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| Template Version 1.4, 6/9/2023    **GENERAL INSTRUCTIONS** – delete this box from the submitted Protocol  This template is for investigators at Boston Medical Center and Boston University Medical Campus who are preparing a detailed protocol. A detailed protocol is required to be attached to the INSPIR submission for initial review of studies that are clinical trials involving medical or surgical interventions, or for any type of investigator-initiated, multi-site clinical trial or clinical trial with NIH funding (see Section [7.2.2.20](https://www.bumc.bu.edu/ohra/hrpp-policies/hrpp-policies-procedures/#_Protocol_Requirements)). *If you have a protocol from an external sponsor or cooperative group, attach that protocol to the INSPIR submission and do not use this template.* Investigators may also choose to use this template for studies that are not clinical trials. For further guidance and example text for any of the sections in this template, please also review the [NIH-FDA Phase 2 and 3 IND/IDE Clinical Trial Protocol Template.](https://osp.od.nih.gov/wp-content/uploads/Protocol-Template-Version-1.0-040717.docx)  Use this template to create a study protocol as follows:   * Red text represents instructions to you – to be deleted from the final version * Blue text represents guidance on suggested content – to be edited and changed to black or replaced with black in the final version. * Black text represents text that should ordinarily be incorporated as-is, if applicable * Green text represents definitions to be used for guidance – to be deleted from the final version   Note that the table of contents is automatically included, so do not change the content or formatting of the headings. Be sure to right click on the table of contents and select “Update field” as the last step before saving the protocol and uploading it to the INSPIR application.  Please make sure to complete the header on this page with the protocol title and version number and date.    The submitted protocol should have no red, green, or blue text (including the header and instruction boxes like this one). |

**PROTOCOL TITLE**

**Protocol Version Number:** Complete

**Protocol Version Date:** day, month, year

**ClinicalTrials.gov number:** Complete – may say “Pending” if number is not yet assigned or “None” if the study will not be registered

**Funding Mechanism:** organization and grant or contract # - may say “Internally Funded” if no external funder

[Include if there is industry support; otherwise, delete heading] **Industry Support provided by:** name of industry

[Include if the study involves an IND or IDE and choose IND or IDE; otherwise, delete heading] **IND / IDE Sponsor:** name of the person who holds the IND or IDE

[Include if the study involves an IND or IDE and choose IND or IDE; otherwise, delete heading] **IND / IDE number:** Complete

**Principal Investigator:** name

**Phone:** Complete

**E-mail:** Complete

[Include if the study has a medical monitor; otherwise, delete heading] **Medical Monitor:** name

**CONFIDENTIAL**

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**Summary of Changes:**

The table should summarize changes of IRB-approved versions of the protocol, including a description of the change and rationale.

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| --- | --- | --- | --- |
| **Version** | **Date** | **Description of Change** | **Brief Rationale** |
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# List of Abbreviations

[Complete this table with all disease or study-specific abbreviations/acronyms. Add rows as needed]

|  |  |
| --- | --- |
| **Abbreviation** | **Abbreviation definition** |
|  |  |

# Protocol Summary

Limit to 1-2 pages

|  |  |
| --- | --- |
| **Title:** | Study title. |
| **Population:** | Study population, sample size, sex, age, vulnerable populations if any. |
| **Intervention:** | For drugs: name, dose, route of administration, regimen; for other interventions: name, method, timing. |
| **Objectives:** | Study objectives. |
| **Design/Methodology:** | Study arms, randomization, schedule of interventions and assessments. You may refer to a detailed schematic, table of visits and assessments, and/or other visual representation of the study design in the Appendix. |
| **Total Study Duration:** | Time from when the study opens to enrollment until completion of data analysis |
| **Subject Participation Duration:** | Time it will take to conduct the study for each individual participant. |

# Background/Rationale & Purpose

## Background Information

Include as appropriate:

* A brief description of the health condition or research question that the study will address
* The name and description of the study intervention/investigational product
* Discussion of important research and literature (cite references and list them in Section 16) and current practice that provides background and scientific justification for the study and applicable clinical, epidemiological, or public health background or context of the study
* Known risks and potential benefits (briefly, these are addressed in detail later in the protocol)
* Importance of the study and any relevant treatment issues or controversies
* Any pertinent pre-clinical data and prior experience with intervention

This study will be conducted in compliance with the protocol, applicable regulatory requirements, and policies and procedures of the Boston Medical Center and BU Medical Campus Human Research Protection Program [insert if there is an external IRB of record; otherwise delete] and of the name of IRB of record.

