University of California, San Francisco

PROTOCOL TEMPLATE

**Instructions to User:**

1. **Sections where the text is *italicized*** represent instructions with some example text. All require complete customization for your study. Sections that may not apply to all protocols have italicized instructions highlighted in grey.
2. **Sections and text that are in regular font** represent standard language. In general, these sections should be present in your final protocol and the language should not be changed. However, every protocol is unique and changes to standard sections and language may be necessary to meet the needs of your protocol. Please review the language carefully to make sure that it is accurate for your study.
3. **Sections that are highlighted in grey, but that have regular font,** represent sections or information that needs to be customized as applicable to your study, but the language that is present is generally considered to be standard if that section (or procedure) applies to your protocol.
4. As you customize each section of the protocol, **remove the highlighting and restore the font to regular (from italics)** to denote that section as having been completed.
5. When your protocol is complete, **review** it to ensure that all highlighting and italics have been removed.

**SPONSOR NAME**

**Clinical Research Protocol**

**PROTOCOL NAME**

|  |  |
| --- | --- |
| Protocol Number: |  |
| Version Date: |  |
| Investigational Device: |  |
| IDE Number: |  |
| Study Phase: |  |
| Sponsor-Investigator: | Name (*please note – for academic studies, the sponsor is the Investigator, not the funding agency)*  Address  City, State |
| Funding Organization: |  |
| Site Investigator: | Name:  Telephone:  Fax:  E-mail: |

|  |  |  |
| --- | --- | --- |
| **Approval:** | | |
|  |  |  |
| *PI or Sponsor Signature (Name and Title)* |  | *Date* |
| **This confidential information about an investigational product is provided for the exclusive use of investigators of this product and is subject to recall at any time. The information in this document may not be disclosed unless federal or state law or regulations require such disclosure. Subject to the foregoing, this information may be disclosed only to those persons involved in the study who have a need to know, with the obligation not to further disseminate this information.** | | |

**PROTOCOL AGREEMENT**

I have read the protocol specified below. In my formal capacity as Investigator, my duties include ensuring the safety of the study subjects enrolled under my supervision and providing [Sponsor Name] with complete and timely information, as outlined in the protocol. It is understood that all information pertaining to the study will be held strictly confidential and that this confidentiality requirement applies to all study staff at this site. Furthermore, on behalf of the study staff and myself, I agree to maintain the procedures required to carry out the study in accordance with accepted GCP principles and to abide by the terms of this protocol.

Protocol Number: Number

Protocol Title: Title

Protocol Date: TBD

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | | |  |  |
| *Investigator Signature* | | |  | *Date* |
|  | | | | |
| *Print Name and Title* | | | | |
| *Site #* |  |  | | |
| *Site Name* |  | | | |
| *Address* |  | | | |
|  |  | | | |
|  |  | | | |
|  |  | | | |
| *Phone Number* |  | | | |

**TABLE OF CONTENTS**

[**1.0 PURPOSE OF THE INVESTIGATION**](#h.3znysh7)

[1.1. Name of investigational device](#h.2et92p0)

[1.2. Intended use of the investigational device](#h.tyjcwt)

[1.3. Objectives of the clinical investigation](#h.3dy6vkm)

[1.3.1. Primary objective](#h.1t3h5sf)

[1.3.2 Secondary objective(s).](#h.4d34og8)

[1.4 Anticipated duration of the clinical investigation](#h.2s8eyo1)

[**2.0 CLINICAL PROTOCOL**](#h.17dp8vu)

[2.1 Protocol number and title](#h.3rdcrjn)

[2.2 Protocol version number and date](#h.26in1rg)

[2.3 Study design](#h.lnxbz9)

[2.3.1 General study design](#h.35nkun2)

[2.3.2 Study design schematic](#h.1ksv4uv)

[2.4 Subject selection](#h.44sinio)

[2.4.1 General characteristics of the proposed subject population(s)](#h.2jxsxqh)

[2.4.2 Anticipated number of research subjects](#h.z337ya)

[2.4.3 Inclusion criteria](#h.3j2qqm3)

[2.4.4 \_ Exclusion criteria](#h.1y810tw)

[2.5 Study procedures](#h.4i7ojhp)

[2.5.1 Screening procedures](#h.2xcytpi)

