OR refer to Section 19, Schedule of Events Table>*
* *Administer initial study intervention*

***Week/Day (Insert time) Follow-up assessments of study endpoints and safety***

* *<List specimens to be collected, examinations or imaging or laboratory assays to be performed, questionnaires to be completed OR refer to Section 19, Schedule of Events Table>*

***Week/Day (Insert time) Follow-up assessments of study endpoints and safety***

* *<List specimens to be collected, examinations or imaging or laboratory assays to be performed, questionnaires to be completed OR refer to Section 19, Schedule of Events Table>*

***Week/Day (Insert time) End of Study Assessments***

* *<List specimens to be collected, examinations or imaging or laboratory assays to be performed, questionnaires to be completed OR refer to Section 19, Schedule of Events Table>*

***Week/Day (Insert time) Follow-up Telephone Call***

* *<List questionnaires to be completed OR refer to Section 19, Schedule of Events Table>*

# Key Roles

<Insert Text>

*Provide a list of persons, companies, and/or groups serving in key roles in the conduct or oversight of the trial. This should include the sponsor’s medical expert for the trial (medical monitor), investigator responsible for conducting the trial (principal investigator (PI)), qualified clinician responsible for the site’s clinical decisions (site investigator), and any clinical laboratory(ies) or other institutions involved in the trial. Other key roles may include the NIH point of contact (program director or officer), regulatory specialist, biostatistician, data coordinating center (DCC), data management center, data manager, or industry partner.*

*Include the following information for each individual:*

*Name, degree, title*

*Institution Name*

*Address*

*Phone Number*

*Email*

# Introduction, Background Information and Scientific Rationale

## Background Information and Relevant Literature

<Insert Text>

*This section should contain a background discussion of the target disease state to which the investigational product(s) hold promise and any pathophysiology relevant to potential study treatment action.*

*Provide an overview of the literature and data relevant to the trial, which help to support the rationale for the trial. Discuss importance of the study and any relevant treatment issues or controversies. Also include the relevant literature establishing the validity of any scales, evaluation tools, etc. which may be used in the study to assess study endpoints. References should be listed in section 17.*

## Name and Description of the Investigational Agent

<Insert Text>

*In this section include the name and description of the study intervention (drug, device, biologic, etc.) This section should contain a description of the investigational agent, its make-up, chemical properties and any relevant physical properties, including any available pharmacologic data. Specify the FDA approval status and include the IND Number or justify how the drug meets the IND Exemption criteria if applicable.*

*For device studies this section should include a description of the device, including category of the device, and overview of its intended use or purpose in the research study. Specify the FDA approval status and include the IDE Number or Non-Significant Risk rationale if applicable.*

### Preclinical Data

<Insert Text>

*Summarize the available non-clinical data (in vitro or in vivo studies) that have potential clinical significance. Include both supportive and adverse event data.*

### Clinical Data to Date

<Insert Text>

*Summarize the available clinical study data (published or available unpublished data) with relevance to the protocol under construction -- if none is available, include a statement that there is no available clinical research data to date on the investigational product. Please see examples below of the potential types of clinical data that may be available [This is not an exhaustive list].*

### Dose Rationale (if applicable)

<Insert Text>

*For studies involving an agent that will be dosed, describe the rationale for choosing the dose and summarize the available literature, preclinical and clinical studies and risks supporting the selected dose(s).*

## Rationale

<Insert Text>

State the problem or question under study (e.g., describe the disease and current limitations of knowledge or therapy). Include a statement of the hypothesis. Include a justification for the route of administration, dosage, dosing regimen of the study agent, intervention periods, and selection of study population. Describe the rationale for the type and selection of control (e.g. placebo, no treatment, active drug, dose-response, historical). Discuss known or potential problems associated with the control group chosen in light of the specific disease and therapies being studied.

## Potential Risks & Benefits

### Known Potential Risks

<Insert Text>

*Include a discussion of known potential risks from either clinical or nonclinical studies. If a package insert 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 Investigator’s 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 or the IB, the risk information discussion will result from published literature and should be included and referenced appropriately.*

*Describe in detail any physical, psychological, social, legal, economic, or any other risks to participants by virtue of participation in the study that the PI foresees, addressing each of the following:*

* *Immediate risks*
* *Long-range risks*
* *Rationale for the necessity of exposing human participants to such risks*
* *Why the value of the information to be gained outweighs the risks involved*
* *If risk is related to proposed procedures included in protocol, any alternative procedures that have been considered and explanation on why alternative procedures not included*

*If vulnerable populations are included, list the risks as they pertain to each vulnerable population.*

*Note: For studies that enroll adults without capacity to consent, and are a minor increase than minimal risk, an ICM and MRC may be required. Alternatively, justification for why the study is minimal risk and/or an ICM and MRC is not required must be included.*

*Please refer to Section on Persons who Lack Capacity to Provide Informed Consent for Research and Surrogate Consent of the* [*NYU Langone Health Institutional Review Board and Human Subjects Research Protection Program Policies and Procedures*](https://med.nyu.edu/research/office-science-research/clinical-research/sites/default/files/nyu-som-irb-policies-and-procedures-for-human-subjects-research-protection.docx) *for additional information.*

### Risk of Use of Mobile Health Technology

If applicable:

{Sample Text}

Commercial products or devices made by third party companies, including wearable fitness trackers, wearable sleep monitors, mobile apps for use on smartphone and tablets, websites and web apps, and types of computer software that permit screen sharing, record keystrokes, gain access to device files and/or use location tracking technology may be used to collect study data. These devices will be used in accord with the Terms of Service (TOS) and/or the End User License Agreements (EULA) provided by the product or device vendor. Use of such products and devices may result in loss of privacy and risk of breach of confidentiality. These products and devices will only be used to collect study data with IRB approval and if the subject has agreed to all applicable Terms of Service and EULAs. The participant will be advised to read the full EULA or TOS before agreeing to use the product. Any risks associated are outlined in the informed consent, as follows: ADD HERE IN SUMMARY IF APPLICABLE as noted in TOS or EULA

{End Sample Text}

### Known Potential Benefits

<Insert Text>

*Include a discussion of known potential benefits from either clinical or nonclinical studies. If a package insert 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 or the IB, the potential benefit information discussion will result from published literature and should be included and referenced appropriately.*

*Describe in detail any physical, psychological, social, legal, economic, or any other potential benefits to participants by virtue of participation in the study that the PI foresees, addressing each of the following:*

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

*If vulnerable populations are included, list the benefits as they pertain to each vulnerable population.*

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

# Objectives and Purpose

*Provide a detailed description of the primary objective and any secondary objectives of the study. An objective is the reason for performing the study in terms of the scientific question to be answered. The primary objective is the main question. This objective generally drives statistical planning for the trial (e.g., calculation of the sample size to provide the appropriate power for statistical testing. Note: do not include statistical analysis here.). Secondary objectives are goals that will provide further information on the use of the intervention.*

*Express each objective as a statement of purpose (e.g., to assess, to determine, to compare, to evaluate) and include the general purpose (e.g., feasibility, acceptability, efficacy, effectiveness, safety) and/or specific purpose (e.g., dose-response, superiority to placebo, effect of an intervention on disease incidence, disease severity, or health behavior).*

## Primary Objective

<Insert Text>

## Secondary Objectives (if applicable)

<Insert Text>

# Study Design and Endpoints

## Description of Study Design

<Insert Text>

*The scientific integrity of the trial and the credibility of the data from the trial depend substantially on the trial design. A description of the trial design should be consistent with the Protocol Summary**and include:*

* *The type/design of trial to be conducted (e.g., placebo-controlled, double-blinded, parallel design, open-label, dose escalation, dose-ranging);*
* *Phase of the trial;*
* *The number of study groups/arms;*
* *Single or multi-center;*
* *Name of study agent/intervention(s);*
* *Changes in scheduling, such as dose escalations; and*
* *Any stratifications.*

## Study Endpoints

### Primary Study Endpoints

<Insert Text>

*Specify the primary endpoint used to determine primary efficacy. Although the critical efficacy measurements may seem obvious, the protocol should indicate how the selected primary endpoint(s) is linked to achieving the primary objective. This section should include an explanation of why primary endpoint(s) was chosen and its importance and role in the analysis and interpretation of study results. Generally, there should be just one primary endpoint that will provide a clinically relevant, valid, and reliable measure of the primary objective. Additional primary endpoints may require an adjustment to the sample size calculations and p-value threshold. For example: The primary endpoint will be % change in variable X between the baseline visit and visit 12.*

### Secondary Study Endpoints

<Insert Text>

*Secondary endpoints should be specified and may include, for example, endpoints related to efficacy, safety, or both. The protocol should indicate how the selected secondary endpoints are linked to either adding more information about the primary objective or addressing secondary objectives. This section should include an explanation of why secondary endpoints were chosen and their importance and role in the analysis and interpretation of study results.*

### Exploratory Endpoints

<Insert Text>

*Exploratory endpoints should be specified; for example, treatment comparisons and subgroup analysis with an exploratory (e.g., hypothesis generating) purpose.*

# Study Enrollment and Withdrawal

*The following subsections should include a description of the study population, participant recruitment, and issues related to participant withdrawal. The study population should be appropriate for the stage of the study and the development stage of the study agent.*

*Use the following guidelines when developing participant eligibility criteria to be listed in Sections 5.1 Participant Inclusion Criteria and 5.2 Participant Exclusion Criteria:*

* *The eligibility criteria should provide a definition of participant characteristics required for study entry/enrollment.*
* *If participants require screening, distinguish between screening participants vs enrolling participants. Determine if screening procedures will be performed under a separate screening consent form.*
* *The risks of the intervention should be considered in the development of the inclusion/exclusion criteria so that risk is minimized.*
* *The same criterion should not be listed as both an inclusion and exclusion criterion (e.g., do not state age >18 years old as ̠an inclusion criterion and age ≤18 years as an exclusion criterion).*
* *Identify specific laboratory tests or clinical characteristics that will be used as criteria for enrollment or exclusion.*
* *If reproductive status (i.e., pregnancy, lactation, reproductive potential) is an eligibility criterion, provide specific contraception requirements (e.g., licensed hormonal or barrier methods).*

## Inclusion Criteria

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

1. <Insert Text>

*Create a numbered list of criteria that an individual must meet to be eligible to participate in the study.*

*Some criteria to consider for inclusion are: provision of appropriate consent and assent, willingness and ability to participate in study procedures, age range, health status, diagnosis or symptoms, background medical treatment, laboratory ranges, and use of appropriate contraception. Additional criteria should be included as appropriate for the study design and risk.*

## Exclusion Criteria

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

1. <Insert Text>

*Create a numbered list of criteria that would exclude an individual from study enrollment. Some criteria to consider for exclusion are: pre-existing conditions or concurrent diagnoses, concomitant use of other medication(s) or devices, known allergies, other factors that would cause harm or increased risk to the participant or close contacts, or preclude the participant’s full adherence with or completion of the study. Additional criteria should be included as appropriate for the study design and risk.*

## Vulnerable Subjects

<Insert Text>

*If vulnerable subjects are included, provide justification. Children, pregnant women, fetuses, neonates, and prisoners are considered vulnerable populations under federal regulation. The elderly, students, employees, and persons with decisional incapacity are also generally considered vulnerable participants and in need of greater protection.*

*If persons with decisional incapacity are included,*

If the study intends to enroll children, pregnant women, prisoners, or other vulnerable populations, refer to applicable section of 45 CFR Part 46 Subpart B – Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research (45 CFR Part 46.201-46.207); Subpart C – Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects (45 CFR Part 46.301-46.306); Subpart D – Additional Protections for Children Involved as Subjects in Research (45 CFR Part 46.401-46.409).

Please refer to these regulations and Office for Human Research Protections (OHRP) guidelines when choosing the study population. Note that these regulations apply if any participants are members of the designated population even if it is not the target population (for example, if a participant becomes a prisoner during the study). Refer to: <http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#46> and <http://www.hhs.gov/ohrp/archive/irb/irb_guidebook.htm>.

### Adults without Capacity to Consent

*Summarize how the disorder, condition or factor that prevents the individual from having capacity to consent is an intrinsic characteristic of the research population such that the research could not otherwise be conducted on subjects who have capacity. Provide evidence that the use of such a procedure or intervention presents a reasonable opportunity to further the understanding of the etiologist, prevention, diagnosis, pathophysiology, or alleviation or treatment of a condition or disorder.*

*Note that for research in which recruitment of individuals with impaired consent capacity is not expected at the time of IRB submission, judgment that prospective subjects have the capacity to consent to the research can ordinarily be made informally during routine interactions with the individual during the consent process. An investigator who questions a prospective subject’s capacity to consent may not enroll the individual and should consult with the IRB.*

### Assessment of Capacity

Assessment of capacity will be done by *{choose one: licensed MDs with experience treating this patient population or other licensed clinicians (e.g. social workers, nurses) with experience treating this patient population}*. The assessors are *{choose one:}* independent of the study team or study team members that are identified in Research Navigator *{or}* do not need to be independent because *{explain}.*

The individual performing the assessment and/or monitoring ongoing capacity will perform *{name of tool or assessment}*. *The IRB recommends use of assessments commonly used in clinical care to assess capacity to consent for their own clinical care. If no specific tool would be used, state this and explain why.*

The results of the capacity assessment *{choose one:}* will/will not be placed in the subject’s medical record. *{If results will be placed in the medical record, add:}* Prospective subjects will be informed that the results of the assessment may be added to their medical record and that this may affect their subsequent medical care. *{If results will not be placed in the medical record, explain why}. Note that where the reason for lack of capacity is mental illness, New York State law requires that a psychiatrist or licensed psychologist document this determination in the individual’s medical record in a signed and dated progress note [New York State Public Health Law 2994-C].*

Prospective subjects will be informed of the results of the capacity assessment after it’s conducted. If an individual is found not to have the capacity to consent, the assessor will explain this to the individual. The assessor will provide the necessary resources and referrals for further care and evaluation.

*For multi-site research with sites outside of New York State, who are relying on NYULH IRB, state that a description of the site-specific plan to enroll subjects who lack capacity and assess capacity as indicated will be submitted with each site approval, and the description will indicate how state-specific laws or requirements impact the enrollment of this population. Submit this description as a separate site-specific addendum in the site record.*

### Surrogate Consent

Surrogate order will be followed in order of priority: court appointed LAR, health care proxy, spouse if not legally separated from subject – or domestic partner-/adult son or daughter, parent, grandparent, adult grandchild who maintains regular contact with subject as to be familiar with subject’s activities, health, or beliefs).

*For multi-site research with sites outside of New York State, who are relying on NYULH IRB, state the site-specific order of priority, if different than above.*

The surrogate will be informed that the prospective subject was invited to take part in the study, that a capacity

assessment was conducted, and that the subject was determined to lack the capacity to provide informed

consent. The surrogate will be informed whether or not the result will be added to the subject’s medical record

or impact their clinical care. The surrogate will then be given a description of the nature of the research and

asked if they agree to provide consent on behalf of the incapacitated subject.