## Rationale and Purpose

Describe why it makes sense to do this study and the importance/value of the information to be gained. Provide information on the current standard of care for the condition under investigation and why this study intervention/product could represent an improvement, if appropriate. Describe what is innovative or new and useful about the potential solutions including any new and enabling ideas or technologies, new approaches, and/or unique resources developed or that will be accessed. Provide justification for the proposed use of the intervention in this manner and within the study population. Describe the rationale for the type and selection of control, if there is one (e.g. placebo, active drug, dose-response, historical) and study design (e.g., non-inferiority as opposed to superiority). Include a statement of the hypothesis.

# Objectives

## Study Objectives

Provide a detailed description of the one primary objective and any secondary and (if applicable) exploratory 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). Secondary objectives are goals that will provide further information on the use of the intervention. Exploratory objective(s) serve as a basis for explaining or supporting findings of primary analyses and for suggesting further hypotheses for later research.

Express each objective as a statement of purpose (e.g., to assess, to determine, to compare, to evaluate). Remember to include an objective related to safety, if the study involves greater than minimal risk.

## Study Outcome Measures

The sections below should include the methods for assessing how the objectives are met.

An outcome measure is a specific measurement or observation used to assess the effect of the study intervention. Outcome measures should be prioritized and should correspond to the study objectives and hypotheses being tested. Give succinct but precise definitions of the outcome measures used to address the study’s primary objective and key secondary objectives (e.g., specific laboratory tests that define safety or efficacy, clinical assessments of disease status, assessments of psychological characteristics, assessments of individual or group oral health behaviors, assessments of healthcare visit attendance, etc.), and briefly explain why they were chosen. Include the study visits or time points at which data will be recorded or samples will be obtained.

### Primary Outcome Measures

Generally, there should be just one primary outcome measure that will provide a clinically relevant, valid, and reliable measure of the primary objective. The primary outcome measure is the basis for concluding that the study met its objective, and its importance and role in the analysis and interpretation of study results should be defined.

### Secondary Outcome Measures

List additional outcome measures. Secondary outcome measures are those that may provide supportive information about the study intervention’s effect on the primary objective or demonstrate additional effects on the disease or condition. Secondary outcome measures may include, for example, endpoints related to efficacy, safety, or both.

### Exploratory Outcome Measures

List exploratory outcome measures, if any. Exploratory outcome measures may include clinically important events that are expected to occur too infrequently to show a treatment effect or outcome measures that for other reasons are thought to be less likely to show an effect but are included to explore new hypotheses. If there are no exploratory outcome measures, state this.

# Study Design

The scientific integrity of the trial and the credibility of the data from the trial depend substantially on the trial design. This section should include, as applicable (but not be limited to):

* A brief description of the type/design of trial to be conducted (e.g., randomized, placebo-controlled, masking, parallel group, cross-over, open-label, dose-escalation, dose-ranging)
* A description of the randomization process if applicable
* A description of the study population (e.g., healthy/sick, inpatient/outpatient, demographic groups). Do not list detailed inclusion/exclusion criteria here, as these will be listed in later sections.
* A brief discussion of the rationale for design features
* Phase of trial, if applicable
* The number of study groups/arms and descriptions
* Planned variation in intervention dose or schedule (e.g., dose escalation)
* A brief summary of methods for collecting data for assessment of study objectives
* Other protocol-specific details, such as centralization of evaluations (e.g., central laboratory or central reading center for clinical scans)

[Include if a schematic of the study design is in the Appendix; otherwise, delete sentence] See the Appendix for a schematic of the study design.

# Potential Risks and Benefits

## Risks

Describe in detail any reasonably foreseeable physical, psychological, social, legal, economic, or any other anticipated risks to study subjects. Include risks of study intervention and other study procedures. Describe procedures to minimize risks.

One or more of the following may serve as the source of risk information:

* Package insert for a licensed product
* Device brochure for a marketed device
* Investigator’s Brochure (IB) for an investigational product or device
* Preclinical data reports
* Literature search and review (cite references and list them in Section 16)

## Potential Benefits

Describe the potential physical, psychological, social, legal, or any other anticipated benefits to subjects. Even if the study may not provide direct benefit to subjects, the importance of the knowledge that may result from the study must be described. Note: Compensation to subjects is not considered a “benefit.”

## Analysis of Risks in Relation to Benefits

Describe how risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result.