[2.5.2 Study treatment or diagnostic product procedures](#h.1ci93xb)

[2.5.3 Allocation to treatment](#h.3whwml4)

[2.5.4 \_ Unblinding](#h.2bn6wsx)

[2.5.5 Treatment adherence](#h.qsh70q)

[2.5.6 Withdrawal of subjects due to non-compliance](#h.3as4poj)

[2.5.7 Procedures to assess efficacy](#h.1pxezwc)

[2.5.8 Procedures to assess safety](#h.49x2ik5)

[2.5.9 Schedule of study visits](#h.2p2csry)

[2.6 Study outcome evaluations](#h.147n2zr)

[2.6.1 Study endpoints](#h.3o7alnk)

[2.6.2 Sample size determination](#h.23ckvvd)

[2.6.3 Outcome data and data analysis](#h.ihv636)

[2.6.4 Data and Safety Monitoring Committee](#h.32hioqz)

[**3.0 RISK ANALYSIS**](#h.1hmsyys)

[3.2 Adverse event reporting](#h.41mghml)

[3.2.1 Adverse event definitions](#h.2grqrue)

[3.2.2 \_ Eliciting adverse effect information](#h.vx1227)

[3.2.3 \_ Recording and assessment of adverse effects](#h.3fwokq0)

[3.2.4 Abnormal test findings](#h.1v1yuxt)

[3.2.5 Causality and severity assessment](#h.4f1mdlm)

[3.2.6 Reporting adverse effects to the FDA](#h.2u6wntf)

[3.2.5 Reporting adverse effects to the responsible IRB](#h.19c6y18)

[3.3 Withdrawal of subjects due to adverse effects](#h.3tbugp1)

[**4.0 DESCRIPTION OF THE INVESTIGATIONAL DEVICE**](#h.28h4qwu)

[**5.0 MONITORING PROCEDURES**](#h.nmf14n)

[**6.0 LABELING**](#h.37m2jsg)

[**7.0 INFORMED CONSENT**](#h.1mrcu09)

[**8.0 IRB INFORMATION**](#h.46r0co2)

[**9.0 OTHER INSTITUTIONS**](#h.2lwamvv)

[**10.0 ADDITIONAL RECORDS AND REPORTS**](#h.111kx3o)

[10.1 Data handling and record-keeping](#h.3l18frh)

[10.2 Record maintenance and retention](#h.206ipza)

**List of Abbreviations**

***Add all other abbreviations referenced in the protocol and delete any not referenced in the protocol.***

|  |  |
| --- | --- |
| **AE** | adverse event |
| **CFR** | Code of Federal Regulations |
| **CRF** | case report form |
| **DMC** | Data Monitoring Committee |
| **DSMB** | Data Safety Monitoring Board |
| **FDA** | Food and Drug Administration |
| **GCP** | Good Clinical Practice |
| **HIPAA** | Health Insurance Portability and Accountability Act of 1996 |
| **ICF** | informed consent form |
| **ICH** | International Conference on Harmonisation |
| **IEC** | Independent Ethics Committee |
| **IRB** | Institutional Review Board |
| **QC** | Quality Control |
| **PI** | Principal Investigator |
| **UADE** | unanticipated adverse device effect |