*{Choose one:}* Before the surrogate signs the consent, the subject will be informed of the surrogate’s identity if

not already aware and will be given the chance to assent. Subjects who object to the capacity assessment,

surrogate, or participation will not be enrolled, unless required by law. *{or}* The subject population will not have

or is unlikely to have the ability to communicate, to be informed of the identity of the surrogate, or to assent to

participation in the research.

### Ongoing Assessment of Capacity

*{Choose one:}* At each study visit, subjects will have direct interaction with the licensed clinicians referenced above. If the licensed clinicians have any concerns about the subject’s capacity, a formal capacity assessment will be conducted as described above. *{or}* At each study visit, subjects will have a formal capacity assessment to determine whether there has been any change in their capacity to assent or provide consent.

Over the course of the study, it is possible that a subject who had capacity at enrollment may lose capacity or capacity may fluctuate. A surrogate will be proactively identified at the time of enrollment and the study team will remain in contact with the surrogate over course of study. The PI will take steps to ensure people with some decisional impairment make a voluntary and informed decision. Such steps include involvement of a trusted individual in the decision-making process, allocation of additional time for the consent process, waiting periods after initial discussion before enrollment, repetitive teaching, oral or written recall tests, and / or audiovisual presentations, or group sessions.

*{Add the following statements, as applicable:}*

Subjects who regain capacity will be re-consented with the latest consent version and informed of all research procedures performed to date and all research procedures that remain to be performed. Subjects will have the opportunity to continue in or withdraw from study.

Subjects who lose capacity will continue in the study only if their LAR is consented.

Subjects who lose capacity and do not have surrogate consent by an LAR will be withdrawn.

Subjects who appear to be unduly distressed will be withdrawn from the research in a manner consistent with

good clinical practice.

Regular communication with the surrogate will be maintained.

### Independent Consent Monitors

*Describe the involvement of independent consent monitors (ICMs) and medically responsible clinicians (MRCs). NYU Langone Health IRB and Human Subjects Research Protection Program Policies and Procedures require this for (1) any study involving more than a minor increase over minimal risk or (2) any study involving a minor increase over minimal risk with no prospect of direct benefit. The IRB will usually require use of ICMs and MRCs for any study involving a minor increase over minimal risk with the prospect of direct benefit.*

*Note: ‘Minimal risk’ means risks no greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.*

*A “minor increase over minimal risk” means that the increase in the probability and magnitude of harm is only slightly more than minimal risk, any potential harms associated with the procedure will be transient and reversible in consideration of the nature of the harm, and there is no or an extremely small probability that subjects will experience significant pain, discomfort, stress or harm.*

*For minimal risk research, state:* The study involves minimal risk to subjects we have chosen not to use an ICM or MRC.

*For minor increase over minimal risk studies, include one of the following:* The study involves a minor increase over minimal risk with the prospect of direct benefit but we have chosen not to use an ICM or MRC. This safeguard is not necessary because *{state why}.*

*{or}*

The following individual will serve as the ICM: *{State name and title).* This individual is unaffiliated with the

research and will be present during the informed consent process as an advocate for the rights and wellbeing

of potential and current research subjects. The ICM will also:

* Verify consent is properly obtained.
* Confirm subjects are enrolled only when appropriate consent procedures are followed.
* Confirm LARs understand the goals and risks of the research.
* Provide independent assurance that a subject is enrolled in research only when there is sufficient evidence that participation is consistent with the subject’s preferences and/or interests.
* Be familiar with the subject population and have clinical trial experience.
* Be instructed to report any consent violations or irregularities to the IRB, if observed.

The ICM will be present during the consent process of *{choose one:}* a percentage of subjects: *{state the*

*percent}*. *This figure should be determined by the size of the targeted subject population, the complexity of the*

*research, and the risks of the research {or}* a random selection of subjects.

The ICM will provide confirmation of compliance with the process above at the time of study continuing review.

The following individual will serve as MRC: *{state name and title).* This individual is a licensed medical doctor who is skilled and experienced in working with the research population and is unaffiliated with the research and will serve as an advocate for the rights and wellbeing of potential and current research subjects. This individual is available to answer questions of subjects and / or their LARs. The same individual may serve as both ICM and MRC.

## Strategies for Recruitment and Retention

<Insert Text>

*Identify strategies for participant recruitment and retention,* *e.g. from investigator or sub-investigator clinical practices, referring physicians, advertisement, etc. See the Research and Recruitment Unit’s Participant Recruitment Overview of Resources eBook for information on tools and services available to address common needs:* [*https://central.nyumc.org/research/site/Pages/Participant-Recruitment-Resources.aspx*](https://central.nyumc.org/research/site/Pages/Participant-Recruitment-Resources.aspx)*.*

*Include details as to whether or not the recruitment plan proposes to use any NYULMC media services (communications, marketing, etc.) social media (e.g.: Facebook, Twitter, blogging, etc.) Note: All recruitment materials which will be seen by potential participants need to be approved by the IRB. Include numbers of women and minorities expected to be recruited, or provide justification if women and/or minorities will not be recruited.*

*Describe how participants will be identified and recruited for the study. The identification of participants must protect participants’ privacy. Privacy refers to persons and their interest in controlling the access of others to themselves. Include the following:*

*• The time and place where informed consent will take place.*

*• The nature of the information subjects will be asked to give about themselves.*

*• Who receives and can use the information.*

*For example, persons might not want to be seen entering a place that might stigmatize them, such as a pregnancy-counseling center that is clearly identified as such by signs on the front of the building.*

*If the study requires long-term participant participation, describe procedures that will be used to enhance participant retention (e.g., multiple methods for contacting participants, visit reminders).*

*In addition, consider inclusion of the following information:*

* *Target sample size; identify anticipated number to be screened in order to reach the target enrollment (should be consistent with information contained in* ***Section 10.5, Sample Size****);*
* *Anticipated accrual rate;*
* *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; and*
* *Types of advertisements planned (e.g. national newspaper, local flyers; specific names are not needed), and a statement that any advertisements must be approved by the IRB/EC for the site.*

### Use of DataCore/Epic Information for Recruitment Purposes

*This section, including the following information, is required if this study includes utilization of DataCore/Epic information for recruitment purposes.*

* *How the data will be gathered from EPIC (e.g. DataCore will request a report)*
* *How the data will be used (be specific regarding the purpose e.g. subject identification, informing subjects, initial discussion of subject eligibility, etc.]*
* *List of the study team members ( by role not name) who will have access to the EPIC search results*
* *All data points and PHI that will be used for the search*
* *When the data will be discarded after use and how the data will discarded*
* *Parameters (how many times the study team will search EPIC over the course of the study and/or how often queries regarding eligible subjects will run during the course of the study)*
* *The method used to notify the treating physician (if any, and if no explain why)*
* *A description of how the patients will be contacted (email, phone, text, mailed letters etc.)*

*Notes:*

1. *When sending recruitment information by email, SendSafe Secure email MUST be used to contact patients. NYU Langone does not permit sending any patient health information via unencrypted email.*
2. *Note: Ensure that all recruitment tools i.e., direct mailing letter, direct calling phone script, MyChart message language, etc. are uploaded in the recruitment section.*

*For additional information on recruitment methods please see:*

*Guidance on Recruitment of Research Subjects*

*Guidance on Advertising*

*{Begin sample text}*

This study will utilize EPIC to identify subjects.

Any recruitment information sent by email will utilize Send Safe email.

Once potential subjects have been identified, the study team will notify the treating physician (TP) that they have patients eligible to participate as follow: *{Include one or more of the following options to describe how patients will be contacted or include a description of your own.}*

* Provide TP with a list, advertisement, letters or oral script to use when contacting potential subjects
* TP and Research PI send letter to all potential subjects (letter must have both TP and Research PI's name)
* TP agrees to permit study team to directly contact potential subjects on behalf of TP.
* TP has been notified that the study team will contact potential subjects directly, by letter, phone, email, or the MyChart portal etc.

Once contact is made, approved recruitment language will be used to communicate the reason they are being contacted and subjects will be asked if they are interested in participating in this specific study. Should the potential subjects agree, the study team will provide the subjects with information regarding the next steps for participation.

If a subject requests information regarding opting out of further recruitment for all research, subjects will be directed to contact research-contact-optout@nyumc.org or 1-855-777-7858.

*{End sample text}*

## Duration of Study Participation

<Insert Text>

*This refers to the duration of the study participants’ participation and not simply the duration of the study. This should include screening, study intervention phase and any follow up time period.*

## Total Number of Participants and Sites

<Insert Text>

*Include the number of participants that will be enrolled at NYUMC and the number of participants that will be enrolled elsewhere if applicable. Specify whether any subjects will be recruited at international sites. Enrolled for the intent and purpose of the IRB, means the consent form was signed.*

*{Begin sample text}*

Recruitment will end when approximately \_\_\_ participants are enrolled. It is expected that approximately \_\_\_ participants will be enrolled in order to produce \_\_\_ evaluable participants.

*{End sample text}*

## Participant Withdrawal or Termination

### Reasons for Withdrawal or Termination

*Provide a list of reasons participation may be terminated (e.g. safety reasons, failure of subject to adhere to protocol requirements, subject consent withdrawal, disease progression, etc.). 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 at any time.*

*{Begin sample text}*

Participants are free to withdraw from participation in the study at any time upon request. An investigator may terminate participation in the study 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
* The participant meets an exclusion criterion (either newly developed or not previously recognized) that precludes further study participation

*{End sample text}*

### Handling of Participant Withdrawals or Termination

<Insert Text>

*Describe efforts that will be made to continue follow-up of withdrawn or terminated participants or participants who discontinue study agent but remain in the study for follow-up, especially for safety and efficacy study endpoints (if applicable). Every effort must be made to undertake protocol-specified safety follow-up procedures to capture AEs, serious adverse events (SAEs), and unanticipated problems (UPs). The investigator should attempt to obtain at a minimum survival data on all participants lost to follow-up. Include details regarding the methods that will be used prior to stating that a participant is lost to follow up (e.g. number of phone calls to participant, phone calls to next-of-kin if possible, certified letters, etc.). In studies of implantable devices, a discussion should be included of any pertinent information that will be provided to withdrawn or terminated patients (e.g., how to replace batteries, how to obtain replacement parts, who to contact).*

*If abrupt termination of study treatment could affect subject safety (e.g. in an antihypertensive study, abrupt withdrawal without other intervention might cause hypertensive rebound), describe procedure to transition subject off the study drug or to alternate therapy.*

*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 Section 10, Statistical Considerations.*

## Premature Termination or Suspension of Study

<Insert Text>

*List possible reasons for termination or temporary suspension of the study (e.g., study closure based on PI decision or sponsor/funder decision). For any study that is prematurely terminated or temporarily suspended, the PI will promptly inform the IRB and sponsor and provide the reason(s) for the termination or temporary suspension. State what criteria or review will be done to determine if study can resume.*

*{Begin sample text}*

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 <investigator, funding agency, the IND/IDE sponsor and regulatory authorities>. If the study is prematurely terminated or suspended, the PI will promptly inform the IRB and will provide the reason(s) for the termination or suspension.

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 of futility

Study may resume once concerns about safety, protocol compliance, data quality are addressed and satisfy the sponsor, IRB and/or FDA.

*{End sample text}*

# Study Agent (Study drug, device, biologic, vaccine etc.) and/or Procedural Intervention

*The following subsections should describe the study agent and/or procedural intervention that is being tested for safety and effectiveness in the clinical investigation, and any control product being used in the clinical investigation. The study agent may be a drug (including a biological product), imaging agent, or device. Note: This also includes a product with a marketing authorization when used or assembled (formulated or packaged) in a way different from the approved form, when used for an unapproved indication or when used to gain further information about an approved use.*

*If multiple study agents are to be evaluated in the trial, Section 6.1 Study Agent(s) and Control Description should clearly differentiate between each product. Address placebo or control product within each part of Section 6.1. If the control product is handled differently than the study agent, be sure to state how they are each handled separately. If the control product is handled the same as the study agent, state as such. In addition, all sections may not be relevant for the trial. If not relevant, note as not applicable in that section.*

## Study Agent(s) and Control Description

<Insert Text>

*Include a detailed description of the investigational product, including its constituent substances or parts, and the form (tablet, capsule, liquid, cream, single use device, etc.).*

*If study is IND exempt or IDE is not required (e.g. if the device is not a significant risk device), provide justification here.*

### Acquisition

<Insert Text>

*Describe how the study agent and control product will be acquired and shipped to the investigator (e.g., a study agent may be supplied by the manufacturer or IND/IDE sponsor; an approved product may be acquired from the hospital pharmacy).*

### Formulation, Appearance, Packaging, and Labeling

<Insert Text>

*Describe the formulation, appearance, packaging, and labeling of the study agent and control product as supplied. Information in this section can usually be obtained from the IB or the package insert. The package insert may be attached as an appendix to the protocol. This section should include the name of the manufacturer of the study agent and control product. Also, discuss availability of product (e.g., investigational or commercially marketed) and if the product proposed is available for human use in the form, route, dose planned in this trial or if product must be formulated to meet the trial plan.*

### Product Storage and Stability

<Insert Text>

*Describe study agent and control product’s storage needs. Include storage requirements and stability (e.g., temperature, humidity, security, and container). Provide additional information regarding stability and expiration time for studies in which multidose vials are utilized (i.e., the seal is broken).*

### Preparation

<Insert Text>

*Describe the preparation of study agent and control product, including what preparation is required by study staff and/or study participant. Include thawing, diluting, mixing, and reconstitution/preparation instructions, as appropriate. If study drug is stored, mixed/prepared or dispensed from the NYULMC Investigational Drug Service (IDS) that should be noted here, including the contact number to that service office. The IDS can also provide standard language text for this section of the protocol. Detailed information may be provided in a separate document such as a Manual of Procedures (MOP) or standard operating procedure (SOP).*

### Dosing and Administration

<Insert Text>

*Describe the procedures for selecting each participant's dose of study agent and control product. The timing of dosing (e.g., time of day, interval) and the relation of dosing to meals should be described. Any specific instructions to study participants about when or how to take the dose(s) should be described. Include any specific instructions or safety precautions for administration of the study agent. Discuss the maximum hold time once thawed/mixed, if appropriate, before administration.*

### Route of Administration

<Insert Text>

*Describe the planned route of administration (e.g., oral, nasal, intramuscular).*

### Starting Dose and Dose Escalation Schedule

<Insert Text>

*State the starting level of the study agent and control product.*

*If applicable, describe the dose escalation scheme and treatment regimen (using exact dose, rather than percentages). State any minimum period required before a participant’s dose might be raised to the next higher dose or dose range.*

### Dose Adjustments/Modifications/Delays

<Insert Text>

*If applicable, the protocol should state the conditions under which a dose change will be made, particularly in regard to failure to respond or to toxic or untoward changes in stipulated indicators (e.g., white blood cell count in cancer chemotherapy). Address dose modifications for specific abnormal laboratory values of concern or other AEs that are known to be associated with the planned study agent. The protocol must state explicitly the dose-limiting effects that are anticipated. Provide criteria that will be used to determine dose escalations. If a participant is responding positively to treatment, the protocol should specify whether treatment would progress to still higher doses. If appropriate, provide a dose de-escalation schema with treatment modifications. Do not restate reasons for withdrawal of participants. Cross-reference relevant sections, as appropriate.*