# Study Subject Selection

## Subject Inclusion Criteria

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

* Inclusion criteria; if there are multiple cohorts, stratify into separate groups

## Subject Exclusion Criteria

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

* Exclusion criteria; do not duplicate what is already listed in the Inclusion criteria above. Exclusion criteria are criteria that would exclude a potential subject even if they met all of the inclusion criteria. If no exclusion criteria, say “None.”

# Study Intervention

The study intervention may involve an investigational drug or device, an approved drug or device, a behavioral intervention, and/or a surgical or other intervention. Provide a detailed description of the intervention, including any placebo or other control interventions. If this is study does not involve an intervention, please state “None.”

If the study is testing drug/biologic(s) include the following:

* A justification for the route of administration, planned maximum dosage, and dosing regimen, including starting dose, of the study intervention(s) and control product(s), as applicable.
* How the study product will be acquired
* The formulation, packaging, and labeling of the product as supplied
* Product distribution, storage and stability
* Dosage, preparation, and administration
* Instructions for modification of dose due to toxicity or other reason.
* Accountability procedures and compliance assessment

If you are testing a drug/biologic and you are not certain whether the use of the drug/biologic requires

submission of an Investigational New Drug (IND) application to the FDA, please review the Decision Chart

[here](https://www.bumc.bu.edu/irb/files/2021/09/Flow-Diagram_Use-of-FDA-Regulated-Drug-or-Biologic-in-Human-Subjects-Research.pdf). If you determine that you think the use of this drug/biologic meets criteria for IND exemption under

21 CFR 312.2, please note that you will be required to attach a detailed justification to your INSPIR

Submission explaining how/why these criteria are met.

If the study is testing a device include the following:

* The name of the device
* Device size(s)
* Device model(s)
* Description of each component
* Device settings and programming (if applicable)
* Duration of implant or exposure (if applicable)
* Frequency of exposure (if applicable
* The manufacturer or supplier of the device
* Where the device will be stored
* Whether the device will be supplied at no cost

# Recruitment and Retention Procedures

### Recruitment Procedures

Describe methods for participant recruitment. The recruitment methods may be described broadly here in the protocol (for example, pre-screening of medical records and use of study flyers), but note that you will need to describe your recruitment methods in detail in the INSPIR application, and therefore you should be designing the specifics of your recruitment strategies now. The INSPIR application will ask you to indicate which of the following recruitment methods you will use, so please start thinking about these now (and delete the below table in the final protocol version). See more information on recruitment methods [**here**](https://wwwapp.bumc.bu.edu/ocr/ClinicalResearchNewsletter/article.aspx?article=882) and [**here**](https://www.bumc.bu.edu/crro/files/2023/05/CRRO-Seminar_May-2023_Recruitment-Best-Practices.pdf):

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Flyers/Brochures/Posters | Recruitment Company (BuildClinical, TrialSpark, etc) | Medical record/clinic schedule review of patients of PI/co-Is | Recruitment registries | Clinician referrals | Opt-out correspondence (letters, MyChart) with follow-up phone call |
| Advertisements (radio, tv, websites, social media) | Approval for re-contact in prior study consent form | Tabling/Community events | Inpatient recruitment | Approach at clinical appointment and/or waiting room | Use of Listservs (with approval from Listserv steward(s)) |

For multi-site studies, please also include a description of the type and number of recruitment sites (e.g., inpatient hospital setting, student health service, community center), and the anticipated number of participants to be recruited from each site.

### Retention Procedures

If the study requires long-term subject participation, describe procedures that will be used to enhance participant retention (e.g., multiple methods for contacting participants, visit reminders, incentives for visit attendance). If the study does not require long-term subject participation, state this.

# Screening Procedures

If the study will involve clinical screening procedures (such as fasting or blood draws) or the collection of information by direct contact with potential subjects prior to consenting them using the primary consent form for the study, describe those screening procedures. Describe the consent process for the screening procedures. The screening consent procedures may be described broadly here in the protocol, but note that you will need to describe your screening consent procedures in detail in the INSPIR application, and therefore you should be designing the specifics of the screening procedures now. If there are no such screening procedures, state this.

# Consent Procedures

Describe methods for obtaining informed consent. The consent procedures may be described broadly here in the protocol (for example, the consent process will take place at the first visit prior to any study procedures), but note that you will need to describe your consent procedures in detail in the INSPIR application, and therefore you should be designing the specifics of your consent procedures now.

