Abbott	Clinical Investigation Plan Cover Page

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LBBAP Data Collection Registry
Study Document No: [redacted]
Version B
Date: 02-JUL-2024

Sponsor

Abbott
15900 Valley View Ct.
Sylmar, CA 91342
USA

Clinical Investigation Plan

LBBAP Data Collection Registry

Version Number	B
Date	February 6, 2023
Planned Number of Sites and Region(s)	Up to 20 sites worldwide.
Clinical Investigation Type	The LBBAP data collection registry is a retrospective, observational, non-randomized, multi-center registry.
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Sponsor	Abbott 15900 Valley View Ct. Sylmar, CA 91342 USA
CIP Author of Current Version	[redacted]

[redacted]

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SITE PRINCIPAL INVESTIGATOR SIGNATURE PAGE

I have read and agree to adhere to the clinical investigation plan and all regulatory requirements applicable in conducting this clinical investigation.

Site Principal Investigator

Printed name:
Signature:
Date:

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COMPLIANCE STATEMENT:

This clinical investigation will be conducted in accordance with this Clinical Investigation Plan, the Declaration of Helsinki, applicable Good Clinical Practices and regulations (e.g., US 21 CFR Part 50, 21 CFR Part 56, 21 CFR Part 812 and OUS ISO14155:2020) and the appropriate local legislation(s). The most stringent requirements, guidelines or regulations must always be followed. The conduct of the clinical investigation will be approved by the appropriate Institutional Review Board (IRB)/Ethics Committee (EC) of the respective investigational site and by the applicable regulatory authorities (e.g., FDA, PMDA, MHRA, etc.).

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1.0 INTRODUCTION

This registry is a retrospective, observational, non-controlled chart review conducted to support an indication expansion of the Tendril STS 2088 lead to include pacing/sensing in the left bundle branch area.

This clinical investigation will be conducted in accordance with this CIP. All investigators involved in the conduct of the clinical investigation will be qualified by education, training, or experience to perform their tasks and this training will be documented appropriately.

1.1 Background and Rationale

1.1.1 Background

Patients with cardiac disease may exhibit symptoms associated with electrical conduction abnormalities, such as bradycardia (sinus node dysfunction and/or heart block), thereby requiring implantation of a permanent dual-chamber (atrioventricular) or single-chamber (ventricular) pacemaker. However, these pacing modalities are associated with alteration of the normal electrical conduction due to right ventricular (RV) pacing,[1-3] leading to accelerated progression of left ventricular dysfunction, heart failure, and increasing the risk of heart failure hospitalization and atrial fibrillation.[4, 5] Patients with electrical conduction abnormalities may also present with associated ventricular desynchrony causing further cardiac disease progression into heart failure with impaired left ventricular function.[6]

Physiological pacing achieved by His-bundle pacing (HBP) and left bundle branch area pacing (LBBAP) has emerged as an alternative pacing strategy for patients with pacemaker indications. While HBP can be considered an ideal form of physiological pacing as it activates the heart through the native His-Purkinje conduction system resulting in synchronized contraction of the ventricles obviating RV pacing-related complications, its widespread clinical utility has been limited by technical challenges including lead delivery, accurate His-bundle capture (selective vs. non-selective), and early battery depletion due to high pacing thresholds over time. Left bundle branch area pacing (LBBAP), on the other hand, has been suggested as an effective alternative to overcome the limitations of HBP attributed to the anatomic and histological characteristics of the LBB.[7]

The left bundle branch (LBB) is surrounded by dense myocardial tissue providing a large target zone for pacing owing to its thick, band-like structure.[7] Moreover, the LBB can be activated from the main trunk, the posterior fascicle or the septal fascicle.[7, 8] Therefore, LBBAP presents a lesser technical challenge compared to HBP.