### Duration of Therapy

<Insert Text>

*Discuss the duration of therapy for each active phase and what duration is the minimum necessary for an “evaluable” participant (should be consistent with Section 10, Statistical Considerations and/or Statistical Analysis Plan (SAP)).*

### Tracking of Dose

<Insert Text>

*Discuss what procedures will be in place to monitor dosing and adherence for each participant.*

### Device Specific Considerations

<Insert Text>

*If conducting a study with a device, the following information should be included, otherwise note as not-applicable:*

* *Device size(s)*
* *Device model(s)*
* *Device settings and programming (if applicable)*
* *Duration of implant or exposure (if applicable)*
* *Frequency of exposure (if applicable)*

## Study Agent Accountability Procedures

<Insert Text>

*Describe plans for how and by whom the study agent(s) will be distributed including participation of a drug repository or pharmacy, frequency of product distribution, amount of product shipped, documentation of adequate and safe handling, and plans for return of unused product.*

*This section should include regular drug reconciliation checks (i.e. how much drug was assigned and whether participants actually received assigned dose or received dose properly, how much remains, how much drug was inadvertently damaged, etc. --- e.g. “Regular study drug reconciliation will be performed to document drug assigned, drug consumed, and drug remaining. This reconciliation will be logged on the drug reconciliation form, and signed and dated by the study team.”)*

*This section should note the procedures for final reconciliation of the site’s drug supply at the end of the study, and whether study drug is to be shipped back to a source or destroyed on site. If drug is to be shipped back to a source, note the address and contact information here.*

## Study Behavioral or Social Intervention(s)

<Insert Text>

*If the study does not use a behavioral or social intervention, delete this section, including the heading and associated subheadings.*

*Provide a general description of the behavioral and social intervention(s) included in this study. If one or more intervention(s) will be compared to a control intervention or to treatment as usual, include a general description of these. Detailed descriptions of behavioral or social intervention(s), including any intervention manuals, scripts, participant hand-outs, etc., can be provided in a separate Manual of Procedures (MOP).*

### Administration of Intervention

<Insert Text>

*Describe whether the intervention will be delivered in-person or in some other modality. If in-person, describe who will administer the intervention. If not in-person, describe how participants will access the intervention. Describe the number of sessions to be delivered, the frequency of session delivery, and the approximate duration of each session.*

### Procedures for Training Interventionalists and Monitoring Intervention Fidelity

<Insert Text>

*Describe the training and supervision of staff who will administer the intervention, or of staff who will facilitate participants’ accessing the intervention. Describe the procedures for monitoring intervention fidelity, including how interventionists’ fidelity to the intervention manual will be documented and assessed, what criteria will signal inadequate fidelity, and how re-training or replacement of interventionists will be managed. If audio or video recordings of sessions will be used to monitor intervention fidelity, describe the coding system to be used to extract fidelity data from these recordings, and how fidelity coders will be selected and trained.*

### Assessment of Subject Compliance with Study Intervention

<Insert Text>

*If applicable, include in this section plans for compliance assessment (e.g., questionnaires, telephone follow-up contacts, direct observation).*

## Study Procedural Intervention(s) Description

<Insert Text>

*If the study does not use a procedural intervention, delete this section, including the heading and associated subheadings.*

*Describe the dental, surgical or other medical procedural intervention(s) that will be tested in the study. If one or more intervention(s) will be compared to a control intervention or to treatment as usual, include a general description of these. Detailed descriptions of the intervention(s), including any intervention manuals, detailed procedures, participant handouts, etc., can be provided in a separate MOP.*

### Administration of Procedural Intervention

<Insert Text>

*Include information about who will administer the intervention and how the intervention will be administered. In addition, describe the schedule of the intervention procedure(s), including the number of interventions, frequency of the intervention delivery, and the approximate duration of each intervention.*

### Procedures for Training of Clinicians on Procedural Intervention

<Insert Text>

*Describe any means used to standardize the surgical or procedural intervention (e.g., single operator, calibration, images, minimal time of therapy required, specialized required instruments and/or materials, required measurements). Describe any re-standardization or re-evaluation procedures and time intervals between reassessments.*

### Assessment of Clinician and/or Participant Compliance with Study Procedural Intervention

<Insert Text>

*If applicable, include in this section plans for compliance assessment (e.g., questionnaires, research record review, medical record review, laboratory result review, telephone follow-up contacts, direct observation).*

# Study Procedures and Schedule

*The following subsections should include a description of study procedures and outline the schedule of visits and procedures to be performed at each visit.*

*Allowable windows should be stated for all visits. The schedule must include clinic visits and all contacts, e.g., telephone contacts. To determine the appropriate windows, consider feasibility and relevance of the time point to study endpoints (e.g., pharmacokinetic (PK) studies may allow little or no variation, with required time points measured in minutes or hours, whereas a 6-month follow-up visit might have a window of several weeks). Further details should be provided in the MOP.*

## Study Procedures/Evaluations

*In the following subsections, describe procedures for collection of all study data including clinical observations, laboratory results, biospecimens, images, questionnaire responses.*

### Study Specific Procedures

<Insert Text>

*List and describe all study procedures and evaluations to be done as part of the study. All procedures listed here should be specific to the study and not part of standard clinical care.*

*{Begin sample text}*

* *Medical history (describe what is included for history, e.g., time-frame considerations, whether history will be obtained by interview or from medical records)*
* *Medication history (e.g., describe if a complete medication history is needed, or if only medications currently taken should be included; prescription and over-the-counter medications). Assessment of eligibility should include a review of permitted and prohibited medications.*
* *Physical examination (list the vital signs [including height and weight] and organ systems to be assessed. Address details in the MOP.); if appropriate, discuss what constitutes a targeted physical examination and at what visits it may occur.*
* *Radiographic or other imaging assessments. State the specific imaging required and, as appropriate, provide description of what is entailed to perform the specialized imaging. Details describing how to perform the imaging in a standard fashion may be described in a separate document such as a MOP or SOP.*
* *Biological specimen collection and laboratory evaluations. If biological specimen and laboratory procedures require further detail, they may be described in Section 7.2 Laboratory Procedures/Evaluations below, or in a separate document such as a MOP or SOP. At minimum, the biological specimens and purpose should be listed.*
* *A discussion of if the results of any study specific procedures (e.g., radiographic or other imaging or laboratory evaluations) will be provided to participant.*
* *Counseling procedures*
* *Assessment of study agent adherence*
* *Administration of questionnaires or other instruments for patient-reported outcomes, such as a daily diary.*

*{End sample text}*

### Standard of Care Study Procedures

<Insert Text>

*Describe and summarize all procedures completed during the study as part of regular standard of clinical care.*

## Laboratory Procedures/Evaluations

*Include content in this section if it is not already included in Section 7.1 Study Procedures/Evaluations, otherwise note as not-applicable. This section header may be modified to describe other procedures/evaluations such as Imaging Procedures/Evaluations or Surgical Procedures.*

### Clinical Laboratory Evaluations

<Insert Text>

*List all laboratory evaluations 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. 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.*

*{Begin sample text}*

* ***Hematology:*** *hemoglobin, hematocrit, white blood cells (WBC) with differential count, platelet count.*
* ***Biochemistry:*** *creatinine, total bilirubin, alanine aminotransferase (ALT), aspartate*
* *aminotransferase (AST).*
* ***Urinalysis:*** *dipstick urinalysis, including protein, hemoglobin and glucose; if dipstick is abnormal, complete urinalysis with microscopic evaluation is required.*
* ***Pregnancy test****, usually to be done within 24 hours prior to study intervention and results must be available prior to administration of study product.*

*{End sample text}*

### Other Assays or Procedures

<Insert Text>

*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 or refer to the study’s MOP. If more than one laboratory will be used, specify which assays will be done by each laboratory.*

### Specimen Preparation, Handling, and Storage

<Insert Text>

*Special instructions for the preparation, handling, and storage of specimens should be explained clearly in this section (or refer to the study’s MOP), including specific time requirements for processing, required temperatures, aliquots of specimens, where they will be stored, and how they will be labeled.*

### Specimen Shipment

<Insert Text>

*State the frequency with which specimens are to be shipped and to what address. Include contact information for laboratory personnel. Include days and times shipments are allowed, and any labeling requirements for specimen shipping. Also, include any special instructions such as dry ice or wet ice or the completion of a specimen-tracking log (or refer to the study’s MOP).*

## Study Schedule

*This section should include a description of those procedures/evaluations planned throughout the study. Consideration should be given to the level of detail included in the protocol versus the MOP, noting that any changes to the protocol require a protocol amendment or will need to follow the plan outlined in Section 14.3, Protocol Deviations.*

### Screening

<Insert Text>

*Include a description of only those procedures/evaluations necessary to assess whether a participant meets eligibility criteria. Discuss the sequence of events that should occur during screening and the decision points regarding eligibility. List the time frame prior to enrollment within which screening procedures/evaluations must be performed (e.g., within 28 days prior to enrollment).*

*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, describe how written informed consent will be obtained prior to review of that information or whether a waiver of consent will be sought from the IRB.*

*{Begin sample text}*

**Screening Visit (Day -28 to -1)** *<include a window that is appropriate for the study>*

* Obtain informed consent of potential participant verified by signature on written informed consent for screening form.
* Review medical history to determine eligibility based on inclusion/exclusion criteria.
* Review medications history to determine eligibility based on inclusion/exclusion criteria.
* Perform medical examinations needed to determine eligibility based on inclusion/exclusion criteria.
* Collect blood/urine for <specify tests>.
* Schedule study visits for participants who are eligible and available for the duration of the study.
* Provide participants with <specify instructions needed to prepare for first study visit>.

*{End sample text}*

### Enrollment/Baseline

<Insert Text>

*Include a description of those procedures/evaluations necessary to assess or confirm whether a participant still meets the eligibility criteria and may be enrolled and those procedures/evaluations that are required at baseline for later endpoint comparison after study intervention (e.g., baseline signs and symptoms prior to administration of study agent).*

*Discuss the sequence of events that should occur during enrollment and/or initial administration of study agent. List any special conditions that must be achieved at this visit (e.g., results of the pregnancy test must be negative and available prior to administration of study product). List the procedures for administering the study agent and follow-up procedures after administration (e.g., assessment of vital signs).*

*{Begin sample text}*

**Enrollment/Baseline Visit (Visit 1, Day 0)**

* Obtain informed consent of potential participant verified by signature on study informed consent form.
* Verify inclusion/exclusion criteria.
* Obtain urine pregnancy test.
* Obtain demographic information, medical history, medication history, alcohol and tobacco use history.
* Record vital signs, results of examinations, other assessments.
* Collect blood/urine for <specify baseline laboratory tests required for the study>.
* Administer the study treatment.
* <Specify procedures, instructions provided to participants, observations after the intervention>.

*{End sample text}*

### Intermediate Visits

*Include a discussion of procedures/evaluations required to assess or confirm study endpoints and study evaluations. Discuss the sequence of events that should occur during the visit, if applicable. Include, as applicable, counseling, medications, assessment of AEs, etc. Consider specifying an appropriate range of time, or visit window, when the visit should occur to allow feasible scheduling, safety and other data collection considerations.*

*If multiple follow-up visits are planned, repeat for each visit, providing a study-appropriate window for each visit.*

#### Visit 2

<Insert Text>

*{Begin sample text}*

**Visit 2 (Day X+/-Y)** *<include a window that is appropriate for the study>*

* Record adverse events as reported by participant or observed by investigator.
* Record vital signs, results of <specify examinations or other assessments, including the information to be recorded>.
* Collect blood/urine for <specify follow-up laboratory tests>.
* Administer the study agent or provide additional medication to the participant, in accordance with <specify procedures, instructions provided to participants>.
* Record participant’s adherence to treatment program.

*{End sample text}*

### Final Study Visit

<Insert Text>

*Include a discussion of procedures/evaluations required to assess or confirm study endpoints and study evaluations. Define when the final study visit should occur. Describe provisions for follow-up of ongoing AEs/SAEs. Consider discussing if or when participants will be informed of study results. Consider specifying an appropriate range of time, or visit window, when the visit should occur to allow feasible scheduling, data collection and study completion considerations.*

*{Begin sample text}*

***Final Study Visit (Visit X, Day X+/-Y)*** *<include a window that is appropriate for the study>*

* *Record adverse events as reported by participant or observed by investigator.*
* *Record vital signs, results of <specify examinations or other assessments, including the information to be recorded>.*
* *Collect blood/urine for <specify final laboratory tests>.*
* *Record participant’s adherence to treatment regimen.*
* *Provide <specify final instructions> to participant.*

*{End sample text}*

### Withdrawal/Early Termination Visit

<Insert Text>

*Specify which of the procedures/evaluations required for the final study visit should be done at a termination visit if the subject withdraws or if early termination occurs, provided that the participant is willing.*

### Unscheduled Visit

<Insert Text>

*Specify how unscheduled visits(s) will be handled and documented.*

## Concomitant Medications, Treatments, and Procedures

<Insert Text>

*Include content in this section if applicable, or if not already addressed elsewhere in this section, otherwise note as not-applicable.*

*This section should be consistent with the medication restrictions in the inclusion/exclusion criteria. Describe the data that will be recorded related to permitted concomitant medications, treatments, and/or procedures. Include details about when the information will be collected (e.g., screening, all study visits). Describe how allowed concomitant therapy might affect the outcome (e.g., drug-drug interaction, direct effects on the study endpoints) and how the independent effects of concomitant and study agents could be ascertained.*

*{Begin sample text}*

All concomitant prescription medications taken during study participation will be recorded on the case report forms (CRFs). For this protocol, a prescription medication is defined as a medication that can be prescribed only by a properly authorized/licensed clinician. Medications to be reported in the CRF are concomitant prescription medications, over-the-counter medications and non-prescription medications.

*{End sample text}*

## Justification for Sensitive Procedures

<Insert Text>

*Provide justification for any sensitive procedures (e.g., use of placebo, medication withdrawal, provocative testing, and deception).*

### Precautionary Medications, Treatments, and Procedures

<Insert Text>

*If applicable, list all medications, treatments, and/or procedures for which there are precautions for concomitant use with the study agents. Include instructions for dose modification, if appropriate. Describe any drug and food interactions and toxicities for standard agents that are likely to be given in conjunction with this protocol.*

## Prohibited Medications, Treatments, and Procedures

<Insert Text>

*Include content in this section if applicable, or if not already addressed elsewhere in this section, otherwise note as not-applicable.*

*List all medications, treatments, and/or procedures that are NOT permitted on study. Include drugs from the exclusion criteria if they are also prohibited while the participant is on study. Describe what action will be taken if prohibited medications, treatments or procedures are indicated for care (e.g., early withdrawal.)*

*{Begin sample text}*

Treatment with <list specific drugs> will not be permitted unless discussed with and approved by the <study medical monitor/sponsor/investigator>.

