Clinical Study Protocol

Evoke Study: A prospective, multicenter, randomized double-blind study examining the safety and efficacy of using the Evoke™ Spinal Cord Stimulator (SCS) System with feedback to treat patients with chronic pain of the trunk and/or limbs.

Study ID: SCLSH1503
Revision: [redacted]
Date: [redacted]

IDE Number: G150266

Sponsor:
Saluda Medical Americas, Inc.
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TABLE OF CONTENTS

1 CLINICAL PROTOCOL SUMMARY

Title	A prospective, multicenter, randomized, double-blind study examining the safety and efficacy of using the Evoke™ Spinal Cord Stimulator (SCS) System with feedback to treat patients with chronic pain of the trunk and/or limbs. (Evoke Study)
Investigational Device	Evoke Spinal Cord Stimulator (SCS) System
Treatment Groups	Investigational: Evoke SCS with feedback [redacted] The feedback control uses Evoked Compound Action Potential (ECAP) measurements to provide consistent stimulation based on the subjects neural response during physiological changes and movement by automatically adjusting the level of stimulation current required to meet the subject's requested target level. Control: Evoke SCS without feedback [redacted]
Randomization	1:1
Study Purpose	This study will evaluate the safety and efficacy of the Saluda Medical Evoke SCS System with feedback control to treat chronic pain of the trunk and/or limbs.
Targeted Indication For Use	The Evoke SCS System is indicated as an aid in the management of chronic, intractable pain of the trunk and/or limbs, including unilateral or bilateral pain associated with the following: failed back surgery syndrome, intractable low back pain and leg pain.
Study Design	This study is a prospective, multicenter, randomized, double-blind clinical trial designed to assess the safety and efficacy of the Saluda Medical Evoke SCS System for the treatment of subjects suffering from chronic, intractable pain of the trunk and/or limbs. This study will compare the Saluda Medical Evoke SCS System with feedback (Investigational) to Saluda Medical Evoke SCS System without feedback (Control).
Sample Size	[redacted]
Analysis Populations	[redacted] nd .

Study Sites	Up to 20 US sites.
Study Duration	[redacted]
Primary Objective	[redacted]
Study Success Criteria	[redacted]
Primary Endpoint	The primary endpoint is a composite endpoint, where a subject is deemed a success if: • They experience a 50% reduction in overall trunk and limb pain as determined by the Visual Analog Scale (VAS) at the 3-month visit, AND • They have no increase in baseline pain medications within 4 weeks of the 3-month visit
Secondary Endpoints for Hierarchical Testing	[redacted]
Other Secondary Endpoints	A number of additional secondary endpoints will also be collected and assessed across study visits. These endpoints include the following: [redacted]

Inclusion Criteria	Subjects enrolled in this study must meet the following inclusion criteria, as determined by the Investigator: 1. Subject is male or female between the ages of 18 and 80 years. 2. Have been diagnosed with chronic, intractable pain of the trunk and/or limbs, which has been refractory to conservative therapy for a minimum of 6 months. 3. VAS leg pain score ≥ 6 cm. 4. VAS back pain score ≥ 6 cm. 5. VAS overall trunk and limb pain score ≥ 6 cm. 6. Be an appropriate candidate for an SCS trial and the surgical procedures required in this study based on the clinical judgment of the Investigator. 7. Prescribed pain medications have been stable for at least 30 days prior to the baseline evaluation. 8. ODI score of 41-80 (severely disabled or crippled) out of 100 at the baseline evaluation. 9. Be willing and capable of giving informed consent and able to comply with study-related requirements, procedures, and visits. 10. The subject's primary back pain is located such that lead placement will be in the thoracolumbar region.
Exclusion Criteria	Subjects enrolled in this study must not meet the following exclusion criteria, as determined by the Investigator: 1. Have a medical condition or pain in other area(s), not intended to be treated with SCS, that could interfere with study procedures, accurate pain reporting, and/or confound evaluation of study endpoints, as determined by the Investigator. 2. Have evidence of an active disruptive psychological or psychiatric disorder or other known condition significant enough to impact perception of pain, compliance of intervention, and/or ability to evaluate treatment outcomes. 3. Are not a surgical candidate due to a diagnosis of an uncontrolled coagulation disorder, bleeding diathesis, progressive peripheral vascular disease, uncontrolled diabetes mellitus, or morbid obesity. 4. Have an existing drug pump and/or SCS system or another active implantable device such as a pacemaker, deep brain stimulator (DBS), or sacral nerve stimulator (SNS). 5. Have prior experience with SCS. 6. Have a condition currently requiring or likely to require the use of MRI or diathermy. 7. Have a life expectancy of less than 1 year. 8. Have an active systemic infection or local infection in the area of the surgical site. 9. Be allergic, or have shown hypersensitivity, to any materials of the neurostimulation system which come in contact with the body. 10. Be pregnant or nursing (if female and sexually active, subject must be using a reliable form of birth control, be surgically sterile, or be at least 2 years post-menopausal). 11. Have a documented history of substance abuse (narcotics, alcohol, etc.) or substance dependency in the 6 months prior to the baseline evaluation. 12. Be concomitantly participating in another clinical study. 13. Be involved in an injury claim under current litigation or have pending/approved worker's compensation claim.