# Study Procedures

[Include; a schedule of events that lists all visits/contacts and procedures at each visit/contact **must** be included in the Appendix] See the Appendix for the schedule of events.

Include a description of all study visits and all other contacts, such as telephone and/or email/text contacts. Include length of visits, whether visits are remote or in-person, and visit windows, considering feasibility and relevance of the time point to study outcome measures (e.g., pharmacokinetic 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).

Describe evaluations/procedures necessary to assess or confirm whether a subject will meet eligibility criteria and may be enrolled. Describe in detail all tests and procedures at follow-up visits. Include a table that lists visits and procedures at each visit, either in this section or as an appendix. Describe the final study visit as well as an early termination visit, as necessary.

Include the total study duration (anticipated time between the beginning of study activities to the completion of data analysis) and the subject participation duration (the time between enrollment and the end of study activities for an individual subject).

Describe all clinical and laboratory evaluations. Make sure to clarify as needed which procedures would happen anyway, if the subject were not in the research, and which procedures are happening due to the research. Any special handling, processing, or shipping of laboratory specimens should be described, including long-term storage for research purposes.

As appropriate, describe intervention-assignment procedures, randomization procedures, and reasons subjects may be withdrawn from the study without their consent. Describe any procedures necessary in the case of early termination or withdrawal of subjects.

If the study is blinded, describe procedures for masking, maintaining the blinding, and procedures for unblinding study intervention for a particular subject due to safety reasons.

# Assessment of Safety and Data Safety Monitoring Plan (DSMP)

## Definitions for Safety Assessment

[Edit if necessary to make these definitions specific to the study. Non-medical studies will require editing of the definition of Adverse Event. Include any specific provisions for pregnancy in female subjects and/or in female partners of male subjects.]

The following definitions will be used in the assessment of safety:

*Adverse Event (AE)*is any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject’s participation in the research, whether or not considered related to the subject’s participation in the research.

*Serious Adverse Event (SAE)* is any adverse event that

1. results in death;
2. is life-threatening;
3. results in inpatient hospitalization or prolongation of existing hospitalization;
4. results in a persistent or significant disability/incapacity;
5. results in a congenital anomaly/birth defect; or
6. based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition (examples of such events include allergic bronchospasm requiring intensive treatment in the emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse).

*Life-threatening* means that the event places the subject at immediate risk of death from the event as it occurred.

*Unanticipated Problem*is defined as an event, experience or outcome that meets **all three** of the following criteria:

* is unexpected; AND
* is related or possibly related to participation in the research; AND
* suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

*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

*Unexpected* means the nature, severity, or frequency of the event is not consistent with either:

* the known or foreseeable risk of adverse events associated with the procedures involved in the research that are described in (a) the protocol–related documents, such as the IRB-approved research protocol, any applicable investigator brochure, and the current IRB-approved informed consent document, and (b) other relevant sources of information, such as product labeling and package inserts; or
* the expected natural progression of any underlying disease, disorder, or condition of the subject(s) experiencing the adverse event and the subject’s predisposing risk factor profile for the adverse event.

[Include if the study involves a device; otherwise, delete definition]

*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.

## Safety Review

Both the risks listed in Section 4.1 and unknown risks will be monitored as follows: a description of what risks will be monitored, by whom, and how often; how Adverse Events will be evaluated for severity, seriousness, relatedness, and expectedness; how events that are not Adverse Events will be assessed for expectedness, relatedness, and suggesting new risks; when and how aggregate Adverse Events will be evaluated to determine whether there are trends that could affect subject safety; and when and how the blind may be broken to assess events/outcomes by study arm. If there is an independent monitoring committee (such as a Data and Safety Monitoring Board), you MUST also include a **charter document** as an appendix that describes the purposes and specific functions and processes of the safety monitoring entity.

### Multi-Site Safety Monitoring

If this is a multi-site study, describe plans for coordination of safety monitoring. Describe the processes for communication among sites concerning information relevant to the protection of participants, such as Serious Adverse Events, Unanticipated Problems, interim results, and protocol modifications. If this is not a multi-site study, state this.

## Reporting Plans

The below instructions and template language are for use in studies where the BMC/BU Medical Campus IRB is the IRB of record for the activities conducted at BMC/BU Medical Campus. For studies that are ceded to an external IRB, please ensure you modify the below as-needed to follow the reporting policies of the IRB of record. Please work with the study team from the IRB of record to create this section.