*{End sample text}*

## Prophylactic Medications, Treatments, and Procedures

<Insert Text>

*List all medications, treatments, and/or procedures that will be provided as prophylaxis on study. For injectable medications, describe if topical numbing medications such as Emla cream may be used.*

## Rescue Medications, Treatments, and Procedures

<Insert text>

*List all medications, treatments, and/or procedures that may be provided on study for “rescue therapy.”*

*This section should be consistent with the medications restrictions in Section 5.1, Participant Inclusion Criteria and Section 5.2, Participant Exclusion Criteria.*

## Participant Access to Study Agent at Study Closure

<Insert Text>

*Describe obligations to continue beneficial interventions after participants are no longer enrolled in the study.*

# Assessment of Safety

*The subsections below are intended to highlight the specific assessments related to safety and the aspects of the study which are intended to ensure the safety of trial participants. This should be consistent with the NYUSOM IRB guidelines. Consider developing this section in consultation with the study Medical Monitor. Consider the risks of the study agent and other study procedures and the characteristics of the study population (e.g., vulnerable populations such as children). This section should be tailored for specific study characteristics, including but not limited to the following:*

* *The study involves an investigational new drug or investigational device*
* *The study involves washout from current medication regimen*
* *The study involves treatment with placebo to population with diagnosed disease*
* *The study requires selection of an appropriate toxicity grading scale*
* *The study involves risks to individuals other than research participants (e.g., household or intimate contacts or communities, study clinicians, pharmacists or interventionists, etc.)*
* *Reporting of certain events (e.g., suspected child abuse or substance abuse) is mandatory because of the study population or study design characteristics*
* *The study is conducted at multiple sites, and will require centralized safety oversight*

*In developing the sections below, consider the risks of the study agent. Review and reference the IB, package insert, literature and other sources that describe the study agent. Consider and describe how participant’s risk will be minimized in the sections below.*

## Specification of Safety Parameters

<Insert Text>

*Reference safety parameters that are study endpoints (Section 4.2, Study Endpoints). Include other parameters if not primary/secondary endpoints. Describe safety parameters that will be recorded in the safety reporting system. “Recording” refers to documenting data in the study database. Define what data will require reporting for protection of human subjects.*

### Definition of Adverse Events (AE)

*{Begin required text}*

An ***adverse event*** (AE) is any symptom, sign, illness or experience that develops or worsens in severity during the course of the study. Intercurrent illnesses or injuries should be regarded as adverse events. Abnormal results of diagnostic procedures are considered to be adverse events if the abnormality:

* results in study withdrawal
* is associated with a serious adverse event
* is associated with clinical signs or symptoms
* leads to additional treatment or to further diagnostic tests
* is considered by the investigator to be of clinical significance

*{End required text}*

### Definition of Serious Adverse Events (SAE)

*Provide the definition of an SAE being used for the clinical trial. The FDA definition of an SAE is used in this template. Note: The example text provided is from the drug regulations (i.e., (21 CFR 312.32 (a)). There is no definition for SAE in the device regulations. Therefore, investigators should develop an appropriate definition for their study. This definition could include an unanticipated adverse device effect, but an SAE is broader than that definition. According to 21 CFR 812.3(s), an “unanticipated adverse device effect means any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.”*

*{Begin sample text}*

**Serious Adverse Event**

Adverse events are classified as serious or non-serious. A ***serious adverse event*** is any AE that is:

* fatal
* life-threatening
* requires or prolongs hospital stay
* results in persistent or significant disability or incapacity
* a congenital anomaly or birth defect
* an important medical event

Important medical events are those that may not be immediately life threatening, but are clearly of major clinical significance. They may jeopardize the subject, and may require intervention to prevent one of the other serious outcomes noted above. For example, drug overdose or abuse, a seizure that did not result in in-patient hospitalization, or intensive treatment of bronchospasm in an emergency department would typically be considered serious.

All adverse events that do not meet any of the criteria for serious should be regarded as ***non-serious adverse events***.

*{End sample text}*

### Definition of Unanticipated Problems (UP)

*{Begin sample text}*

**Unanticipated Problems Involving Risk to Subjects or Others**

Any incident, experience, or outcome that meets all of the following criteria:

* Unexpected in nature, severity, or frequency (i.e. not described in study-related documents such as the IRB-approved protocol or consent form, the investigators brochure, etc)
* Related or possibly related to participation in the research (i.e. possibly related means there is a reasonable possibility that the incident experience, or outcome may have been caused by the procedures involved in the research)
* Suggests that the research places subjects or others at greater risk of harm (including physical, psychological, economic, or social harm).

*{Additional sample text for device protocols}*

This definition could include an unanticipated adverse device effect, any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects (21 CFR 812.3(s)).

*{End sample text}*

## Classification of an Adverse Event

### Severity of Event

<Insert Text>

*All AEs will be assessed by the clinician using a protocol defined grading system. Describe the method of grading an AE for severity. For example, many toxicity tables are available for use and are adaptable to various study designs. Selection of a toxicity table or severity scale should be made in consultation with the Medical Monitor.*

*{Begin sample text}*

For AEs not included in the protocol defined grading system, the following guidelines will be used to describe severity.

* **Mild** – Events require minimal or no treatment and do not interfere with the participant’s daily activities.
* **Moderate** – Events result in a low level of inconvenience or concern with the therapeutic measures. Moderate events may cause some interference with functioning.
* **Severe** – Events interrupt a participant’s usual daily activity and may require systemic drug therapy or other treatment. Severe events are usually potentially life-threatening or incapacitating.

*{End sample text}*

### Relationship to Study Agent

<Insert Text>

*All AEs will have their relationship to study agent or study participation assessed with a level of specificity appropriate to the study design. Describe the method of determining the relationship of an AE to a study agent. Some protocols may use a binary assessment (related/not related); others may have a scale of relatedness (definitely related, probably related, possibly related, unlikely or unrelated). Evaluation of relatedness must consider etiologies such as natural history of the underlying disease, concurrent illness, concomitant therapy, study-related procedures, accidents, and other external factors. In a clinical trial, the study agent must always be suspect.*

*{Begin sample text}*

*The clinician’s assessment of an AE's relationship to study agent (drug, biologic, device) is part of the documentation process, but it is not a factor in determining what is or is not reported in the study. If there is any doubt as to whether a clinical observation is an AE, the event should be reported. All AEs must have their relationship to study agent assessed. In a clinical trial, the study product must always be suspect. To help assess, the following guidelines are used.*

* ***Related*** *– The AE is known to occur with the study agent, there is a reasonable possibility that the study agent caused the AE, or there is a temporal relationship between the study agent and event. Reasonable possibility means that there is evidence to suggest a causal relationship between the study agent and the AE.*
* ***Not Related*** *– There is not a reasonable possibility that the administration of the study agent caused the event, there is no temporal relationship between the study agent and event onset, or an alternate etiology has been established.*

*{Alternative text}*

*For all collected AEs, the clinician who examines and evaluates the participant will determine the AE’s causality based on temporal relationship and his/her clinical judgment. The degree of certainty about causality will be graded using the categories below.*

* ***Definitely Related*** *– There is clear evidence to suggest a causal relationship, and other possible contributing factors can be ruled out. The clinical event, including an abnormal laboratory test result, occurs in a plausible time relationship to drug administration and cannot be explained by concurrent disease or other drugs or chemicals. The response to withdrawal of the drug (dechallenge) should be clinically plausible. The event must be pharmacologically or phenomenologically definitive, with use of a satisfactory rechallenge procedure if necessary.*
* ***Probably Related*** *– There is evidence to suggest a causal relationship, and the influence of other factors is unlikely. The clinical event, including an abnormal laboratory test result, occurs within a reasonable time after administration of the drug, is unlikely to be attributed to concurrent disease or other drugs or chemicals, and follows a clinically reasonable response on withdrawal (dechallenge). Rechallenge information is not required to fulfill this definition.*
* ***Possibly Related*** *– There is some evidence to suggest a causal relationship (e.g., the event occurred within a reasonable time after administration of the trial medication). However, other factors may have contributed to the event (e.g., the participant’s clinical condition, other concomitant events). Although an AE may rate only as “possibly related” soon after discovery, it can be flagged as requiring more information and later be upgraded to “probably related” or “definitely related,” as appropriate.*
* ***Unlikely to be related*** *– A clinical event, including an abnormal laboratory test result, whose temporal relationship to drug administration makes a causal relationship improbable (e.g., the event did not occur within a reasonable time after administration of the trial medication) and in which other drugs or chemicals or underlying disease provides plausible explanations (e.g., the participant’s clinical condition, other concomitant treatments).*
* ***Not Related*** *– The AE is completely independent of study drug administration, and/or evidence exists that the event is definitely related to another etiology. There must be an alternative, definitive etiology documented by the clinician.*

*{End sample text}*

### Expectedness

<Insert Text>

*Expected adverse reactions are AEs that are common and known to occur for the study agent being studied and should be collected in a standard, systematic format using a grading scale based on functional assessment or magnitude of reaction. Describe the method of determining the expectedness of an AE. Expectedness refers to the awareness of AEs previously observed, not on the basis of what might be anticipated from the properties of the study agent.*

*An AE or suspected adverse reaction is considered "unexpected" if it is not listed in the IB or is not listed at the specificity or severity that has been observed; or, if an IB is not required or available, is not consistent with the risk information described in the general investigational plan or elsewhere in the protocol, as amended. For example, under this definition, hepatic necrosis would be unexpected (by virtue of greater severity) if the IB referred only to elevated hepatic enzymes or hepatitis. Similarly, cerebral thromboembolism and cerebral vasculitis would be unexpected (by virtue of greater specificity) if the IB listed only cerebral vascular accidents. "Unexpected," as used in this definition, also refers to AEs or suspected adverse reactions that are mentioned in the IB as occurring with a class of drugs or as anticipated from the pharmacological properties of the drug, but are not specifically mentioned as occurring with the particular drug under investigation.*

*{Begin sample text}*

<Insert name> will be responsible for determining whether an AE is expected or unexpected. An AE will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the risk information previously described for the study agent.

*{End sample text}*

## Time Period and Frequency for Event Assessment and Follow-Up

<Insert Text>

*Describe how AEs and SAEs will be identified and followed until resolved or considered stable. Also describe how UPs will be recorded. Specify procedures for recording and follow-up of AEs, SAEs, and UPs that are consistent with the information contained within Section 7, Study Procedures and Schedule, including what assessment tools will be used to monitor AEs. Include duration of follow-up after appearance of events (e.g., 1 week, 2 months).*

*An unsolicited AE would occur without any prompting or in response to a general question such as “Have you noticed anything different since you started the study, began the study agent, etc.” A solicited AE is one that is specifically solicited such as “Have you noticed any dry mouth since you started the study medication?”*

* *Describe which AEs will be collected as solicited events. Plan the reporting and data collection system to avoid double capture (captured both as an unsolicited and a solicited AE).*
* *Describe how unsolicited events will be captured.*
* *Include time period of collection (e.g., Days 0 -28) and note how long SAEs are collected – usually collected through entire study.*

*{Begin sample text}*

The occurrence of an AE or SAE may come to the attention of study personnel during study visits and interviews of a study participant presenting for medical care, or upon review by a study monitor. All AEs including local and systemic reactions not meeting the criteria for SAEs will be captured on the appropriate RF. Information to be collected includes event description, time of onset, clinician’s assessment of severity, relationship to study product (assessed only by those with the training and authority to make a diagnosis), and time of resolution/stabilization of the event. All AEs occurring while on study must be documented appropriately regardless of relationship. All AEs will be followed to adequate resolution.

Any medical condition that is present at the time that the participant is screened will be considered as baseline and not reported as an AE. However, if the study participant’s condition deteriorates at any time during the study, it will be recorded as an AE. UPs will be recorded in the data collection system throughout the study.

Changes in the severity of an AE will be documented to allow an assessment of the duration of the event at each level of severity to be performed. AEs characterized as intermittent require documentation of onset and duration of each episode.

The PI will record all reportable events with start dates occurring any time after informed consent is obtained until 7 (for non-serious AEs) or 30 days (for SAEs) after the last day of study participation. At each study visit, the investigator will inquire about the occurrence of AE/SAEs since the last visit. Events will be followed for outcome information until resolution or stabilization.

All unresolved adverse events should be followed by the investigator until the events are resolved, the subject is lost to follow-up, or the adverse event is otherwise explained. At the last scheduled visit, the investigator should instruct each subject to report any subsequent event(s) that the subject, or the subject’s personal physician, believes might reasonably be related to participation in this study. The investigator should notify the study sponsor of any death or adverse event occurring at any time after a subject has discontinued or terminated study participation that may reasonably be related to this study. The sponsor should also be notified if the investigator should become aware of the development of cancer or of a congenital anomaly in a subsequently conceived offspring of a subject that has participated in this study.

*{End sample text}*

## Reporting Procedures – Notifying the IRB

*This section describes the requirements for reporting specific types of unanticipated problems, including adverse events. For NYUSOM reporting requirements and timelines refer to the following for* [*NYULMC IRB*](file:///C:\Users\mdutt\AppData\Local\Microsoft\Windows\Temporary%20Internet%20Files\Content.Outlook\E7H27SJR\somapps.med.upenn.edu\pennmanual\secure\pm\reporting) *definition of reportable events and reporting timelines. See:* [*https://med.nyu.edu/research/research-resources/clinical-research/resources-researchers-study-teams/human-research-regulatory-affairs/submitting-to-institutional-review-board/nyu-school-medicine-institutional-review-boards*](https://med.nyu.edu/research/research-resources/clinical-research/resources-researchers-study-teams/human-research-regulatory-affairs/submitting-to-institutional-review-board/nyu-school-medicine-institutional-review-boards)

*In the following subsections, describe the protocol-specific reporting procedures, including the individual responsible for each step (e.g., PI, DCC, 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 and life-threatening events*
* *Other SAEs*
* *Other AEs*
* *Other UPs*

*The example text in the following sections may be customized by including IRB-specified reporting time frames or protocol-specific parameters (safety issues) that need to be reported in an expedited fashion, either to the IRB, sponsor, or other regulatory body.*

### Adverse Event Reporting

<Insert Text>

*Describe the AE reporting procedures, including timeframes. Include description and a flow chart of when events are reported to various oversight and regulatory groups, and what study staff are responsible for completing and signing off on the AE reports. Describe who will receive notification of AEs.*

### Serious Adverse Event Reporting

<Insert Text>

*Describe the SAE reporting procedures, including timeframes. Include description and a flow chart of when events are reported to various oversight and regulatory groups, and what study staff are responsible for completing and signing off on the SAE reports. Describe who will receive notification of SAEs.*

*Generally, any AE considered serious by the PI or Sub-investigator or which meets the definition of an SAE included in Section 8.1.2, Definition of Serious Adverse Event must be submitted on an SAE form to the DCC if one exists for the study. If a study is overseen by a Data and Safety Monitoring Board (DSMB), the DSMB may request to receive real-time notification of all SAEs or only SAEs thought to be related to study agent.*