In regard to clinical outcome, it has been reported that LBBAP provides stable and reliable lead parameters at short and intermediate follow-up.[8-11] The need for a back-up RV lead is deemed unnecessary and device programming is simplified.[8, 12] Furthermore, reported complication rates of the 1343 published cases remain low with LBBAP,[13] and increased threshold at follow-up is infrequent thereby minimizing the need for lead revision.[14] Improvements on clinical outcomes of LBBAP compared to RVP has been further demonstrated by Sharma et al. using results from the Geisinger-Rush Conduction System Pacing Registry with a large multicenter cohort. It has been concluded that LBBAP was associated with a significant reduction in the composition outcome of all-cause mortality, heart failure or upgrade to bi-ventricular pacing.[15]

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1.1.2 Rationale for Conducting this Clinical Investigation

LBBAP has emerged as a feasible and safe alternative to traditional pacing modalities with clinical and electrophysiological advantages. This is a retrospective, observational, non-controlled chart review real-world evidence registry to evaluate the safety and effectiveness of LBBA pacing/sensing in patients already implanted with the Tendril STS 2088 lead. The LBBAP data collection registry is designed to support future indication expansion of the existing Tendril STS 2088TC lead to include conduction system pacing in the left bundle branch area (LBBAP). This LBBAP data collection registry is designed in accordance with FDA's guidance documents: Considerations for the Use of Real-World Data and Real-World Evidence To Support Regulatory Decision-Making for Drug and Biological Products – December 2021 and Considerations for the Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices – August 2017. Tendril STS 2088TC bradycardia lead is currently market approved under P960013/S46 on May 26, 2009 and CE-marked under CE Cert no. 17 09 01 14607 104 on June 16, 2009, and is indicated for permanent sensing and pacing in either the right atrium or the right ventricle in combination with a compatible pacemaker, implantable cardioverter defibrillator (ICD) or cardiac resynchronization therapy (CRT-P/CRT-D) device.

2.0 CLINICAL INVESTIGATION OVERVIEW

2.1 Clinical Investigation Objective

The objective of this LBBAP data collection registry is to evaluate the safety and effectiveness of LBBA pacing/sensing in patients already implanted with the Tendril STS 2088 lead.

2.2 Device(s) Used in the Clinical Investigation

2.2.1 Name of the Device(s) Under Investigation

Table 1 outlines the devices included in the registry.

Table 1: Devices Used in the Registry

Device name	Model/Type	Manufacturer	Region/ Country	Investigational or Market Released
Any Abbott market-approved Pacemaker, defibrillator, and/or /CRT device	Any market-approved models	Abbott/St. Jude Medical	All geographies	Market released
Any market-approved pacing, defibrillation, and/or CRT lead(s) – non-LBBAP lead	Any market-approved models	All	All geographies	Market released
Abbott market-approved lead(s) implanted in LBBAP location	Tendril™ STS 2088	Abbott/St. Jude Medical	All geographies	Market released

Merlin Patient Care System	Any market approved model	Abbott/St. Jude Medical	All geographies	Market released
Delivery catheter and other implant tools	Any market-approved model	All	All geographies	Market released

2.2.2 Indication for Use/Intended Purpose

All devices used in this registry are market released. Refer to the specific device IFU for the indications for use.

The Tendril™ STS 2088 leads are indicated for permanent sensing and pacing in either the right atrium or the right ventricle in combination with a compatible device.

2.2.3 Description of the Device(s) Under Investigation

Please refer to the country- and device-specific IFU for additional information regarding the devices used in this clinical investigation.

3.0 CLINICAL INVESTIGATION DESIGN

This is a retrospective, observational, non-controlled, chart review registry designed to evaluate the safety and effectiveness of LBBA pacing/sensing in patients already implanted with the Tendril STS 2088 lead.

Data from a minimum of 220 attempted subjects will be included in order to have 190 evaluable subjects in this registry. The chart review will be conducted at up to 20 participating centers worldwide.

The clinical investigation is a retrospective chart review and therefore involves no pain, discomfort, fear, and any other foreseeable risk as possible for subjects.

3.1 Clinical Investigation Procedures and Follow-up Schedule

The flowchart and the follow-up requirements of this clinical investigation are described below.