The Principal Investigator at BMC/BU Medical Campus will report Unanticipated Problems, safety monitors’ reports, and Adverse Events to the BMC/BU Medical Center IRB in accordance with IRB policies:

* Unanticipated Problems occurring at BMC/BU Medical Campus [include if this is a multi-site study and the BMC/BU Medical Campus IRB is the IRB of record; otherwise delete] and external sites will be reported to the BMC/BU Medical Campus IRB within 7 days of the investigator learning of the event.
* [include if there is no safety monitoring entity (such as a medical monitor or Data Safety Monitoring Board]; otherwise delete] Adverse Events (including Serious Adverse Events) will be reported in summary at the time of continuing review, along with a statement that the pattern of adverse events, in total, does not suggest that the research places subjects or others at a greater risk of harm than was previously known.
* [include the next two bullets if there is a safety monitoring entity (such as a medical monitor or Data Safety Monitoring Board]; otherwise delete both bullets] Reports from safety monitors with recommended changes will be reported to the IRB within 7 days of the investigator receiving the report.
* Reports from safety monitors with no recommended changes will be reported to the IRB at the time of continuing review.

[Include if multi-site study; otherwise delete] The Principal Investigators at name of external site(s) will additionally follow the reporting policies and procedures of their local IRB.

[Include if there is one or more safety monitoring entity; otherwise, delete paragraph] The Principal Investigator will report Unanticipated Problems and Adverse Events to name of entity; schedule of reporting requirements

[Include if there is one or more safety monitoring entity; otherwise, delete paragraph] Name of entity will communicate its reports and recommendations as follows: schedule of reporting by the safety monitoring entity to the PI, IRB, and/or sponsor.

## Stopping Rules

[Include if the study has no stopping rules; otherwise, omit sentence] The study has no pre-defined stopping rules.

[Include if the study does have stopping rules; otherwise, omit next two paragraphs] A subject will be withdrawn from active participation in the study if adverse event(s) require subject withdrawal.

The study will be stopped if rules are met for stopping such as for safety, futility, etc.

# Data Handling and Record Keeping

## Confidentiality

Include

* procedures for maintaining subject confidentiality for data and/or biospecimens
* any special data security requirements
* any plans for sharing data and/or biospecimens, identified or de-identified
* any plans for registering and updating on ClinicalTrials.gov.

[Include if the study has an external sponsor or lead site, modified as applicable; otherwise, delete] The study monitor or other authorized representatives of the sponsor / name of lead site 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 subjects in this study. The clinical study site will permit access to such records.

## Study Documentation, Source Data, and Case Report Forms (CRFs)

[review the below Definitions for guidance, and then delete Definitions in green from final protocol]

**Definitions:**

Source data

All information in original records and certified copies of 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 (original records or certified copies).

Source documents

Original documents, data, and records (e.g., 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 copies, 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).

Case Report Form (CRF)

A printed, optical, or electronic document designed to record all of the protocol required information to be reported to the sponsor on each trial subject. If source data is entered directly onto the CRF then that data should be initialed or signed and dated by the research team member generating that source data.

Describe the various sources of data for the study and means of collecting the data, including onto source documents and CRFs. Explain how you will first record the data, whether it will be onto hardcopy data collection forms or entered directly into an electronic system such as REDCap, or a combination of both methods. If you plan to utilize the EPIC encounter/progress note function to record any research data, then describe this process. If you will directly enter source data into an electronic system, the electronic system must have an audit trail (for example, REDCap has this functionality, but Excel does not). Source data may already exist, such as clinical data from the subject’s medical record that you plan to use for research purposes, or, it may be generated by study procedures. Provide explicit description that any “source data” that is generated/collected from study procedures and that is recorded onto hardcopy or electronic “source documents” will meet ALCOA-C criteria (Attributable, Legible, Contemporaneous, Original, Accurate, Complete).

Please note that if you are investigating a drug or device and are utilizing an electronic system to maintain your study records and/or use electronic signatures, your system must be compliant [with Part 11 requirements](https://www.fda.gov/media/75414/download). You do not need to detail Part 11 compliance in the protocol but you should begin planning for this when choosing your electronic system. At BMC and BU Medical Campus, local Part 11 compliant systems are listed [here](https://www.bumc.bu.edu/irb/part-11-compliance/).

[Include and modify as applicable] Corrections on data collection forms: If any entry error has been made to hardcopy data collection forms, to correct such an error, a single straight line will be drawn through the incorrect entry and the correct data will be entered above it. All such changes will be initialed and dated. There will be no erasures or white-out on CRFs. For clarification of illegible or uncertain entries, the clarification will be printed above the item, then initialed and dated.