	14. Had surgery and/or interventional procedure to treat back and/or leg pain within 90 days (if surgery) and 30 days (if any other procedure) prior to the baseline evaluation. 15. Subject is a prisoner. 16. Being treated with electroconvulsive therapy (ECT) or transcranial magnetic stimulation (rTMS). 17. Subject is unwilling or unable to discontinue and remain off of any medication used to treat chronic pain that is not FDA approved for chronic pain. 18. Subject has pain due to peripheral vascular disease or angina. 19. Subject is on anticoagulation therapy that would preclude their ability to undergo the implant procedure.

2 BACKGROUND

2.1 Disease and Current Treatment

[redacted]

[redacted]

2.2 Summary of Prior Preclinical and Clinical Experience

[redacted]

[redacted]

[redacted]

[redacted]

2.3 Rationale for the Clinical Study

[redacted]

[redacted]

3 DEVICE DESCRIPTION AND INDICATION FOR USE

3.1 Device Description

3.1.1 Investigational Device

[redacted]

[redacted]

[redacted]

Figure 1: [redacted]

[redacted]

3.1.2 Control Device

[redacted]

3.2 Target Indication for Use

[redacted]

4 STUDY PURPOSE AND OBJECTIVES

4.1 Study Purpose

[redacted]

4.2 Primary Objective

[redacted]

4.3 Secondary Objectives

[redacted]

5 STUDY DESIGN

5.1 Overview

[redacted]

[redacted]

Figure 2 [redacted]

5.2 Randomization

[redacted]

5.3 Blinding

This is a double-blind study. Neither the subjects nor the Investigator or their staff, will be informed which treatment group a subject has been assigned to. In addition, the independent adjudication committee will be blinded to the subjects' treatment assignments. [redacted]

[redacted]

[redacted]

5.4 Minimization of Bias

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

6 STUDY POPULATION

6.1 Study Sites

Study subjects will be enrolled at up to 20 US sites.

6.2 Inclusion Criteria

Subjects enrolled in this study must meet the following inclusion criteria, as determined by the Investigator:

1. Subject is male or female between the ages of 18 and 80 years.

2. Have been diagnosed with chronic, intractable pain of the trunk and/or limbs, which has been refractory to conservative therapy for a minimum of 6 months.

3. VAS leg pain score ≥ 6 cm.

4. VAS back pain score ≥ 6 cm.

5. VAS overall trunk and limb pain score ≥ 6 cm.

6. Be an appropriate candidate for an SCS trial and the surgical procedures required in this study based on the clinical judgment of the Investigator.

7. Prescribed pain medications have been stable for at least 30 days prior to the baseline evaluation.

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9. Be willing and capable of giving informed consent and able to comply with study-related requirements, procedures, and visits.

10. The subject's primary back pain is located such that lead placement will be in the thoracolumbar region.

6.3 Exclusion Criteria

Subjects enrolled in this study must not meet the following exclusion criteria, as determined by the Investigator:

1. Have a medical condition or pain in other area(s), not intended to be treated with SCS, that could interfere with study procedures, accurate pain reporting, and/or confound evaluation of study endpoints, as determined by the Investigator.

2. Have evidence of an active disruptive psychological or psychiatric disorder or other known condition significant enough to impact perception of pain, compliance of intervention, and/or ability to evaluate treatment outcomes.

3. Are not a surgical candidate due to a diagnosis of an uncontrolled coagulation disorder, bleeding diathesis, progressive peripheral vascular disease, uncontrolled diabetes mellitus, or morbid obesity.

4. Have an existing drug pump and/or SCS system or another active implantable device such as a pacemaker, deep brain stimulator (DBS), or sacral nerve stimulator (SNS).