*According to CFR 21 CFR 312.32(c)(1), “the sponsor must notify FDA and all participating investigators … in an IND safety report of potential serious risks, from clinical trials or any other source, as soon as possible, but in no case later than 15 calendar days after the sponsor determines that the information qualifies reporting … In each IND safety report, the sponsor must identify all IND safety reports previously submitted to FDA concerning a similar suspected adverse reaction, and must analyze the significance of the suspected adverse reaction in light of previous, similar reports or any other relevant information. The sponsor must report any suspected adverse reaction that is both serious and unexpected. The sponsor must report an adverse event as a suspected adverse reaction only if there is evidence to suggest a causal relationship between the drug and the adverse event, such as:*

*(A) A single occurrence of an event that is uncommon and known to be strongly associated with drug exposure (e.g., angioedema, hepatic injury, Stevens-Johnson Syndrome);*

*(B) One or more occurrences of an event that is not commonly associated with drug exposure, but is otherwise uncommon in the population exposed to the drug (e.g., tendon rupture);*

*(C) An aggregate analysis of specific events observed in a clinical trial (such as known consequences of the underlying disease or condition under investigation or other events that commonly occur in the study population independent of drug therapy) that indicates those events occur more frequently in the drug treatment group than in a concurrent or historical ̮control group.”*

*Furthermore, according to 21 CFR 312.32(̮c)(2), “the sponsor must also notify FDA of any unexpected fatal or life-threatening suspected adverse reaction as soon as possible but in no case later than 7 calendar days after the sponsor’s initial receipt of the information.”*

*As noted previously, an unanticipated adverse device effect could be considered an SAE (Section 8.1.2, Definition of Serious Adverse Event). For IDE studies, according to 21 CFR 812.150(a)(1), “an investigator shall submit to the sponsor and to the reviewing IRB a report of any unanticipated adverse device effect occurring during an investigation as soon as possible, but in no event later than 10 working days after the investigator first learns of the effect.” In addition, according to 21 CFR 812.150(b)(1), “A sponsor who conducts an evaluation of an unanticipated adverse device effect under 812.46(b) shall report the results of such evaluation to FDA and to all reviewing IRB's and participating investigators within 10 working days after the sponsor first receives notice of the effect. Thereafter the sponsor shall submit such additional reports concerning the effect as FDA requests.”*

### Unanticipated Problem Reporting

<Insert Text>

*Describe the UP reporting procedures, including timeframes. Include description and a flow chart of when events are reported to various oversight and regulatory groups, and what study staff are responsible for completing and signing off on the UP report forms.*

*{Begin sample text}*

Incidents or events that meet the OHRP criteria for UPs require the creation and completion of an UP report form. It is the site investigator’s responsibility to report UPs to their IRB and to the DCC/study sponsor. The UP report will include the following information:

* Protocol identifying information: protocol title and number, PI’s name, and the IRB project number;
* A detailed description of the event, incident, experience, or outcome;
* An explanation of the basis for determining that the event, incident, experience, or outcome represents an UP;
* A description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the UP.

To satisfy the requirement for prompt reporting, UPs will be reported using the following timeline:

* UPs that are SAEs will be reported to the IRB and to the DCC/study sponsor within <insert timeline in accordance with policy> of the investigator becoming aware of the event.
* Any other UP will be reported to the IRB and to the DCC/study sponsor within <insert timeline in accordance with policy> of the investigator becoming aware of the problem.
* All UPs should be reported to appropriate institutional officials (as required by an institution’s written reporting procedures), the supporting agency head (or designee), and OHRP within<insert timeline in accordance with policy> of the IR’s receipt of the report of the problem from the investigator.

### Reporting of Pregnancy

<Insert Text>

*State the study’s pregnancy-related policy and procedure. Include appropriate mechanisms for reporting to the DCC or NIH, the IND or IDE sponsor, study leadership, IRB, and regulatory agencies. Provide appropriate modifications to study procedures (e.g., discontinuation of treatment while continuing safety follow-up, requesting permission to follow pregnant women to pregnancy outcome).*

## Reporting Procedures – Notifying the Study Sponsor

*Reporting to the study sponsor should be consistent with regulatory and/or sponsor requirements for the study. If the study involves a NYUSOM sponsor, investigators from all participating sites should report all unexpected and related adverse events, regardless of whether they are serious or not, and all unanticipated problems to the NYUSOM sponsor.*

*{Begin sample text}*

*{Sample text for drug or biologic protocols}*

The study clinician will complete a SAE Form within the following timelines:

* All deaths and immediately life-threatening events, whether related or unrelated, will be recorded on the SAE Form and submitted to the DCC/study sponsor within 24 hours of site awareness. See Section 1, Key Roles for contact information.
* Other SAEs regardless of relationship will be submitted to the DCC/study sponsor within 72 hours of site awareness.

All SAEs will be followed until satisfactory resolution or until the site investigator deems the event to be chronic or the adherence to be stable. Other supporting documentation of the event may be requested by the DCC/study sponsor and should be provided as soon as possible.

As a follow-up to the initial report, within the following 48 hours of awareness of the event, the investigator shall provide further information, as applicable, on the unanticipated event or the unanticipated problem in the form of a written narrative. This should include a copy of the completed Unanticipated Problem form, and any other diagnostic information that will assist the understanding of the event. Significant new information on ongoing unanticipated adverse effects shall be provided promptly to the study sponsor.

*{Additional sample text for device protocols}*

The study investigator shall complete an Unanticipated Adverse Device Effect Form and submit to the study sponsor and to the reviewing IRB as soon as possible, but in no event later than 10 working days after the investigator first learns of the effect. The study sponsor contact information is provided in Section 1, Key Roles.

As a follow-up to the initial report, within the following 48 hours of awareness of the event, the investigator shall provide further information, as applicable, on the unanticipated event or the unanticipated problem in the form of a written narrative. This should include a copy of the completed Unanticipated Problem form, and any other diagnostic information that will assist the understanding of the event. Significant new information on ongoing unanticipated adverse effects shall be provided promptly to the study sponsor.

The study sponsor is responsible for conducting an evaluation of an unanticipated adverse device effect and shall report the results of such evaluation to FDA and to all reviewing IRBs and participating investigators within 10 working days after the sponsor first receives notice of the effect. Thereafter the sponsor shall submit such additional reports concerning the effect as FDA requests.

*{End sample text}*

## Reporting Procedures – Notifying the FDA

*If this protocol is being conducted under an FDA IND or IDE held by an NYU faculty member, it is the responsibility of the study regulatory sponsor (i.e. the IND or IDE holder) to report all adverse events to the FDA in the Annual Report and all unanticipated, related and serious adverse events to the FDA. Delete this section if the study is not being conducted under a NYULMC faculty-held IND or IDE.*

The study sponsor is required to report certain study events in an expedited fashion to the FDA. These written notifications of adverse events are referred to as IND/IDE safety reports.

The following describes the IND safety reporting requirements by timeline for reporting and associated type of event:

* ***Within 7 calendar days*** *(via telephone or facsimile report)*

Any study event that is:

* associated with the use of the study drug
* unexpected,
* fatal or life-threatening
* ***Within 15 calendar days*** *(via written report)*

Any study event that is:

* associated with the use of the study drug,
* unexpected, and
* serious, but not fatal or life-threatening

-or-

* a previous adverse event that was not initially deemed reportable but is later found to fit the criteria for reporting (reporting within 15 calendar days from when event was deemed reportable).

Any finding from tests in laboratory animals that:

* suggest a significant risk for human subjects including reports of mutagenicity, teratogenicity, or carcinogenicity.

The following describes the IDE safety reporting requirements by timeline for reporting and associated type of event:

* ***Within 10 working days*** *(via telephone or facsimile report)*

Any study event that is:

* associated with the use of the study device, and
* unanticipated,

regardless of the seriousness of the event.

* ***Within 5 working days*** *(via written report)*
* Protocol deviation to protect the life of the subject in emergency
* Withdrawal of IRB approval
* Lack of informed consent

**Additional reporting requirements**

Sponsors are also required to identify in IND safety reports all previous reports concerning similar adverse events and to analyze the significance of the current event in light of the previous reports.

**Reporting Process**

Adverse events may be submitted on FDA Form 3500A (MEDWATCH Form; see Attachment XXXX), or in a narrative format. If supplied as in a narrative format, the minimum information to be supplied is noted above at the beginning of section 8.3. The contact information for submitting IND safety reports is noted below:

[Include the FDA Division, contact person, telephone number and fax number here]

The following describes the IDE safety reporting requirements by timeline for reporting and associated type of event:

• Within 10 working days (via telephone or facsimile report)

Any study event that is:

– associated with the use of the study device, and

– unanticipated,

regardless of the seriousness of the event.

• Within 5 working days (via written report)

– Protocol deviation to protect the life of the subject in emergency

– Withdrawal of IRB approval

– Lack of informed consent

## Reporting Procedures – Participating Investigators

<Insert Text>

*For multi-center clinical trials, in addition to reporting certain unanticipated problems and adverse events noted above to the FDA, it is the responsibility of the study sponsor to report those same adverse events or findings to participating investigators. Delete this section if it is not applicable.*

## Study Halting Rules

<Insert Text>

*Describe safety findings that would prompt temporary suspension of enrollment and/or study agent until a safety review is convened (either routine or ad hoc). The objective of the safety review is to decide whether the study (or study agent for an individual or study cohort) should continue per protocol, proceed with caution, be further investigated, be discontinued, or be modified and then proceed. Suspension of enrollment (for a particular group, a particular study site or for the entire study) is a potential outcome of a safety review.*

*Subsequent review of serious, unexpected, and related AEs by the Medical Monitor, DSMB, IRB, the sponsor(s), or the FDA or relevant local regulatory authorities may also result in suspension of further study agent administration at a site. The FDA and study sponsor(s) retain the authority to suspend additional enrollment and study agent for the entire study, as applicable.*

*Examples of findings that might trigger a safety review are the number of SAEs overall, the number of occurrences of a particular type of SAE, severe AEs/reactions, or increased frequency of events.*

*This section should be consistent with Section 5.6, Premature Termination or Suspension of Study and Section 10.4.7.1, Safety Review.*

*{Begin sample text}*

Administration of study agent will be halted when three grade 3 AEs determined to be “probably related” are reported to the DCC. The DCC will notify the study sponsor and investigators immediately when the third grade 3 event is reported and enrollment screens will stop accepting new study participants. The study sponsor will inform the DSMB members within 24 hours of this occurrence and will provide the DSMB with AE listing reports. The DSMB will convene an ad hoc meeting by teleconference or in writing as soon as possible. The DSMB will provide recommendations for proceeding with the study to the study sponsor/NIH. The study sponsor will inform the FDA of the temporary halt and the disposition of the study.

*{End sample text}*

## Safety Oversight

<Insert Text>

*Appropriate safety oversight should be considered for each trial. This could include a Data Safety Monitoring Committee (DSMC), Data Safety Monitoring Board (DSMB), and/or a Medical Monitor.*

***DSMC****: An independent group of experts that advises the study investigators for Phase I and some Phase II trials. The primary responsibility of the DSMC is to monitor participant safety. The DSMC considers study-specific data as well as relevant background information about the disease, test agent, and target population under study.*

***DSMB****: An independent group of experts that advises the study investigators. 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 trial. The DSMB considers study-specific data as well as relevant background knowledge about the disease, test agent, or patient population under study. For example, a DSMB may be convened if a study meets one or more of the following criteria: will generate randomized, blinded data; is a multi-center protocol which presents more than minimal risk to participants; uses gene transfer or gene therapy methodology; or requires special scrutiny because of high public interest or public perception of risk.*

***Medical Monitor****: An independent medical expert that advises the study investigators and monitors participant safety. A study may choose to employ the services of, or may be appointed a Medical Monitor. The role of the Medical Monitor is to 1) Review all AEs on a regular basis throughout the trial; 2) be available to advise the investigators on trial-related medical questions or problems, and 3) evaluate cumulative participant safety data and make recommendations regarding the safe continuation of the study. The Medical Monitor will remain blinded throughout the conduct of the clinical trial unless unblinding is warranted to optimize management of an adverse event or for other safety reasons.*

*Independent oversight is an important component to ensure human subjects’ protection 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 in the study and the frequency of meetings. 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. The DSMB Charter should be provided with protocol to FDA and NIH for review.*

*For more information on determining the need for a DSMB and other information about the constitution and management of a DSMB, see the FDA Guidance Document: “Guidance for Clinical Trial Sponsors on the Establishment of Clinical Trial Data Monitoring Committees”*

[*www.fda.gov/downloads/RegulatoryInformation/Guidances/ucm127073.pdf*](http://www.fda.gov/downloads/RegulatoryInformation/Guidances/ucm127073.pdf)

*{Begin sample text}*

It is the responsibility of the Principal Investigator to oversee the safety of the study at his/her site. This safety monitoring will include careful assessment and appropriate reporting of adverse events as noted above, as well as the construction and implementation of a site data and safety-monitoring plan. Medical monitoring will include a regular assessment of the number and type of serious adverse events.

Safety oversight will be under the direction of a DSMB composed of individuals with the appropriate expertise, including <list expertise>. The DSMB will meet at least semiannually to assess safety and efficacy data on each arm of the study. The DSMB 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/NIH staff/other>.

*{End sample text}*

# Clinical Monitoring

<Insert Text>

*Site monitoring is conducted to ensure that the rights and well-being of human subjects are protected, that the reported trial data are accurate, complete, and verifiable, and that the conduct of the trial is in compliance with the currently approved protocol/amendment(s), with GCP, and with applicable regulatory requirement(s). Monitoring refers to the methods used by sponsors of investigational studies, or Contract Research Organizations (CROs) delegated site monitoring responsibilities, to oversee the conduct of, and reporting of data from, clinical investigations. Site monitoring includes ensuring appropriate clinical investigator supervision of study site staff and third party contractors. Monitoring activities include communication with the clinical investigator and study site staff; review of the study site’s processes, procedures, and records; and verification of the accuracy of data submitted to the sponsor.*

*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 agent, 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.*

*{Begin sample text for studies in which a separate CMP is being used}*

Clinical site monitoring is conducted to ensure that the rights and well-being of human subjects are protected, that the reported trial data are accurate, complete, and verifiable, and that the conduct of the trial is in compliance with the currently approved protocol/amendment(s), with 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 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.

*{Sample text for studies in which a separate CMP is not being used}*

Clinical site monitoring is conducted to ensure that the rights and well-being of human subjects are protected, that the reported trial data are accurate, complete, and verifiable, and that the conduct of the trial is in compliance with the currently approved protocol/amendment(s), with 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.
* Each clinical site will perform internal quality management of study conduct, data collection, documentation and completion. An individualized quality management plan will be developed to describe a site’s quality management.