Figure 1: Clinical Investigation Flow Chart

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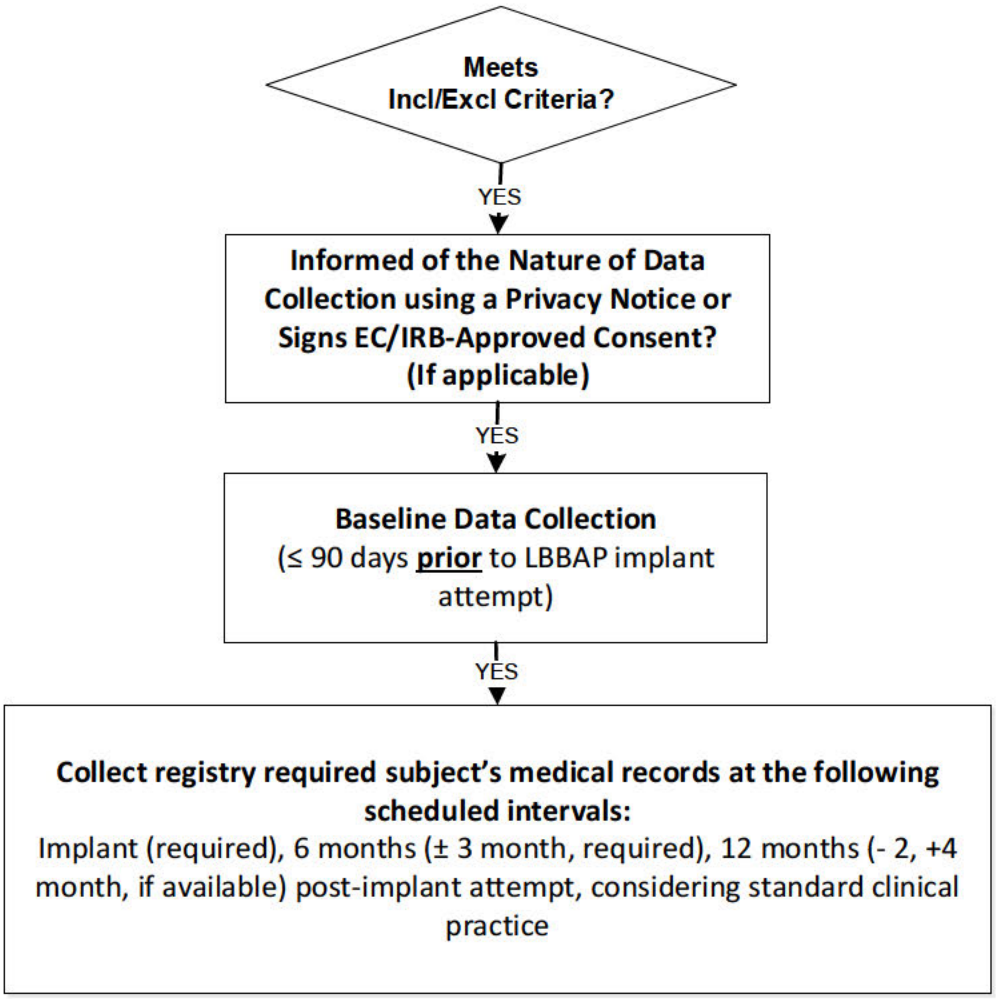

Data included in this LBBAP data collection registry will be from subjects followed for 6 months (± 3 months) after attempted implant of LBBAP location. Data will be collected from previously occurring visits at pre-implant (baseline, required), implant (required), 6 months (±3 months, required), and 12 months (-2, +4months, optional).

3.2 Measures Taken to Avoid and Minimize Bias and Achieve Systemic Data Collection

To avoid bias, investigators should screen records from every patient with an attempted implant of the Tendril™ STS 2088 lead in the LBBA. Enrollment of consecutive subjects should be attempted.

This registry is designed in accordance with FDA's guidance documents: Considerations for the Use of Real-World Data and Real-World Evidence To Support Regulatory Decision-Making for Drug and Biological Products – December 2021 and Considerations for the Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices – August 2017.

The following measures will be taken, but not limited, to ensure that the registry collects both successful and unsuccessful device implantations.

- Sites should retain an enrollment log which links the subject ID and identifiable information for traceability purposes in order to address inquiries from regulatory agencies, as needed.
- Sites should review patient medical records (i.e., electronic health records) and submit only de-identified data through Case Report Forms (CRFs).
- Sites should make all the effort to collect both successful and unsuccessful LBBAP implantation attempts for the time being applicable to the purpose of this registry by utilizing a device inventory list and/or sales data relevant to the usage of the Tendril™ STS 2088 lead.
- Monitoring by the sponsor will be conducted using a risk-based approach to maintain the reliability and data integrity of the data included in this registry (see details in section 10.6).