5. Have prior experience with SCS.

6. Have a condition currently requiring or likely to require the use of MRI or diathermy.

7. Have a life expectancy of less than 1 year.

8. Have an active systemic infection or local infection in the area of the surgical site.

9. Be allergic, or have shown hypersensitivity, to any materials of the neurostimulation system which come in contact with the body.

10. Be pregnant or nursing (if female and sexually active, subject must be using a reliable form of birth control, be surgically sterile, or be at least 2 years post-menopausal).

11. Have a documented history of substance abuse (narcotics, alcohol, etc.) or substance dependency in the 6 months prior to the baseline evaluation.

12. Be concomitantly participating in another clinical study.

13. Be involved in an injury claim under current litigation or have pending/approved worker's compensation claim.

14. Had surgery and/or interventional procedure to treat back and/or leg pain within 90 days (if surgery) and 30 days (if any other procedure) prior to the baseline evaluation.

15. Subject is a prisoner.

16. Being treated with electroconvulsive therapy (ECT) or transcranial magnetic stimulation (rTMS).

17. Subject is unwilling or unable to discontinue and remain off of any medication used to treat chronic pain that is not FDA approved for chronic pain.

18. Subject has pain due to peripheral vascular disease or angina.

19. Subject is on anticoagulation therapy that would preclude their ability to undergo the implant procedure.

7 STUDY ASSESSMENTS

[redacted]

[redacted]

[redacted]

8 STUDY PROCEDURES

[redacted]

[redacted]

[redacted]

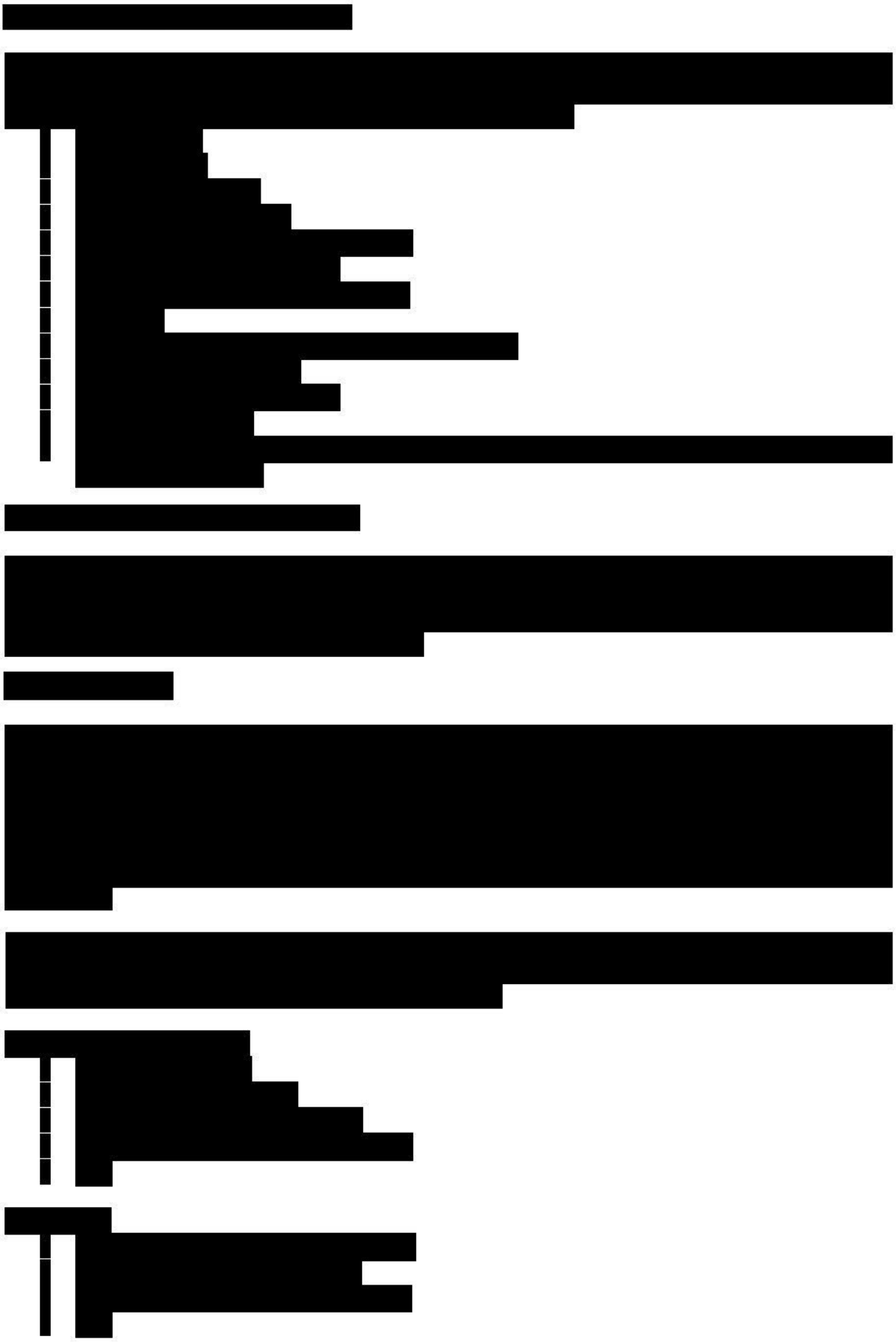
[redacted]