**Protocol Synopsis**

|  |  |
| --- | --- |
| **TITLE** |  |
|  |  |
| **SPONSOR** |  |
|  |  |
| **FUNDING ORGANIZATION** |  |
| **NUMBER OF SITES** |  |
|  |  |
| **RATIONALE** | *This should be very brief – 2 paragraphs or so, just highlighting why it makes sense to study devixce X in these patients and that there is a medical need.* |
|  |  |
| **STUDY DESIGN** | *This is a multi-center, randomized feasibility study.* |
|  |  |
| **PRIMARY OBJECTIVE** |  |
|  |  |
| **SECONDARY OBJECTIVES** |  |
|  |  |
| **NUMBER OF SUBJECTS** |  |
|  |  |
| **SUBJECT SELECTION**  **CRITERIA** | Inclusion Criteria:  Exclusion Criteria: |
|  |  |
| **INVESTIGATIONAL DEVICE / INTENDED USE** | *Product XX*  *Describe intended use* |
|  |  |
| **CONTROL GROUP OR OTHER STUDY ARMS (if applicable)** | *Product XX*  *Describe intended use.* |
|  |  |
| **DURATION OF SUBJECT PARTICIPATION AND DURATION OF STUDY** | *Subjects will be on study for up to 28 days*  ***Screening:*** *up to 7 days*  ***Treatment:*** *5 days (subjects to be admitted to the hospital)*  ***Follow-up:*** *16 days*  *The total duration of the study is expected to be XXX. XXX months for subject recruitment and XXX for final subject follow-up.* |
| **E** |  |
| **CONCOMMITANT MEDICATIONS** | Allowed:  Prohibited: |
|  |  |
| **EFFICACY EVALUATIONS** | *Observations and/or measurements* |
| **PRIMARY ENDPOINT** |  |
| **SECONDARY ENDPOINTS** |  |
| **OTHER EVALUATIONS** | *Observations and/or measurements* |
| **SAFETY EVALUATIONS** | *Procedures, laboratory tests, or other measures from baseline to XXX*  *Incidence of adverse events* |
| **PLANNED INTERIM ANALYSES** | *Fill in details of DMC or DMP. Sample text:* When approximately 50% of subjects have completed the study, an interim analysis for safety will be conducted by an independent data monitoring committee. Serious adverse events will be monitored by the committee on an ongoing basis throughout the study. |
|  |  |
| **STATISTICS**  **Primary Analysis Plan** | *Describe plan for analyzing the primary endpoint.* |
| **Rationale for Number of Subjects** |  |

# 1.0 PURPOSE OF THE INVESTIGATION

* 1. **Name of investigational device**

*Specify the name of the investigational device.*

* 1. **Intended use of the investigational device**

*Summarize the intended use of the investigational device.*

* 1. **Objectives of the clinical investigation**
     1. **Primary objective**

*Describe the primary objective of the proposed clinical investigation. For example:*

* *Evaluate the efficacy of the device in humans or a certain clinical population*
* *Evaluate safety issues associated with the use of the device*
* *Evaluate device design characteristics*
* *Assess certain human factors (patient or operator) associated with the use of the device*
* *Study other specified device characteristics or device application considerations*
* *Obtain preliminary data for use in designing a subsequent pivotal study of the device*

### 1.3.2 Secondary objective(s).

*Describe any secondary objective(s) of the proposed clinical investigation of the device.*

## 1.4 Anticipated duration of the clinical investigation

*Provide a best estimate of the number of months or years it will take to complete the proposed feasibility study of the device.*

# 2.0 CLINICAL PROTOCOL

## 2.1 Protocol number and title

*For example: ABC001: [title of the clinical study]*

## 2.2 Protocol version number and date

*For example: Version 1.0, December 10, 2011. Number subsequent versions consecutively and include the date of the current version.*

## 2.3 Study design

### 2.3.1 General study design

*Describe the type/design (e.g., open-label, observational) of the proposed clinical study.*

### 2.3.2 Study design schematic

*Provide a schematic diagram of the study design, procedures, and stages.*

## 2.4 Subject selection

### 2.4.1 General characteristics of the proposed subject population(s)

*Provide a general description of the characteristics of the proposed subject population(s).*

*Provide a justification for the suitability of this (these) population(s) for the purpose of the investigation.*

### 2.4.2 Anticipated number of research subjects

*Indicate that “enrollment” into the investigation is defined as providing informed consent for study participation (as per University IRB policies).*

*Specify the estimated total number of subjects to be enrolled into the clinical study and the anticipated number of subjects expected to complete the study.*

### 2.4.3 Inclusion criteria

*List the specific criteria for including subjects for participation in the clinical study. Note that these criteria should be inclusive of diagnostic criteria and, where appropriate, confirmatory laboratory tests applicable to the specific disease or condition to be treated or diagnosed by the investigational device. In the case of an investigational device intended to prevent a disease or condition, the criteria for subject inclusion should provide for evidence of susceptibility and exposure to the condition against which prophylaxis is desired.*

### 2.4.4 Exclusion criteria

*List the specific criteria for excluding subjects from participation in the clinical study.*

## 2.5 Study procedures

### 2.5.1 Screening procedures

*Describe or list the procedures that will be performed to verify subject eligibility for participation in the clinical study.*