3.3 Suspension or Early Termination of the Clinical Investigation

While no formal statistical rule for early termination of the clinical investigation for insufficient effectiveness of the device under investigation is defined, the Sponsor reserves the right to discontinue the clinical investigation at any stage or reduce the follow-up period with suitable written notice to the investigator. Possible reason(s) may include, but are not limited to:

- Further product development is cancelled
- Inability to gather adequate patient data

3.3.1 Subject Follow-up for Early Termination or Suspension of Registry

If the Sponsor suspends or prematurely terminates the clinical investigation at an individual site in the interest of safety, the Sponsor will inform all other Principal Investigators.

If suspension or premature termination occurs, the Sponsor will remain responsible for providing resources to fulfill the obligations from the CIP and existing agreements.

The investigator will be requested to return all clinical investigation materials to the Sponsor and provide a written statement to the IRB/EC (if applicable). All applicable clinical investigation documents shall be subject to the same retention policy as detailed in [Section 11.5] of the CIP.

A Principal Investigator, IRB/EC, or regulatory authority may also suspend or prematurely terminate participation in the clinical investigation at the investigational site(s) for which they are responsible. The investigators will follow the requirements specified in the Clinical Trial Agreement.

If a suspended investigation is to be resumed, a prior approval should be obtained from the EC/IRB (if applicable) and a notification should be sent to the regulatory bodies (if applicable).

4.0 ENDPOINTS

4.1 Primary Safety Endpoint and Rationale

The primary safety endpoint evaluates freedom from LBBAP lead related serious adverse device effects (SADEs) through 6 months post-implant attempt.

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The primary safety endpoint evaluates a LBBAP lead related SADE rate which is an appropriate measure for safety and consistent with the primary safety endpoints used for evaluating performance of the transvenous right ventricular lead. It is appropriate to evaluate the safety through 6 months since it is known that a great majority of complications occur through 3 - 6 months after the implantation.[16]

4.2 Primary Effectiveness Endpoint and Rationale

The primary effectiveness endpoint evaluates the composite success rate of acceptable capture thresholds and sense amplitudes for LBBAP at 6 months post-implant. This analysis will be performed with only patients who are successfully implanted with the Tendril™ STS 2088 lead in the LBBA (see details in section 6.1.2). Acceptable ranges for sensing and pacing are shown below:

Parameter	Acceptable values
Pacing voltage	Pacing threshold ≤ 2.0V
Sense amplitude	LBBA sense amplitude ≥ 5.0 mV or ≥ value at implant

The primary effectiveness endpoint evaluates the ability to pace and sense when the Tendril™ STS 2088 lead is implanted in the LBBA. The evaluation of a composite success rate of acceptable pacing thresholds and sense amplitudes is similar to the primary effectiveness endpoints used in for a prior transvenous pacing lead (Tendril FSR 1699T). The 6-month timepoint for assessing the primary effectiveness endpoint is an appropriate time period since these electrical measurements have been demonstrated to be stable starting as early as 1 month post-implant.[17]

4.3 Descriptive Endpoints

Descriptive endpoints are reported using only summary statistics and no hypothesis tests will be performed.

- Demographics (if provided): sex at birth, age range
- Indication for pacemaker or CRT-P/D implant
- Cardiovascular (CV) history and other significant medical conditions
- Procedure and device-related adverse events
- Implant success rate for LBBAP lead and reasons for unsuccessful implant
- Number of repositioning attempts at implant
- Overall procedure time: skin-to-skin
- Implant procedure time: vascular access to lead fixation
- Fluoroscopy time and radiation dose
- Implant tools used (i.e., catheter, stylet, etc.): manufacturer, model#
- Capture threshold, pulse width, sense amplitude, and pacing impedance at all follow-up visits
- Mortality
- QRS duration and morphology (if available)
- NYHA classification (if available)
- LVEF, LVEDV, LVESV (if available)

5.0 SUBJECT SELECTION AND WITHDRAWAL

5.1 Subject Population

This clinical investigation will enroll adult male and female subjects over the age of 18 years, who have undergone an attempt of the Tendril™ STS 2088 lead implant in the LBBA and have 6 months of follow-up in their medical records after LBBAP implant attempt.