[redacted]

[redacted]

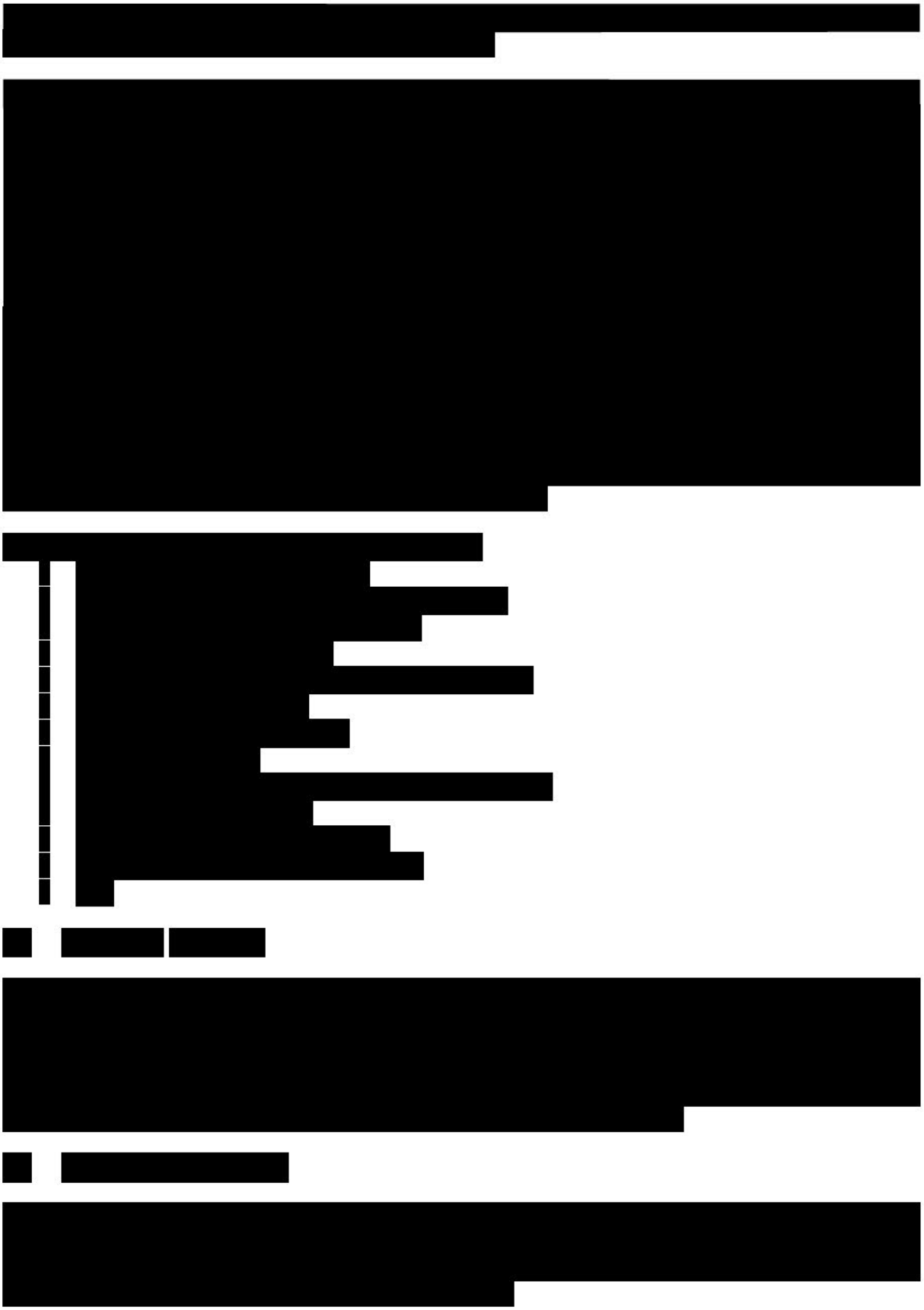
[redacted]

[redacted]



8.5 Implant Procedure Phase

[redacted]



[redacted]

9 ADVERSE EVENTS

9.1 Adverse Event Definitions

[redacted]

[redacted]

9.2 Adverse Event Recording and Reporting

9.2.1 Adverse Event Recording

Investigators are responsible for providing a description of all AEs, including the clinical outcome for the subject. Investigators will evaluate each event for seriousness, severity, and relatedness to the procedure, device, or stimulation therapy. Investigators must supply the Sponsor with any additional information related to safety reporting of a particular event.