### 2.5.2 Study treatment or diagnostic product procedures

*Describe, in detail, the study treatment or diagnostic products (e.g., the investigational device and, if applicable, comparative devices or products) that will be administered to each study group or arm of the proposed clinical investigation; to include, for each study treatment or diagnostic product, the product name and FDA-approval status, dose or dose range (if applicable), route/mode of administration, dosing or exposure schedule, and treatment or exposure duration.*

*Describe, if applicable, any plans for dose or exposure reductions or increases based on the data accrued with study progression.*

### 2.5.3 Allocation to treatment

*If the proposed clinical study involves multiple treatment arms, describe the plan and procedures for allocating subjects to the various treatment or diagnostic arms of the study so as to ensure comparability between test groups and any control groups with regard to pertinent variables such as gender, severity or duration of disease, and use of therapy other than the investigational device*

### 2.5.4 Unblinding

*If the proposed clinical study is blinded, describe the procedures for breaking the blind should a given subject suffer a serious adverse event wherein knowledge of the identity of the study treatment or diagnostic product received by the subject is necessary for effective emergency treatment of the event.*

### 2.5.5 Treatment adherence

*If applicable, describe the procedures that will be used to assess subject compliance with the assigned study treatment or diagnostic product regimen.*

### 2.5.6 Withdrawal of subjects due to non-compliance

*If applicable, specify the criteria and procedures for withdrawing subjects from study participation due to subject non-compliance with study procedures or the investigator’s instructions.*

*Specify if subjects withdrawn from study participation due to non-compliance will be replaced and, if so, the corresponding procedures for their replacement.*

### 2.5.7 Procedures to assess efficacy

*If applicable, specify the parameters (i.e., observations and/or measurements) that will be used to evaluate the efficacy of the study treatment or diagnostic product(s); to include the methods and timing for assessing, recording, and analyzing these parameters. If the proposed clinical study does not involve evaluation(s) of the efficacy of the investigational device, state this.*

### 2.5.8 Procedures to assess safety

*Specify the parameters (i.e., procedures, laboratory tests, or other measures) that will be used to evaluate the safety of the study treatment or diagnostic product(s); to include the methods and timing for assessing, recording, and analyzing these parameters.*

### 2.5.9 Schedule of study visits

*Incorporate, as a referenced appendix, a table that summarizes the protocol procedures that will be performed at screening, for treatment or diagnosis, and at follow-up, as applicable.*

## 2.6 Study outcome evaluations

### 2.6.1 Study endpoints

*Summarize the primary and, if applicable, secondary endpoints or outcomes that will be evaluated in the clinical study.*

### 2.6.2 Sample size determination

*Specify the number of subjects planned to be enrolled and describe the reason for choice of sample size. Include reflections on (or calculations of) the power of the study and clinical justification. For example: The sample size for this protocol was determined by xxxx.*

### 2.6.3 Outcome data and data analysis

*Describe the specific observations and/or measurements that will form the basis for evaluating the primary and, if applicable, secondary endpoints or outcomes of the clinical study.*

*Describe how these data will be evaluated in addressing the feasibility objective(s) of the clinical study and/or in making a decision to proceed with further clinical investigation of the investigational device.*

### 2.6.4 Data and Safety Monitoring Committee

*If a Data and Safety Monitoring Committee will be used, describe the composition and operations of the Data and Safety Monitoring Committee that will provide oversight of the clinical study.*

# 3.0 RISK ANALYSIS

**3.1 Anticipated risks**

*Describe all increased risks to which the subjects (including normal controls, if applicable) will be exposed as a result of their participation in the clinical study and how these risks will be minimized..*

*Provide an analysis of the risk-to-benefit ratio of study participation and a justification for the investigation in light of these risks.*

## 3.2 Adverse event reporting

### 3.2.1 Adverse event definitions

**Unanticipated adverse device effect (UADE):** 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 IDE 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.

**Associated with the investigational device:** There is a reasonable possibility that the adverse effect may have been caused by the investigational device.

**Life-threatening adverse effect:** Any adverse effect that places the subject, in the view of either the investigator or the sponsor, at immediate risk of death from the effect **as it occurred**. It does not include a reaction that, had it occurred in a more severe form, might have caused death.