*{End sample text}*

# Statistical Considerations

*The following subsections should describe the statistical tests and analysis plans for the protocol. They should indicate how the study will answer the most important questions with precision and a minimum of bias, while remaining feasible. Many elements below can be found in ICH Guidance for Industry E9 Statistical Principles for Clinical Trials and the CONSORT statement which describes standards for improving the quality of reporting randomized controlled trials. If a separate SAP will be developed, respective subsections below can be summarized. At a minimum, the following subsections should be included in the protocol:*

* *10.2 Statistical Hypotheses,*
* *10.3 Analysis Datasets,*
* *10.4.1 General Approach,*
* *10.4.2 Analysis of the Primary Efficacy Endpoint(s),*
* *10.4.3 Analysis of the Secondary Endpoint(s),*
* *10.4.4 Safety Analyses,*
* *10.4.6 Baseline Descriptive Statistics,*
* *10.4.7 Planned Interim Analyses (if applicable),*
* *10.4.11 Exploratory Analyses, and*
* *10.5 Sample Size.*

## Statistical and Analytical Plans (SAP)

<Insert Text>

*State whether there will be a formal SAP. A formal SAP should be completed prior to database lock and unblinding of the study data. The SAP generally includes additional statistical analysis detail (e.g., more detail of analysis populations, summary of statistical strategies).*

## Statistical Hypotheses

<Insert Text>

*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.*

## Analysis Datasets

<Insert Text>

*Clearly identify and describe the analysis datasets (e.g., which participants will be included in each). As a guide, this may include, but is not limited to, any or all of the following:*

* *Intention-to-Treat (ITT) Analysis Dataset (i.e., all randomized participants)*
* *Modified Intention-to-Treat Analysis Dataset (e.g., participants who took at least one dose of investigational product and/or have some particular amount of follow-up outcome data)*
* *Safety Analysis Dataset: defines the subset of participants for whom safety analyses will be conducted (e.g., participants who took at least one dose of investigational product)*
* *Evaluable or Per-Protocol Analysis Dataset: defines a subset of the participants in the full analysis (ITT) set who complied with the protocol sufficiently to ensure that these data would be likely to represent the effects of treatment according to the underlying scientific model (e.g., participants who took at least 80% of investigational product for 80% of the days within the maintenance period)*
* *Other Datasets*

## Description of Statistical Methods

*The following subsections should include a description of the planned statistical methods. The section should contain the key elements of the analysis plan, but does not need to be a full reiteration of a detailed study analysis plan created by the study biostatistician. The full SAP, if there is one, can then be a stand-alone document that can undergo edits and versioning outside of the protocol and therefore not trigger an IRB re-review with every version or edit – as long as the key elements of the analysis plan do not change – otherwise IRB review is required.*

### General Approach

<Insert Text>

*State the proposed formal design of the study (e.g., two-period crossover, two-by-three factorial parallel group, or case-control). If the design or interventions are complex, reference to Schematic of Study Design may be appropriate. As a guide, the following should be addressed, as appropriate:*

* *For descriptive statistics, describe how categorical and continuous data will be presented (e.g., percentages, means with standard deviations, median, range).*
* *For inferential tests, indicate the p-value for statistical significance (Type I error) and whether one or two-tailed.*
* *Indicate whether covariates will be pre-specified in the sections below or later in a SAP.*
* *State whether checks of assumptions (e.g., normality) underlying statistical procedures will be performed and whether any corrective procedures will be applied (e.g., transformation or nonparametric tests).*

### Analysis of the Primary Efficacy Endpoint(s)

<Insert Text>

*For each primary endpoint:*

* *Define the measurement or observation and describe how it is calculated, if not readily apparent*
* *Describe the scale (nominal/binary/categorical, ordinal, interval); state if it is measured as a single endpoint/summary measure or repeated measure*
* *Describe the statistical procedure(s) that will be used to analyze the primary endpoint (e.g., multiple regression, repeated measures mixed models, logistic regression, Analysis of Covariance (ANCOVA)). Describe the covariates and factors in the model. Provide your rationale for covariates and how they will be selected to achieve a parsimonious model. If the decision to specify covariates is deferred for the SAP, indicate here.*
* *Describe how results of statistical procedure(s) will be presented (e.g., adjusted means (Least-squares means (LSMEANS)) with standard errors, odds ratios with 95% confidence intervals, prevalence rates, number-needed-to-treat)*
* *Describe details to check assumptions required for certain types of data (e.g., proportional hazards, transformations or nonparametric tests if non-normal)*
* *Describe the Analysis Set for which the analysis will be conducted, as discussed in Section 10.3, Analysis Datasets*
* *Describe how missing data will be handled (e.g., type of imputation technique, if any, and provide justification), and approach to handling outliers, nonadherence and loss to follow-up*

*Note: if more than one endpoint: the statistical approach for endpoints with the same analytic issues can be described as a group.*

### Analysis of the Secondary Endpoint(s)

<Insert Text>

*For each secondary endpoint:*

* *Define the measurement or observation and describe how it is calculated, if not readily apparent*
* *Describe the scale (nominal/binary/categorical, ordinal, interval); state if it is measured as a single endpoint/summary measure or repeated measure.*
* *Describe the statistical procedure(s) that will be used to analyze the secondary endpoint (e.g., multiple regression, repeated measures mixed models, logistic regression, ANCOVA). Describe the covariates and factors in the model. Provide rationale for covariates and how they will be selected to achieve a parsimonious model. If decision to specify covariates is deferred for the SAP, indicate here.*
* *Describe how results of statistical procedure(s) will be presented (e.g., adjusted means (LSMEANS) with standard errors, odds ratios with 95% confidence intervals, prevalence rates, number-needed-to-treat).*
* *Describe details to check assumptions required for certain types of data (e.g., proportional hazards, transformations or nonparametric tests if non-normal).*
* *Describe the Analysis Set for which the analysis will be conducted as discussed in Section 10.3, Analysis Datasets.*
* *Describe how missing data will be handled (e.g., type of imputation technique, if any, and provide justification), and approach to handling outliers, nonadherence and loss to follow-up.*

*Note: if more than endpoint: the statistical approach for endpoints with the same analytic issues can be described as a group.*

### Safety Analyses

<Insert Text>

*Describe how safety endpoints will be analyzed (e.g., as summary statistics during treatment and/or as change scores from baselines such as shift tables). If your study is evaluating a formal safety endpoint, all of the factors to be included in Section 10.4.2, Analysis of the Primary Efficacy Endpoint(s) should be included here. Describe how AEs will be coded (e.g., Medical Dictionary for Regulatory Activities (MedDRA)), calculated (e.g., each AE will be counted once only for a given participant), presented (e.g., severity, frequency, and relationship of AEs to study agent will be presented by System Organ Class (SOC) and preferred term groupings) and what information will be reported about each AE (e.g., start date, stop date, severity, relationship, outcome, and duration). Also describe how AEs will be ascertained (e.g., adherence and/or PI reported). Adverse events leading to premature discontinuation from the study drug and serious treatment-emergent AEs should be presented either in a table or a listing. The information included here should be consistent with the information contained within Section 8, Assessment of Safety.*

### Adherence and Retention Analyses

<Insert Text>

*Define how adherence to the protocol (e.g., medication consumption) will be assessed, calculated, and verified (if applicable, e.g., plasma assays). Similarly describe measures and calculations for assessing participation, study retention/loss to follow-up, and frequency of and reasons for discontinuation of the intervention.*

### Baseline Descriptive Statistics

<Insert Text>

*Intervention groups should be compared on baseline characteristics, including demographics and laboratory measurements, using descriptive statistics. Discuss planned baseline descriptive statistics, indicate whether inferential statistics will be used.*

### Planned Interim Analysis

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

*The following subsections should describe the types of statistical interim analyses and stopping guidelines (if any) that are proposed, including their timing. Within the two sections below, pre-specify, to the extent possible, the criteria that would prompt an interim review of safety and efficacy data, respectively. Describe who performs the statistical analysis and who reviews the analysis. In addition, discuss whether they are unmasked and how the blinding will be preserved.*

#### Safety Review

<Insert Text>

*Provide details of the proposed rules for stopping study enrollment or study intervention/administration of study product for safety, including whether they pertain to the entire study, specific study arms or participant subgroups, or other components of the study. If statistical rules will be used to halt enrollment into all or a portion of the study, describe the statistical techniques and their operating characteristics, e.g., the probability of stopping under different safety event rates and the associated number of participants that would be enrolled.*

*State which safety endpoints will be monitored, the frequency of monitoring, and the specific definitions of proposed stopping guidelines.*

*This section should be consistent with Section 5.6 Premature Termination or Suspension of Study and Section 8.5 Stopping Rules.*

#### Efficacy Review

<Insert Text>

*Provide the same information as in Section 10.4.7.1 Planned Interim Analyses (Safety Review), but for efficacy endpoints. Also discuss the impact of the interim analysis (if being done) on the final efficacy analyses, particularly on Type I error.*

*If formal interim analyses will be performed, provide unambiguous and complete instructions so that an independent statistician could perform the analyses.*

### Additional Sub-Group Analyses

<Insert Text>

*Describe how the primary endpoint will be analyzed based on age, sex, race/ethnicity or other demographic characteristic(s).*

*Describe how the secondary endpoint(s) will be analyzed based on age, sex, race/ethnicity or other demographic characteristic(s).*

### Multiple Comparison/Multiplicity

<Insert Text>

*Include content in this section if applicable, otherwise note as not applicable. Generally, there should be just one primary endpoint that will provide a clinically relevant, valid and reliable measure of the primary objective. However, if there is more than one primary endpoint or more than one analysis of a particular endpoint, state the statistical adjustment used for Type I error criteria or give reasons why it was considered unnecessary.*

### Tabulation of Individual Response Data

<Insert Text>

*State whether individual participant data will be listed by measure and time point.*

### Exploratory Analyses

<Insert Text>

*Exploratory analyses serve as a basis for explaining or supporting findings of primary analyses and for suggesting further hypotheses for later research. These analyses can’t be used as confirmatory proof for registration trials. All planned exploratory analyses should be specified in the protocol.*

## Sample Size

<Insert Text>

*Include number of participants to recruit, screen, and enroll to meet a goal of evaluable participants for the study. Provide all information needed to validate your calculations, and also to judge the feasibility of enrolling and following the necessary number of participants. In particular, specify all of the following:*

* *Outcome measure used for calculations (almost always the primary variable)*
* *Test statistic*
* *Null and alternate hypotheses*
* *Type I error rate (alpha)*
* *Power level (e.g., 80% power)*
* *Assumed event rate for dichotomous outcome (or mean and variance of continuous outcome) for each study arm, justified and referenced by historical data as much as possible*
* *Assumed dropout rates, withdrawal, cross-over to other study arms, missing data, etc., also justified*
* *Approach to handling withdrawals and protocol violations, i.e., whether participants will be included in the “intent-to-treat” population*
* *Statistical method used to calculate the sample size, with a reference for it and for any software utilized*
* *Method for adjusting calculations for planned interim analyses, if any (Section 10.4.7, Planned Interim Analyses).*

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

*Consider discussing whether the sample size also provides sufficient power for addressing secondary endpoints or exploratory analyses (e.g., subgroup analyses or moderator analyses involving an interaction term, Section 10.4.11, Exploratory Analyses).*

## Measures to Minimize Bias

### Enrollment/Randomization/Masking Procedures

<Insert Text>

*This section should contain a description of enrollment procedures and randomization (if applicable to the study design) and masking procedures. It should include a description or a table that describes how study participants will be assigned to study groups, without being so specific that masking or randomization might be compromised (e.g., the ratio between intervention and placebo groups may be stated but the randomization block sizes should not). It should also include a discussion of the impact of replacement of participants who discontinue early, if allowed, on the statistical analysis/power calculations.*

*Plans for the maintenance of trial randomization codes and appropriate masking for the study should be discussed. The timing and procedures for planned and unplanned breaking of randomization codes should be included. Include a statement regarding when unmasking may occur and who may unmask.*

*Include a discussion of strategies to avoid bias, such as randomization and masking methods, or to decrease variability, such as centralized laboratory assessments. DO NOT include details that might compromise these strategies, such as the size of randomized blocks.*

*A description of the specific procedures to be used to carry out blinding should be provided (e.g., how bottles will be labeled, use of labels that reveal blind-breakage, sealed code list/envelopes, double dummy techniques).*

*Sometimes blinding is attempted but is known to be imperfect because of obvious drug effects in some participants (e.g., dry mouth, bradycardia, fever, injection site reactions, changes in laboratory data). Such problems or potential problems should be identified and, if there are plans to assess the magnitude of the problem or manage it, these should be described (e.g., having endpoint measurements carried out by people shielded from information that might reveal treatment assignment).*

*If the study allows for some investigators to remain unblinded (e.g., to allow them to adjust medication), the means of shielding other investigators should be explained. Measures taken to ensure that the study agent and placebo are indistinguishable and evidence that they are indistinguishable should be described. Measures to prevent unblinding by laboratory measurements, if used, should be described.*

*If blinding is considered unnecessary to reduce bias for some or all of the observations, this should be explained (e.g., use of a random-zero sphygmomanometer eliminates possible observer bias in reading blood pressure and Holter tapes are often read by automated systems that are presumably immune to observer bias). If blinding is considered desirable but not feasible, the reasons and implications should be discussed.*

### Evaluation of Success of Blinding

<Insert Text>

*Include content in this section if applicable, otherwise note as not-applicable. Provide the criteria for determining the success of blinding.*

### Breaking the Study Blind/Participant Code

<Insert Text>

*Provide the criteria for breaking the study blind or participant code. Discuss the circumstances in which the blind would be broken for an individual or for all participants (e.g., for SAEs). Indicate to whom the intentional and unintentional breaking of the blind should be reported.*

# Source Documents and Access to Source Data/Documents

<Insert Text>

*Each participating site will maintain appropriate medical and research records for this trial, in compliance with ICH E6 and regulatory and institutional requirements for the protection of confidentiality of participants. As part of participating in a NIH IC-sponsored or NIH IC -affiliated study, each site will permit authorized representatives of the NIH IC and regulatory agencies to examine (and when permitted by applicable law, to copy) clinical records for the purposes of quality assurance reviews, audits, and evaluation of the study safety, progress, and data validity. Describe in this section who will have access to records.*

*Source data are all information, original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Examples of these original documents and data records include, but are not limited to, hospital records, clinical and office charts, laboratory notes, memoranda, participants’ memory aids or evaluation checklists, pharmacy dispensing records, recorded audio tapes 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 clinical trial. It is acceptable to use CRFs as source documents. If this is the case, it should be stated in this section what data will be collected on CRFs and what data will be collected from other sources.*

*It is not acceptable for the CRF to be the only record of a patient’s participation in the study. This is to ensure that anyone who would access the patient medical record has adequate knowledge that the patient is participating in a clinical trial.*

*{Begin required text}*

Source data is all information, original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents. Examples of these original documents, and data records include: hospital records, clinical and office charts, laboratory notes, memoranda, subjects’ diaries or evaluation checklists, pharmacy dispensing records, 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, subject files, and records kept at the pharmacy, at the laboratories, and at medico-technical departments involved in the clinical trial. It is acceptable to use CRFs as source documents. If this is the case, it should be stated in this section what data will be collected on CRFs and what data will be collected from other sources.