[redacted]

9.3 Independent Adjudication Committee

A blinded independent adjudication committee will be responsible for the review, evaluation, categorization, and adjudication of all AEs that occur during the clinical study. AEs will be reported based on the adjudication committee determination.

10 DEVICE DEFICIENCIES

10.1 Device Deficiency Definitions

[redacted]

10.2 Device Deficiency Reporting

The Investigator shall report all suspected device deficiencies to the Sponsor. Device deficiencies will not necessarily result in an AE. However, if an AE is associated with a device deficiency, the AE shall be documented and reported.

11 STATISTICAL ANALYSIS

The most up-to-date description of the analysis resides in the Statistical Analysis Plan (SAP).

11.1 Timing of Analyses

[redacted]

11.2 Study Endpoints

11.2.1 Primary Composite Endpoint

[redacted]

11.2.2 Secondary Endpoints for Hierarchical Testing

[redacted]

11.2.3 Additional Secondary Endpoints

[redacted]

11.3 Sample Size

[redacted]

11.3.1 Calculation

[redacted]

[redacted]

[redacted]

11.4 General Statistical Procedures

[redacted]

- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]

11.4.1 Assessment of Baseline Characteristics

[redacted]

[redacted]

11.4.2 Assessment of Poolability

[redacted]

[redacted]

11.4.3 Analysis Populations

[redacted]

11.4.4 Handling of Missing Data in Primary and Hierarchical Analyses

[redacted]

[redacted]

[redacted]

[redacted]

- [redacted]
- [redacted]
- [redacted]

[redacted]

11.5 Analysis of Study Endpoints

11.5.1 Primary Composite Endpoint

[redacted]

11.5.2 Hierarchical Secondary Endpoints

[redacted]

11.5.3 Other Secondary Effectiveness Endpoints

[redacted]

11.5.4 Adverse Events

[redacted]

12 RISK ANALYSIS

[redacted]

12.2 Minimization of Risks

[redacted]

[redacted]

12.3 Potential Benefits

[redacted]

12.4 Benefit-Risk Conclusions

[redacted]

13 STUDY ADMINISTRATION

13.1 Study Materials

[redacted]

13.1.2 Handling and Storage

[redacted]

13.1.3 Product Administration

[redacted]

13.1.4 Product Accountability

[redacted]

13.2 Ethics

13.2.1 Institutional Review Board Approval

[redacted]

13.2.2 Informed Consent

[redacted]

13.2.3 Subject Confidentiality

[redacted]

13.3 Data and Quality Management

[redacted]

13.3.1 Data Collection and Management

[redacted]

13.3.2 Monitoring

[redacted]

13.3.3 Audits/Inspections

[redacted]

[redacted]

13.4 Access to Study Records

[redacted]

13.5 Study Site Training

[redacted]

13.6 Investigator Responsibilities

[redacted]

13.7 Investigator Agreement and Financial Disclosure

[redacted]

[redacted]

13.7.1 Investigator Records

[redacted]

13.7.2 Investigator Reports

[redacted]

[redacted]

13.8 Sponsor Responsibilities

[redacted]

13.8.1 Sponsor Representatives

[redacted]

13.9 Deviations to the Protocol

[redacted]

13.10 Amendments to the Protocol

[redacted]

13.11 Completion, Early Termination, or Suspension of the Study

[redacted]

13.12 Record Retention

[redacted]

13.13 Clinical Trials Registry/Database (ClinicalTrials.gov)

This clinical study will be registered on www.ClinicalTrials.gov. Study results will be submitted as required. Per the requirements of 21 CFR Part 50, the ICF will contain a statement that clinical trial information will be entered into this clinical trials registry/database.

13.14 Publication

[redacted]

[redacted]

[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

ABBREVIATIONS AND ACRONYMS

[redacted]

BIBLIOGRAPHY

[redacted]

APPENDIX A: [redacted]