**Serious adverse effect:** An adverse effect is considered “serious” if, in the view of either the investigator or the sponsor, it results in any of the following outcomes:

* death
* a life-threatening AE
* inpatient hospitalization or prolongation of existing hospitalization
* a persistent or significant disability/incapacity
* a congenital anomaly/birth defect.

**Unanticipated adverse effect:** Any adverse effect, the nature, specificity, severity, or frequency of which is not consistent with the risk information in the clinical study protocol or elsewhere in the current IDE application.

### 3.2.2 Eliciting adverse effect information

Clinical study subjects will be routinely questioned about adverse effects at study visits.

### 3.2.3 Recording and assessment of adverse effects

All observed or volunteered adverse effects (serious or non-serious) and abnormal test findings, regardless of treatment group, if applicable, or suspected causal relationship to the investigational device or, if applicable, other study treatment or diagnostic product(s) will be recorded in the subjects’ case histories. For all adverse effects, sufficient information will be pursued and/or obtained so as to permit 1) an adequate determination of the outcome of the effect (i.e., whether the effect should be classified as a *serious adverse effect*) and; 2) an assessment of the casual relationship between the adverse effect and the investigational device or, if applicable, the other study treatment or diagnostic product(s).

Adverse effects or abnormal test findings felt to be associated with the investigational device or, if applicable, other study treatment or diagnostic product(s) will be followed until the effect (or its sequelae) or the abnormal test finding resolves or stabilizes at a level acceptable to the sponsor-investigator.

### 3.2.4 Abnormal test findings

An abnormal test finding will be classified as an *adverse effect* if one or more of the following criteria are met:

* The test finding is accompanied by clinical symptoms
* The test finding necessitates additional diagnostic evaluation(s) or medical/surgical intervention; including significant additional concomitant drug or other therapy (Note: simply repeating a test finding, in the absence of any of the other listed criteria, does not constitute an adverse effect.)
* The test finding leads to a change in study dosing or exposure or discontinuation of subject participation in the clinical study
  + - * The test finding is considered an adverse effect by the sponsor-investigator

### 3.2.5 Causality and severity assessment

The sponsor-investigator will promptly review documented adverse effects and abnormal test findings to determine 1) if the abnormal test finding should be classified as an adverse effect; 2) if there is a reasonable possibility that the adverse effect was caused by the investigational device or other study treatments; and 3) if the adverse effect meets the criteria for a *serious adverse effect*.

If the sponsor-investigator’s final determination of causality is “unknown and of questionable relationship to the investigational device or other study treatments,” the adverse effect will be classified as *associated with the use of the investigational device or other study treatments* for reporting purposes. If the sponsor-investigator’s final determination of causality is “unknown but not related to the investigational device or other study treatments,” this determination and the rationale for the determination will be documented in the respective subject’s case history.

### 3.2.6 Reporting adverse effects to the FDA

For any observed or volunteered adverse event that is determined to be a UADE, the sponsor-investigator will submit an expedited safety report to the FDA’s Center for Devices and Radiological Health. The expedited safety report will consist of:

* a completed Form [FDA 3500A](http://www.fda.gov/opacom/morechoices/fdaforms/3500Aes.pdf)
* a cover letter analyzing the significance of the event

A copy of this safety report will be provided to all participating study investigators.

The completed Form [FDA 3500A](http://www.fda.gov/opacom/morechoices/fdaforms/3500Aes.pdf) and cover letter will be submitted to the FDA as soon as possible and, in no event, later than 10 working days after the sponsor-investigator first receives notice of the adverse effect.

If, following receipt and investigation of follow-up information regarding an adverse effect that was previously determined not to be a UADE, the sponsor-investigator determines that the event does meet the requirements for expedited reporting, the sponsor-investigator will submit a completed [Form FDA 3500A](http://www.fda.gov/opacom/morechoices/fdaforms/3500Aes.pdf) and cover letter as soon as possible, but in no event later than 10 working days, after the determination is made.

Subsequent to the initial submission of a completed [FDA Form 3500A](http://www.fda.gov/opacom/morechoices/fdaforms/3500Aes.pdf), the sponsor-investigator will submit additional information concerning the reported adverse effect as requested by the FDA.