The study case report form (CRF) is the primary data collection instrument for the study. All data requested on the CRF must be recorded. All missing data must be explained. If a space on the CRF is left blank because the procedure was not done or the question was not asked, write “N/D”. If the item is not applicable to the individual case, write “N/A”. All entries should be printed legibly in black ink. If any entry error has been made, to correct such an error, draw a single straight line through the incorrect entry and enter the correct data above it. All such changes must be initialed and dated. DO NOT ERASE OR WHITE OUT ERRORS. For clarification of illegible or uncertain entries, print the clarification above the item, then initial and date it.

*{End required text}*

*{Begin suggested text}*

Access to study records will be limited to IRB-approved members of the study team. The investigator will permit study-related monitoring, audits, and inspections by the IRB/EC, the sponsor, government regulatory bodies, and University compliance and quality assurance groups of all study related documents (e.g. source documents, regulatory documents, data collection instruments, study data etc.). The investigator will ensure the capability for inspections of applicable study-related facilities (e.g. pharmacy, diagnostic laboratory, etc.).

Participation as an investigator in this study implies acceptance of potential inspection by government regulatory authorities and applicable University compliance and quality assurance offices.

*{End suggested text}*

# Quality Assurance and Quality Control

<Insert Text>

*This section will indicate the plans for quality management, the system for assessing the quality of processes within a system. Quality management encompasses quality assurance (QA) and quality control (QC).*

***QA:*** *All those planned and systematic actions that are established to ensure that the trial is performed and the data are generated, documented (recorded), and reported in compliance with GCP and the applicable regulatory requirements(s) (ICH E6 1.46).*

***QC:*** *The operational techniques and activities undertaken within the quality assurance system to verify that the requirements for quality of the trial-related activities have been fulfilled (ICH E6 1.47).*

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

* *How data 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 9, Clinical Monitoring.*

*{Begin sample text}*

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 SOPs, the monitors will verify that the clinical trial is conducted and data are generated, documented (recorded), and reported in compliance with the protocol, GCP, and the applicable regulatory requirements (e.g., Good Laboratory Practices (GLP), Good Manufacturing Practices (GMP)).

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

*{End sample text}*

# Ethics/Protection of Human Subjects

## Ethical Standard

<Insert Text>

*Include in this section the guiding ethical principles being followed by the study.*

*{Begin sample text}*

The investigator will ensure that this study is conducted in full conformity with Regulations for the Protection of Human Subjects of Research codified in 45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56, and/or the ICH E6.

*{End sample text}*

*If the study is conducted at international sites, the statement could be as above and/or could reference compliance with the Declaration of Helsinki, Council for International Organizations of Medical Science (CIOMS), International Ethical Guidelines for Biomedical Research Involving Human Subjects (2002), or another country’s ethical policy statement, whichever provides the most protection to human subjects.*

## Institutional Review Board

<Insert Text>

*Each participating institution must provide for the review and approval of this protocol and the associated informed consent documents and recruitment material by an appropriate IRB registered with the OHRP. Any amendments to the protocol or consent materials must also be approved before they are placed into use. In the US and in other countries, only institutions holding a current US Federal-wide Assurance issued by OHRP may participate.*

*{Begin sample text}*

The protocol, informed consent form(s), recruitment materials, and all participant materials will be submitted to the IRB for review and approval. Approval of both the protocol and the consent form must be obtained before any participant is enrolled. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. All changes to the consent form will be IRB approved; a determination will be made regarding whether previously consented participants need to be re-consented.

*{End sample text}*

## Informed Consent Process

*The following subsections should describe the procedures for obtaining and documenting informed consent of study participants. State if a separate screening consent will be used. If a separate screening consent will not be used, the study consent must be signed prior to conducting study screening procedures.*

*In obtaining and documenting informed consent, the investigator should comply with applicable regulatory requirements and should adhere to 45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56, and/or ICH GCP. Prior to the beginning of the trial, the investigator must have the IRB’s written approval for the protocol and the written informed consent form(s) and any other written information to be provided to the participants.*

### Consent/Assent and Other Informational Documents Provided to Participants

<Insert Text>

*This section should demonstrate that the consent form contains all required regulatory elements. List all consent documents and materials submitted with this protocol. Include consent and/or assent forms, printed or web-based materials, phone scripts and any other related material.*

*If needed, describe special documents or materials (e.g., Braille, another language, audio recording)*

*{Begin sample text}*

Consent forms describing in detail the study agent, study procedures, and risks are given to the participant and written documentation of informed consent is required prior to starting intervention/administering study product. The following consent materials are submitted with this protocol <insert list>.

*{End sample text}*

### Consent Procedures and Documentation

<Insert Text>

*Describe how informed consent will be administered. Describe who will obtain consent (using roles, not names) and how the process of informed consent will be structured to be conducive to rational and thoughtful decision making by the subject/subject’s legally authorized representative. Include information such as:*

* *Where the consent process will take place*
* *How subject privacy will be assured*
* *Whether subjects will be permitted to provide consent at the time of the consent discussion or whether they will be required to come back to provide written informed consent*
* *How the investigators will ensure that subjects comprehend the nature of the study*
* *Steps that will be taken to avoid coercion*

*If the protocol involves multiple consenting sessions, or multiple informed consent forms, describe this information and the associated procedures in detail. If a sample informed consent form is provided in an appendix to the protocol, state so here.*

*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. This section should be consistent with Section 5.3, Vulnerable Subjects when describing consent plans and special considerations for children or other vulnerable participants.*

*If not all subjects will have the capacity to give informed consent, describe how capacity will be assessed. Describe the anticipated degree of impairment relative to their ability to consent to participate in research. Research with persons who have diminished capacity is allowed only for minimal risk or direct benefit studies.* *Clearly document that the investigator has an adequate plan in place to assure an acceptable level of comprehension before consent is obtained. If children and/or decisionally impaired adults will be subjects, include a specific plan to assess comprehension during assent (the subject’s agreement).*

*The PI is responsible for ensuring that valid consent is obtained and documented for all subjects. Specifically describe how consent will be documented and how/where documentation will be stored.*

*{Begin sample text}*

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. Extensive discussion of risks and possible benefits of participation will be provided to the participants and their families. Consent forms will be 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. All participants will receive a verbal explanation in terms suited to their 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 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. The participants may withdraw consent at any time throughout the course of the trial. A copy of the signed informed consent document will be given to the participants for their records. 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.

A copy of the signed informed consent document will be stored in the subject’s research record. The consent process, including the name of the individual obtaining consent, will be thoroughly documented in the subject’s research record. Any alteration to the standard consent process (e.g. use of a translator, consent from a legally authorized representative, consent document presented orally, etc.) and the justification for such alteration will likewise be documented.

*{End sample text}*

## Vulnerable Populations

### Adults without Capacity to Consent

*Summarize how the disorder, condition or factor that prevents the individual from having capacity to consent is an intrinsic characteristic of the research population such that the research could not otherwise be conducted on subjects who have capacity. Provide evidence that the use of such a procedure or intervention presents a reasonable opportunity to further the understanding of the etiologist, prevention, diagnosis, pathophysiology, or alleviation or treatment of a condition or disorder.*

*Note that for research in which recruitment of individuals with impaired consent capacity is not expected at the time of IRB submission, judgment that prospective subjects have the capacity to consent to the research can ordinarily be made informally during routine interactions with the individual during the consent process. An investigator who questions a prospective subject’s capacity to consent may not enroll the individual and should consult with the IRB.*

### Assessment of Capacity

Assessment of capacity will be done by *{choose one: licensed MDs with experience treating this patient population or other licensed clinicians (e.g. social workers, nurses) with experience treating this patient population}*. The assessors are *{choose one:}* independent of the study team or study team members that are identified in Research Navigator *{or}* do not need to be independent because *{explain}.*

The individual performing the assessment and/or monitoring ongoing capacity will perform *{name of tool or assessment}*. *The IRB recommends use of assessments commonly used in clinical care to assess capacity to consent for their own clinical care. If no specific tool would be used, state this and explain why.*

The results of the capacity assessment *{choose one:}* will/will not be placed in the subject’s medical record. *{If results will be placed in the medical record, add:}* Prospective subjects will be informed that the results of the assessment may be added to their medical record and that this may affect their subsequent medical care. *{If results will not be placed in the medical record, explain why}. Note that where the reason for lack of capacity is mental illness, New York State law requires that a psychiatrist or licensed psychologist document this determination in the individual’s medical record in a signed and dated progress note [New York State Public Health Law 2994-C].*

Prospective subjects will be informed of the results of the capacity assessment after it’s conducted. If an individual is found not to have the capacity to consent, the assessor will explain this to the individual. The assessor will provide the necessary resources and referrals for further care and evaluation.

*For multi-site research with sites outside of New York State, who are relying on NYULH IRB, state that a description of the site-specific plan to enroll subjects who lack capacity and assess capacity as indicated will be submitted with each site approval, and the description will indicate how state-specific laws or requirements impact the enrollment of this population. Submit this description as a separate site-specific addendum in the site record*

### Surrogate Consent

Surrogate order will be followed in order of priority: court appointed LAR, health care proxy, spouse if not legally separated from subject – or domestic partner-/adult son or daughter, parent, grandparent, adult grandchild who maintains regular contact with subject as to be familiar with subject’s activities, health, or beliefs).

*For multi-site research with sites outside of New York State, who are relying on NYULH IRB, state the site-specific order of priority, if different than above.*

The surrogate will be informed that the prospective subject was invited to take part in the study, that a capacity

assessment was conducted, and that the subject was determined to lack the capacity to provide informed

consent. The surrogate will be informed whether or not the result will be added to the subject’s medical record

or impact their clinical care. The surrogate will then be given a description of the nature of the research and

asked if they agree to provide consent on behalf of the incapacitated subject.

*{Choose one:}* Before the surrogate signs the consent, the subject will be informed of the surrogate’s identity if

not already aware and will be given the chance to assent. Subjects who object to the capacity assessment,

surrogate, or participation will not be enrolled, unless required by law. *{or}* The subject population will not have

or is unlikely to have the ability to communicate, to be informed of the identity of the surrogate, or to assent to

participation in the research.

### Ongoing Assessment of Capacity

*{Choose one:}* At each study visit, subjects will have direct interaction with the licensed clinicians referenced above. If the licensed clinicians have any concerns about the subject’s capacity, a formal capacity assessment will be conducted as described above. *{or}* At each study visit, subjects will have a formal capacity assessment to determine whether there has been any change in their capacity to assent or provide consent.

Over the course of the study, it is possible that a subject who had capacity at enrollment may lose capacity or capacity may fluctuate. A surrogate will be proactively identified at the time of enrollment and the study team will remain in contact with the surrogate over course of study. The PI will take steps to ensure people with some decisional impairment make a voluntary and informed decision. Such steps include involvement of a trusted individual in the decision-making process, allocation of additional time for the consent process, waiting periods after initial discussion before enrollment, repetitive teaching, oral or written recall tests, and / or audiovisual presentations, or group sessions.

*{Add the following statements, as applicable:}*

Subjects who regain capacity will be re-consented with the latest consent version and informed of all research procedures performed to date and all research procedures that remain to be performed. Subjects will have the opportunity to continue in or withdraw from study.

Subjects who lose capacity will continue in the study only if their LAR is consented.

Subjects who lose capacity and do not have surrogate consent by an LAR will be withdrawn.

Subjects who appear to be unduly distressed will be withdrawn from the research in a manner consistent with

good clinical practice.

Regular communication with the surrogate will be maintained.

## Posting of Clinical Trial Consent Form

Use only if your study is required to post a consent form to clinicaltrials.gov. This section will describe plans for ensuring compliance with Federal Regulations 45 CFR 46.116(h) for clinical trials. Indicate whether:

* the awardee or the Federal department or agency component conducting the trial will post the IRB-approved informed consent form used to enroll subjects on the publicly available Federal website.
* the Federal department or agency supporting or conducting the clinical trial determines that certain information should not be made publicly available on a Federal website (e.g. confidential commercial information), such Federal department or agency may permit or require redactions to the information posted

State that the informed consent form will be posted on the Federal website after the clinical trial is closed to recruitment, **and no later than 60 days after the last study visit by any subject**, as required by the protocol.

<Insert Text>

## Participant and Data Confidentiality

<Insert Text>

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

*Include procedures for maintaining participant confidentiality, any special data security requirements, and record retention per the sponsor’s requirements. Describe who would have access to records, including the investigator and other study staff, the clinical monitor, funding institutions, IND sponsor, representatives of NIH IC, representatives from the IRB, 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 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).*

*For some studies, it may be necessary to obtain a Certificate of Confidentiality. A Certificate of Confidentiality provides protection to researchers and research institutions from being forced to provide identifying information on study participants to any federal, state or local authority. Authorization comes from NIH through section 301 (d) of the Public Health Service Act (42 U.S.C. 241 (d)) which provides the Secretary of Health and Human Services the authority to protect the privacy of study participants.*

*{Begin required text}*

Information about study subjects will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). Those regulations require a signed subject authorization informing the subject of the following:

* What protected health information (PHI) will be collected from subjects in this study
* Who will have access to that information and why
* Who will use or disclose that information
* The rights of a research subject to revoke their authorization for use of their PHI.

In the event that a subject revokes authorization to collect or use PHI, the investigator, by regulation, retains the ability to use all information collected prior to the revocation of subject authorization. For subjects that have revoked authorization to collect or use PHI, attempts should be made to obtain permission to collect at least vital status (i.e. that the subject is alive) at the end of their scheduled study period.

*{End required text}*

*{Begin suggested text}*

Participant confidentiality is strictly held in trust by the participating investigators, their staff, and the sponsor(s) and their agents. 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.

The study monitor, other authorized representatives of the sponsor, representatives of the IRB 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 local IRB and Institutional regulations.

Study participant research data, which is for purposes of statistical analysis and scientific reporting, will be transmitted to and stored at NYU Langone Medical Center. 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 NYU Langone Medical Center 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 NYU Langone Medical Center.

*{Additional text for Certificate of Confidentiality}*

To further protect the privacy of study participants, a Certificate of Confidentiality will be obtained from the 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.

*{Additional text for NIH Data Sharing Policy for Genome-Wide Association Studies (GWAS)}*

This study is a genome-wide association study and will comply with the NIH Policy for Sharing of Data Obtained in NIH Supported or Conducted GWAS, which calls for investigators funded by the NIH for GWAS to 1) share de-identified genetic (genotypic and phenotypic) data through a centralized NIH data repository; and 2) submit documentation that describes how the institutions have considered the interests of the research participants, such as privacy and confidentiality. Submission of data to the NIH GWAS repository will be consistent with the permissions and limitations delineated on the study consent signed by study participants.

*{End suggested text}*

### Research Use of Stored Human Samples, Specimens, or Data

<Insert Text>

*This section should address each of the items listed below:*

* *Intended use of stored samples, specimen or data.*
* *Storage: State whether samples or data will be retained, list type of samples and location of storage.*
* *Tracking: Describe method of tracking, such as the name of the software tracking program or other logging/tracking method*
  + *Disposition at the completion of the study: Describe the disposition of the specimens*
  + *Approach for responding to requests from participants for destruction of samples (if applicable)*

*{Begin sample text}*

* Intended Use: Samples and data collected under this protocol may be used to study <specify condition>. No genetic testing will be performed.
* Storage: Access to stored samples will be limited using <specify approach>. Samples and data will be stored using codes assigned by the investigators. Data will be kept in password-protected computers. Only investigators will have access to the samples and data.
* Tracking: Data will be tracked using <specify approach>.
  + Disposition at the completion of the study: All stored samples will be sent to a <specify repository>. Study participants who request destruction of samples will be notified of compliance with such request and all supporting details will be maintained for tracking.