5.2 Subject Screening and Informed Consent

5.2.1 Subject Recruitment and Screening

Research personnel at each participating center will identify consecutive subjects with an attempt of the Tendril™ STS 2088 lead implant in the LBBA, which comprise the "primary registry" cohort. Subjects are excluded if there is not 6 months (± 3 months) of follow-up data available in the medical records after the LBBAP implant attempt.

A member of the site's clinical investigation team previously trained to the CIP must evaluate patients for the general clinical investigation eligibility criteria, and if applicable, will enter the patients into a site-specific recruitment/screening log. A patient who does not satisfy all general eligibility criteria prior to informed consent (if required) is considered a recruitment failure and should not be enrolled in the clinical investigation.

In case the subject does not meet all inclusion criteria or meets any of the exclusion criteria, the subject is considered a screening failure. The Principal Investigator or the delegated clinical investigation personnel will record the screening failure in the hospital records and on a recruitment/screening log as required.

Each participating site can enroll up to 25 subjects. The sponsor's approval must be obtained to enroll more than 25 subjects in the registry.

5.2.2 Informed Consent

A waiver of Health Insurance Portability and Accountability Act (HIPAA) and a waiver of patient informed consent will be requested at each site's governing IRB/EC.

The Council for International Organizations of Medical Sciences (CIOMS), in a publication issued jointly with the World Health Organization (WHO), has stated that a waiver of the informed consent requirement may be granted by an Ethics Committee, "when the research design involves no more than minimal risk and a requirement of individual informed consent would make the conduct of the research impracticable (for example, where the research involves only excerpting data from subjects' records)"[18]. This publication also states that in such research conditions, "medical records and biological specimens taken in the course of clinical care may be used for research without the consent of the patients/subjects", when approved by Ethics Committee[18].

This is a retrospective data collection registry that collects only de-identified data. The only risks to patients are related to safeguarding of information. The protocol design includes controls to ensure that there is

minimal risk to patients. Safeguards include design of the registry to use only de-identified data and reporting pooled results with no direct identification of any individual patient or study center.

It would be impracticable to require individual informed consent from each patient. A requirement of informed consent could introduce sampling bias into the findings of the registry since the subset of patients who would respond to a solicitation for a chart review and who would provide consent might not be representative of the population.

For sites where the governing IRB/EC has not granted a waiver of informed consent, subject will be either informed of the nature of the data collection project by means of the privacy notice, or will be asked to provide a signed written informed consent, as approved by the IRB/EC. The investigators will be responsible to follow the recommended privacy notice or consent rules before starting data collection within this registry.

5.2.2.1 Special Circumstances for Informed Consent

The following vulnerable populations are excluded from the registry population:

- Individuals under age of 18 or age of legal consent

5.3 Eligibility Criteria

5.3.1 General Eligibility Criteria

Assessment for general eligibility criteria is based on medical records of the site. Patients must meet ALL of the inclusion criteria to be considered for the clinical investigation. If ANY of the exclusion criteria are met, the patient is excluded from the clinical investigation and cannot be enrolled (recruitment failure).

5.3.2 Inclusion Criteria

5.3.2.1 Inclusion Criteria

1) Subject has a de novo attempted implant of the Tendril™ STS 2088 lead in the Left Bundle Branch Area on or before January 31, 2023 and subject's medical records contain data through at least 6 months (+/- 3 months) after LBBAP implant attempt
2) Subject is ≥ 18 years of age or the legal age, whichever age is greater
3) For sites where the governing IRB/EC has not granted a waiver of informed consent, subject has either been informed of the nature of the clinical investigation using a privacy notice or has provided a signed written informed consent, as approved by the IRB/EC (Note: This inclusion criterion is not applicable for sites where the governing IRB/EC or applicable regulation has granted a waiver of patient consent)

5.3.3 Exclusion Criteria

5.3.3.1 Exclusion Criteria

1) Subject was enrolled in another clinical trial during this data collection period that might impact the outcomes of the present registry

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5.4 Subject Enrollment

Subjects are considered enrolled when research personnel at each participating center verify in the health record that all of the inclusion criteria and none of the exclusion criteria are met and, if applicable, local required privacy notice or consent rules have been followed.

5.5 Subject Withdrawal and Discontinuation

This is a retrospective data collection registry, so there will be no case of subject withdrawal and discontinuation.

5.6 Number of Subjects

Data on a minimum of 220 attempted subjects will be included in order to have 190 evaluable subjects in the registry.