### 3.2.5 Reporting adverse effects to the responsible IRB

For any adverse event determined to be a UADE, the sponsor-investigator will submit the completed Form [FDA 3500A](http://www.fda.gov/opacom/morechoices/fdaforms/3500Aes.pdf) and cover letter to the IRB as soon as possible and, in no event, later than 10 working days after the sponsor-investigator first receives notice of the adverse effect.

Follow-up information to reported adverse effects will be submitted to the IRB as soon as the relevant information is available.

## 3.3 Withdrawal of subjects due to adverse effects

*Specify the criteria and procedures for withdrawing subjects from continued exposure to the investigational device or, if applicable, other study treatment or diagnostic product(s) due to an observed or volunteered adverse effect; to include the type and timing of data to be collected from withdrawn subjects.*

*Specify if subjects withdrawn from study participation due to an adverse effect will be replaced and, if so, the corresponding procedures for their replacement.*

# 4.0 DESCRIPTION OF THE INVESTIGATIONAL DEVICE

*Provide a description of each important component, ingredient or element, property, and principle of operation of the investigational device.*

*If applicable, describe any anticipated changes in the device during the investigation. If no changes to the device are anticipated, state this.*

# 5.0 MONITORING PROCEDURES

Independent monitoring of the study for compliance with the clinical protocol and with IDE regulations will be conducted periodically (at a minimum, annually) by qualified staff of [institution]. The address of the [monitoring group] is listed below. Monitoring procedures of the [monitoring group] are listed on the [group] website at:

[list contact information]

The sponsor-investigator and the [institution] will permit direct access of the study monitors and appropriate regulatory authorities to the study data and to the corresponding source data and documents to verify the accuracy of this data.

*Describe the nature and timing of any quality control/quality assurance reviews (independent of the previously described monitoring activities) that will be undertaken by the sponsor-investigator to ensure appropriate conduct of the clinical study and quality and completeness of the accrued study data. Describe the data and safety monitoring plan for the clinical study as outlined in the IRB application.*

# 6.0 LABELING

*Provide copies of all labeling for the device.*

The labeling will contain the statement "CAUTION - Investigational Device. Limited by Federal (or United States) Law to Investigational Use." [§ 812.5(a))].

# 7.0 INFORMED CONSENT

Informed consent will be obtained in accordance with the Declaration of Helsinki, ICH GCP, US Code of Federal Regulations for Protection of Human Subjects (21 CFR 50.25[a,b], CFR 50.27, and CFR Part 56, Subpart A), the Health Insurance Portability and Accountability Act (HIPAA, if applicable), and local regulations.

The Sponsor-Investigator will prepare the informed consent form and HIPAA authorization and provide the documents to IRB for approval. The written consent document will embody the elements of informed consent as described in the International Conference on Harmonisation and will also comply with local regulations. The Sponsor-Investigator will retain an IRB-approved copy of the Informed Consent Form in the study master file.

A properly executed, written, informed consent will be obtained from each subject prior to entering the subject into the trial. Information should be given in both oral and written form and subjects (or their legal representatives) must be given ample opportunity to inquire about details of the study. If a subject is unable to sign the informed consent form (ICF) and the HIPAA authorization, a legal representative may sign for the subject. A copy of the signed consent form will be given to the subject or legal representative of the subject and the original will be maintained with the subject’s records.

# 8.0 IRB INFORMATION

The protocol and consent form will be reviewed and approved by the IRB of each participating center prior to study initiation. UADEs will be reported to the IRB in accordance with the standard operating procedures and policies of the IRB, and the Investigator will keep the IRB informed as to the progress of the study. The Investigator will obtain assurance of IRB compliance with regulations.

Any documents that the IRB may need to fulfill its responsibilities (such as protocol, protocol amendments, Investigator’s Brochure, consent forms, information concerning patient recruitment, payment or compensation procedures, or other pertinent information) will be submitted to the IRB. The IRB’s written unconditional approval of the study protocol and the informed consent form will be in the possession of the Investigator before the study is initiated. The IRB’s unconditional approval statement will be transmitted by the Investigator to the Sponsor or designee prior to the shipment of study supplies to the site. This approval must refer to the study by exact protocol title and number and should identify the documents reviewed and the date of review.