See Section 18 Appendix for the following CRFs/data collection forms: list one or more form by name.

## Study Records Retention

Summarize the record retention plan applicable to the study (taking into account any applicable Institutional, Department, Division or Research Center requirements). Boston Medical Center and Boston University requires that study records be retained for at least seven years after completion of the study. The BMC/BU Medical Campus IRB requires that documentation of informed consent of subjects be retained for at least seven years after the study is closed, unless the IRB waived the requirement for informed consent or documentation of informed consent. Such records may be preserved in hardcopy, electronic or other media form and must be accessible for inspection and copying by authorized individuals.

If your study involves an FDA-regulated product, in addition to record retention times based on the completion of the study, you should add the following based on timing of FDA actions:

Drug/Biologics:

* For Investigational New Drug (IND) research, the FDA requires that sponsors and investigators retain “records and reports required by this part for 2 years after a marketing application is approved for the drug; or if an application is not approved for drug, until 2 years after shipment and delivery of the drug for investigational use is discontinued and the FDA so notified.”

Devices:

* For Investigational Device Exemption (IDE) research, the FDA requires that sponsors and investigators maintain the records “for a period of 2 years after the latter of the following two dates: The date on which the investigation is terminated or completed, or the date that the records are no longer required for purposes of supporting a premarket approval application or a notice of completion of a product development protocol.”

# Statistical Plan

## Study Hypotheses

State the formal, testable, null, and alternative hypotheses for primary and key secondary objectives.

## Sample Size Determination

Describe the statistical methods for determining the sample size for the study. (1) Provide information needed to validate your calculations - i.e., values for all parameters used in calculations. (2) Document feasibility to enroll and follow the necessary numbers of subjects.

## Statistical Methods

Summarize the overall statistical approach to the analysis of the study. This section should contain the key elements of the analysis plan.

State whether there will be a separate Statistical Analysis Plan (SAP). An SAP generally includes additional statistical analysis detail (e.g., more detail of analysis populations, a summary of statistical strategies). If a separate SAP will be developed, this section should be a summary of the SAP. The SAP will need to be attached to the submission in INSPIR.

Clearly describe primary as well as any applicable secondary analyses. 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 minimum bias, while remaining feasible. Consult [ICH Guidance for Industry E9 Statistical Principles for Clinical Trials](https://www.fda.gov/regulatory-information/search-fda-guidance-documents/e9-statistical-principles-clinical-trials) and the [CONSORT statement](http://www.consort-statement.org/) which describe standards for reporting randomized controlled trials.

# Ethics/Protection of Human Subjects

This study is to be conducted according to applicable US federal regulations and institutional policies (which are based in federal regulations, guidance, and ICH Good Clinical Practice guidelines).

This protocol and any amendments will be submitted to the [modify as needed depending on designation of Reviewing IRB] Boston Medical Center and Boston University Medical Campus IRB / Name of IRB of record for formal approval of the study conduct. The decision of the IRB concerning the conduct of the study will be made in writing to the investigator. [Include if there is a separate sponsor; otherwise, omit sentence] A copy of the initial IRB approval letter will be provided to the sponsor before commencement of this study.

All subjects for this study will be provided a consent form describing this study and providing sufficient information for subjects to make an informed decision about their participation in this study. The consent form will be submitted with the protocol for review and approval by the IRB. The consent of a subject, using the IRB-approved consent form, must be obtained before that subject is submitted to any study procedure. Consent will be documented as required by the IRB.

# Literature References

Include a list of relevant literature references in this section. Use a consistent, standard, modern format, which might be dependent upon the required format for the anticipated journal for publication (e.g., N Engl J Med, JAMA, etc). The preferred format is ICMJE.

A full listing of ICMJE style guidelines can be found at:  
International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomedical journals. JAMA. 1997;277:927-34.

You may also refer to:  
[http://www.nlm.nih.gov/bsd/uniform\_requirements.html](http://www.nlm.nih.gov/bsd/uniform_requirements.html%20).

# Appendix

Schedule of Events (required)

As applicable:

Schematic of Study Design

Toxicity Grading Scales

DSMB Charter

Repository Instructions

Biosafety Precautions

Manual of Operations

Laboratory Handling

Pharmacy Manual

IXRS Manual

Case Report Forms (CRFs)

Quality Management Plan

Data Management Plan

Clinical Monitoring Plan

Endpoint Scales

Other Documents