*{End sample text}*

## Future Use of Stored Specimens

<Insert Text>

*If residual specimens will be maintained 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:*

1. *location(s), if other than the clinical site, where specimens or other data will be maintained,*
2. *how long specimens or other data will be stored (specify number of years, indefinitely, or until used up),*
3. *if the site's IRB will review future studies,*
4. *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),*
5. *purpose of future research (or if unknown, state “unknown at this time”),*
6. *whether participation in the storage of specimens is optional and if not, provide a justification*

*Include a statement that genetic testing will or will not be performed.*

*See also Section 13.4, Participant and Data Confidentiality and Section 14.2, Study Records Retention, for further information on future use of study records.*

*{Begin sample text}*

Data collected for this study will be analyzed and stored at the <specify name of 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>, under the supervision of <insert name>, 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 IRs, 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 for research into 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 masking 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 will 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>.

*{End sample text}*

# Data Handling and Record Keeping

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

## Data Collection and Management Responsibilities

<Insert Text>

*Provide details regarding the type(s) of data capture that will be used for the study. Specify whether it will be paper or electronic, distributed or central, batched or ongoing processing, and any related requirements. Indicate expectations for time for submission of CRFs. Further details should be provided in the MOP.*

*Briefly describe steps to be taken to ensure that the data collected are accurate, consistent, complete, and reliable and in accordance with ICH E6. The MOP or a separate data management plan will provide detailed descriptions of source documentation, CRFs, instructions for completing forms, data handling procedures, and procedures for data monitoring.*

*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 DCC. Information should include the role in data collection, review of data, trial 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.*

*Indicate the roles of each party with regard to interpretation of data, plans for analysis, review of tables and listings, and plans for reporting.*

*{Begin sample text}*

Data collection is the responsibility of the clinical trial staff at the site under the supervision of the site PI. 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. Black ink is required to ensure clarity of reproduced copies. When making changes or corrections, cross out the original entry with a single line, and initial and date the change. DO NOT ERASE, OVERWRITE, OR USE CORRECTION FLUID OR TAPE ON THE ORIGINAL.

Copies of the electronic CRF (eCRF) will be provided for use as source documents and maintained for recording data for each participant enrolled in the study. Data reported in the eCRF derived from source documents should be consistent with the source documents or the discrepancies should be explained and captured in a progress note and maintained in the participant’s official electronic study record.

Clinical data (including 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 DCC>. 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.

*{End sample text}*

### Data Collection Tools – Mobile Health Technology

Please consult the Institutional Review Boards’ Guidance on Research with Digital Data Collection Tools, available in the IRB Template Library. Contact MCIT in advance if you intend to use novel technology, applications, or software as indicated in the guidance.  
*{Begin Sample Text}***Products and Device**

The commercial product(s) made by Name third party companies, List name of product (wearable fitness trackers, wearable sleep monitors, mobile apps for use on smartphone and tablets, websites and web apps, and types of computer software) permit pick as applicable screen sharing, record keystrokes, gain access to device files and/or use location tracking technology will be used to collect study data. These devices will be used in accord with the Terms of Service and/or the End User License Agreements (EULA) provided by the product or device vendor. These products and devices will only be used to collect study data with IRB approval and if the subject has agreed to all applicable Terms of Service.

If applicable add

This product(s) may be owned by the participant or provided to the participant by the study team/ mobile health platform.

## Study Records Retention

<Insert Text>

*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. For NIH, grantees must retain records for a period of three years from the date of Federal Financial Report (FFR) submission.*

*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.*

*For non-FDA regulated studies, summarize the record retention plan applicable to the study (taking into account any applicable NYULMC Department, Division or Research Center requirements, or applicable funding sponsor requirements.) The general rule is to retain research data for the longer of 3 years after close-out or 5 years after final reporting/publication, but there are different exceptions that apply to IRB-reviewed research, PHI and FDA studies (among other categories). See Retention of and Access to Research Data Policy at:* [*https://central.nyumc.org/policiesprocedures/Pages/Research.aspx*](https://central.nyumc.org/policiesprocedures/Pages/Research.aspx)

*Investigational product records may be addressed here if not addressed elsewhere in the protocol.*

*{Begin sample text}*

Study documents will be retained for the longer of 3 years after close-out, 5 years after final reporting/publication, or 2 years after the last approval of a marketing application is approved for the drug for the indication for which it is being investigated or 2 years after the investigation is discontinued and FDA is notified if no application is to be filed or if the application has not been approved for such indication. No records will be destroyed without the written consent of the sponsor, if applicable. It is the responsibility of the sponsor to inform the investigator when these documents no longer need to be retained.

*{End sample text}*

## Protocol Deviations

<Insert Text>

*Plans for detecting, reviewing, and reporting deviations from the protocol should be described. A statement should be included to indicate that deviations are not allowed, unless a statement is included in the investigator agreement. Provisions for approval of deviations can be described.*

*{Begin sample text}*

A protocol deviation is any noncompliance with the clinical trial protocol, GCP, or Manual of Procedures (MOP) requirements. The noncompliance may be either on the part of the participant, the investigator, or the study site staff. As a result of deviations, corrective actions are to be developed by the site and implemented promptly.

These practices are consistent with ICH E6:

* 4.5 Compliance with Protocol, sections 4.5.1, 4.5.2, and 4.5.3
* 5.1 Quality Assurance and Quality Control, section 5.1.1
* 5.20 Noncompliance, sections 5.20.1, and 5.20.2.

It is the responsibility of the site PI/study staff to use continuous vigilance to identify and report deviations within <specify number> working days of identification of the protocol deviation, or within <specify number> working days of the scheduled protocol-required activity.

All protocol deviations must be addressed in study source documents, reported to <specify NIH IC> Program Official and <specify DCC>.

Protocol deviations must be reported to the local IRB per their guidelines. The site PI/study staff is responsible for knowing and adhering to their IRB requirements. Further details about the handling of protocol deviations will be included in the MOP.

*{End sample text}*

## Publication and Data Sharing Policy

<Insert Text>

*The publication and authorship policies should be established and clearly outlined 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. Please refer to your specific contract grant and/or Clinical Trials Agreements. If details of the publication policy will be described in the study’s MOP, refer to it here. Where applicable, the study must comply with the NIH Public Access Policy, the Food and Drug Administration Amendments Act of 2007 (FDAAA), and ClinicalTrials.gov. At the end of the study, the PI will make results of the research available to the research community and public at large. For policies relating to NIH-funded studies, refer to NIH Grants Policy Statement Section 8.2.*

*{Begin sample text}*

This study will comply with the NIH Public Access Policy, which ensures that the public has access to the published results of NIH funded research. It requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to the digital archive PubMed Central upon acceptance for publication.

The International Committee of Medical Journal Editors (ICMJE) member journals have adopted a clinical trials registration policy as a condition for publication. The ICMJE defines a clinical trial as any research project that prospectively assigns human subjects to intervention or concurrent comparison or control groups to study the cause-and-effect relationship between a medical intervention and a health outcome. Medical interventions include drugs, surgical procedures, devices, behavioral treatments, process-of-care changes, and the like. Health outcomes include any biomedical or health-related measures obtained in patients or participants, including pharmacokinetic measures and adverse events. The ICMJE policy, and the Section 801 of the Food and Drug Administration Amendments Act of 2007, requires that all clinical trials be registered in a public trials registry such as ClinicalTrials.gov, which is sponsored by the National Library of Medicine. Other biomedical journals are considering adopting similar policies. For interventional clinical trials performed under NIH IC grants and cooperative agreements, it is the grantee’s responsibility to register the trial in an acceptable registry, so the research results may be considered for publication in ICMJE member journals. The ICMJE does not review specific studies to determine whether registration is necessary; instead, the committee recommends that researchers who have questions about the need to register err on the side of registration or consult the editorial office of the journal in which they wish to publish.

FDAAA mandates that a "responsible party" (i.e., the sponsor or designated principal investigator) register and report results of certain "applicable clinical trials":

* Trials of Drugs and Biologics: Controlled, clinical investigations, other than Phase I investigations of a product subject to FDA regulation;
* Trials of Devices: Controlled trials with health outcomes of a product subject to FDA regulation (other than small feasibility studies) and pediatric postmarket surveillance studies.
* NIH grantees must take specific steps to ensure compliance with NIH implementation of FDAAA.

*{End sample text}*

# Study Finances

## Funding Source

<Insert Text>

*This section should describe how the study will be financed, but should not contain specific dollar amounts (e.g. “This study is financed through a grant from the US National Institute of Health”, or “… a grant from the American Heart Association”, etc.) If referral treatments or counseling will be provided, note how the cost of the counseling or referral services will be paid.*

## Costs to the Participant

<Insert Text>

*Describe and justify any costs that the participant will incur as a result of participating in the study. This section should clarify who will pay for procedures associated with the study (ex. agency grant versus departmental funds). Normally, participants should not have to pay for research procedures without direct benefit. No charge may be made to participants if the costs are covered by a grant, contract, or other payment method.*

## Participant Reimbursements or Payments

<Insert Text>

*If participants will be compensated or provided any incentives (e.g. vouchers, iPads) for study participation, describe amount, form and timing of any such compensation in relation to study activities (include financial and non-financial incentives). List the prerequisite condition(s) that must be fulfilled by subjects to receive these payments. The amount must be justified and not constitute undue inducement of the subject to participate in the research or to continue beyond a point that they would have otherwise withdrawn. Note: The IRB requires a prorated system for financial payments. This means that payments are accrued as the study progresses and that participants do not have to complete the entire study to be eligible to receive a payment. This is to protect the subject’s right to withdraw without penalty. Describe who will receive incentives (if not the participant). For example, for minors, state whether the minor or the parent/guardian will receive the incentive. If incapacitated adult, state if the incentive will be provided to the participant or to a guardian.*

*If there are none, either delete this section or state that there are no participant reimbursements or payments.*

*Examples of reimbursements and payments:*

* *Reimbursement for time, travel, parking, meals, etc.*
* *Gifts- any tokens of appreciation given to a research subject, or their family, should be described here*
* *Payment to the subject for time, effort or inconvenience of being in the study*
* *Payment to subject family for time, effort or inconvenience of assisting a family member being in the study*

# Study Administration

*The following subsections should describe the governance of the study and its committee structure. Alternately, this section may describe the role of the study team, its composition (e.g., those listed in Section 1, Key Roles) and describe how study decisions and progress are communicated and reported. Some example text is provided below.*

## Study Leadership

<Insert Text>

*Include content in this section if applicable or rename for the appropriate study leadership body (e.g.: Steering Committee, Executive Committee, Subcommittee, Study Team), otherwise note as not-applicable. This section should reflect the entire scope of the study leadership.*

*{Begin sample text}*

The Steering Committee will govern the conduct of the study. The Steering Committee will be composed of the Study Chairman, the PI of the Coordinating Center, representatives of <sponsoring NIH IC>, the PI of the clinical sites, chairperson of the Study Coordinators subcommittee, and the PI of the Central Biochemistry Laboratory. The Steering Committee will meet in person at least annually.

*{End sample text}*

# Conflict of Interest Policy

<Insert Text>

*This section should include a description of how the study will manage actual or perceived conflicts of interest. All NYUSoM Investigators will follow the applicable* [*Conflict of Interest policies related to research*](file:///\\homedir.nyumc.org\users\home005\wallad04\Personal\Conflict%20of%20Interest%20policies%20related%20to%20research)*. See:* [*https://nyumc.ellucid.com/documents/view/1119*](https://nyumc.ellucid.com/documents/view/1119)

*{Begin sample text}*

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 trial 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 trial. The study leadership in conjunction with the <specify NIH IC> has established policies and procedures for all study group members to disclose all conflicts of interest and will establish a mechanism for the management of all reported dualities of interest.

Any investigator who has a conflict of interest with this study (patent ownership, royalties, or financial gain greater than the minimum allowable by their institution, etc.) must have the conflict reviewed by the NYU Langone Conflict of Interest Management Unit (CIMU) with a Committee-sanctioned conflict management plan that has been reviewed and approved by the study sponsor prior to participation in this study. All NYULMC investigators will follow the applicable conflict of interest policies.

*{End sample text}*

# References

*This is the bibliography section for any information cited in the protocol. It should be organized as any standard bibliography.*

1. Author, Title of work, periodical and associated information.
2. Author, Title of work, periodical and associated information.

# Attachments

These documents are relevant to the protocol, but they are not considered part of the protocol. They are stored and modified separately. As such, modifications to these documents do not require protocol amendments.

*This section should contain all pertinent documents associated with the management of the study. The following lists a few examples of potential attachments:*

* Investigator Agreement (for any investigator, other than sponsor-investigator, who participates in the study)
* Sample Consent Form
* Study Procedures Flowchart/Table
* Study Monitoring Plan
* Core Lab Instructions To Investigators
* Specimen Preparation And Handling (e.g. for any specialized procedures that study team must follow to process a study specimen, and/or prepare it for shipment)
* Drug Conversion Plan (e.g. if there is a special regimen for transitioning a subject from their baseline medication over to study medication)
* Antidote Preparation and Delivery (e.g. special instructions for preparing and delivering any therapy designed to reverse the effects of the study drug, if applicable)

# Schedule of Events

[Guidance and example use noted in blue]

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Activity** | **Visit Name**  [Day or Mo #,  Window] | **Visit Name**  [Day or Mo #,  Window] | **Visit Name**  [Day or Mo #,  Window] | **Visit Name**  [Day or Mo #,  Window] | **Visit Name**  [Day or Mo #,  Window] | Visit Name  [Day or Mo #,  Window] |
| **Study team procedures** |  |  |  |  |  |  |
| Consent | X |  |  |  |  |  |
| Medical History | X |  |  |  |  |  |
| Physical Exam | X |  | X |  | X |  |
| Height | X |  |  |  |  |  |
| Weight | X |  | X |  | X |  |
| Vitals signs | X |  | X |  | X |  |
| Randomization |  | X |  |  |  |  |
| Study drug/device dispensation |  | X |  |  |  |  |
| Participant study drug/device compliance check |  |  | X | X | X | X |
| Subject Survey |  |  | X |  |  | X |
| ***Cardiology assessments*** |  |  |  |  |  |  |
| Electrocardiogram | X |  | X |  | X |  |
| Doppler flow echo cardiogram | X |  |  |  |  |  |
| ***Laboratory Assessments*** |  |  |  |  |  |  |
| Chemistry panel | X |  | X |  | X |  |
| CBC with differential | X |  | X |  | X |  |
| AST and ALT | X |  | X |  | X |  |
| ***Imaging Assessments*** |  |  |  |  |  |  |
| Chest X-ray | X |  |  |  |  |  |