Protocol and/or informed consent modifications or changes may not be initiated without prior written IRB approval except when necessary to eliminate immediate hazards to the patients or when the change(s) involves only logistical or administrative aspects of the study. Such modifications will be submitted to the IRB and written verification that the modification was submitted and subsequently approved should be obtained.

The IRB must be informed of revisions to other documents originally submitted for review; new information that may affect adversely the safety of the patients of the conduct of the study; an annual update and/or request for re-approval; and when the study has been completed.

# 9.0 OTHER INSTITUTIONS

Please refer to section 8 of the IDE application.

# 10.0 ADDITIONAL RECORDS AND REPORTS

## 10.1 Data handling and record-keeping

A Case Report Form (CRF, see Appendix\_\_) will be completed for each subject enrolled into the clinical study. The sponsor-investigator will review, approve and sign/date each completed CRF; the sponsor-investigator’s signature serving as attestation of the sponsor-investigator’s responsibility for ensuring that all clinical and laboratory data entered on the CRF are complete, accurate and authentic.

*Describe the procedures for accounting for any missed, unused, and/or spurious data.*

*Source Data* are the clinical findings and observations, laboratory and test data, and other information contained in *Source Documents*. *Source Documents* are the original records (and certified copies of original records); including, but not limited to, hospital medical records, physician or office charts, physician or nursing notes, subject diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, x-rays, etc. When applicable, information recorded on the CRF shall match the *Source Data* recorded on the *Source Documents*.

*Identify, if applicable, any clinical study data that will be recorded directly on the CRF, whereupon the CRF data is to be considered the Source Data.*

*If an electronic system will be used as the sole instrument for the recording and analysis of clinical and laboratory data related to the safety and/or efficacy of the investigational device, address compliance with the FDA’s electronic records and electronic signatures regulations at* [*21 CFR Part 11*](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=11)*.*

## 10.2 Record maintenance and retention

The sponsor-investigator will maintain records in accordance with 21 CFR 812, Subpart G, to include:

* FDA correspondence related to the IDE application and Investigational Plan; including copies of submitted Form [FDA 3500A](http://www.fda.gov/opacom/morechoices/fdaforms/3500Aes.pdf), supplemental IDE applications, current investigator lists, progress reports, notice of device recall or disposition, and failure to obtain informed consent reports
* IRB correspondence (including approval notifications) related to the clinical protocol; including copies of adverse event reports and annual or interim reports
* Current and past versions of the IRB-approved clinical protocol and corresponding IRB-approved consent form(s) and, if applicable, subject recruitment advertisements
* Signed Investigator’s Agreements and Certifications of Financial Interests of Clinical Investigators
* Curriculum vitae (sponsor-investigator and clinical protocol sub-investigators)
* Certificates of required training (e.g., human subject protections, Good Clinical Practice, etc.) for sponsor-investigator and listed sub-investigators
* Normal value(s)/range(s) for medical/laboratory/technical procedures or tests included in the clinical protocol
* Laboratory certification information
* Instructions for on-site preparation and handling of the investigational device and/or study treatment or diagnostic product(s), and other study-related materials (i.e., if not addressed in the clinical protocol)
* Decoding procedures for blinded trials *(incorporate only if applicable)*
* Master randomization list *(incorporate only if applicable)*
* Signed informed consent forms
* Completed Case Report Forms, signed and dated by sponsor-investigator
* Source Documents or certified copies of Source Documents
* Monitoring visit reports
* Copies of sponsor-investigator correspondence to sub-investigators, including notifications of adverse effect information
* Subject screening and enrollment logs
* Subject identification code list
* Investigational device accountability records, including documentation of device disposal
* Retained biological specimen log *(incorporate only if applicable)*
* Interim data analysis report(s) *(incorporate only if applicable)*
* Final clinical study report.

*Describe how the subject-specific data and Case Report Forms will be coded and how these materials, and the subject identification code list, will be stored so as to protect the subjects’ confidentiality. Specify that subject names or other directly identifiable information will not appear on any reports, publications, or other disclosures of clinical study outcomes.*

The sponsor-investigator will retain the specified records and reports for up to two years after the marketing application is approved for the investigational device; or, if a marketing application is not submitted or approved for the investigational device, until two years after investigations under the IDE have been discontinued and the FDA so notified.