5.7 Total Expected Duration of the Clinical Investigation

The total expected duration of data collection is [redacted] from activation of the first site.

6.0 TREATMENT AND EVALUATION OF ENDPOINTS

As a data collection registry, research personnel at each participating center will collect all of the following data from medical records.

6.1 Assessment time points

6.1.1 Baseline

The baseline refers to the measurements made within 3 months prior to an attempted implant of the Tendril™ STS 2088 lead in the LBBA.

- Demographics (if provided): sex at birth, age range
- Cardiovascular (CV) history and other significant medical conditions
- Cardiac medications
- Indications for pacemaker or CRT-P/D implant
- Intrinsic QRS duration and QRS morphology (if available)
- NYHA classification (if available)
- LVEF, LVEDV, and LVESV (if available)
- Primary indications for device implant

6.1.2 Implant Procedure

The implant procedure is an attempt implant of the Tendril™ STS 2088 lead in the LBBA. Sites report the following measurements from patient's medical record.

- Procedure and device-related adverse events
- Implant success or failure for an LBBAP lead and if not successful, reasons for unsuccessful implant
- Implanted device information
- Number of LBBAP lead repositioning attempts at implant procedure and reason(s) for repositioning
- Overall procedure time: skin-to-skin
- Implant procedure time: vascular access to lead fixation
- Fluoroscopy time and radiation dose
- Implant tools used (i.e., catheter, stylet, etc.): manufacturer, model #
- LBBAP capture threshold, pulse width, sense amplitude, and pacing impedance
- 12-lead ECGs (if available)
- Post-implantation fluoroscopic images in any views (if available)

LBBAP implantation is considered successful if at least one of the following is met,

- Anatomical confirmation of LBBAP with fluoroscopic images (i.e., spatially oriented LBBAP lead implant using RAO or LAO view and contrast injection in RV chamber to confirm deep septal implantation for LBBAP)
- Unipolar-paced QRS morphology demonstrated a Qr or qR pattern in lead V1
- Identification of LBB potential on the sensed electrogram
- Demonstration of transition from nonselective to selective LBB/LV septal capture during threshold testing
- Stimulation to R-wave peak time in lead V5 or V6 < 90 ms

6.1.3 Follow-ups

The post-attempt follow-up visit for LBBAP occurs at 6 months (±3 months), and 12 months (-2, 4 months, optional), considering standard clinical practice.

- LBBAP capture threshold, pulse width, sense amplitude, and pacing impedance
- Adverse event (as applicable)
- Device programming (if available)
- Revision or explant (as applicable)
- Paced QRS duration (if available)
- NYHA classification (if available)
- LVEF, LVEDV, and LVESV (if available)

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6.2 Schedule of Events

CIP Activity	Baseline (≤ 3 months prior to an attempted implant of LBBAP, required)	Implant Attempt (required)	6 Month (±3 months post-attempt, required)*	12 Month (-2, +4 months post-attempt, optional)*
Data transfer notification/Informed consent process (if required by EC/IRB)	X			
Demographics (if provided)	X			
CV history and other significant medical conditions	X			
Implant indication	X			
Cardiac Medications	X			
QRS duration and QRS morphology** (if available)	X	X	X	X
NYHA classification (if available)	X		X	X
LVEF, LVEDV, LVESV (if available)	X	X	X	X
12-lead ECGs (if available)		X		
Post-implantation fluoroscopic images in any views (if available)		X		
Implanted device Information		X		
Number of LBBAP lead repositioning attempts and reason(s) for repositioning		X		
Procedure/fluoroscopy times/radiation dose		X		
Implant tools information		X		
LBBAP capture threshold, pulse width, sense amplitude, lead impedance		X	X	X
Adverse Event		(X)	(X)	(X)
Death	(X)	(X)	(X)	(X)
Product Out of Service		(X)	(X)	(X)
System Revision		(X)	(X)	(X)

(x) if applicable
* If there are multiple visits within the visit window, the closest visit to 6 and 12 months will be captured using the scheduled follow-up CRF and other visit(s) will be captured using the unscheduled follow-up CRF.
** Intrinsic QRS morphology is only applicable at baseline

7.0 Adverse Events

To comply with worldwide standards and guidelines on clinical investigation adverse event reporting, the Sponsor has adopted uniform and worldwide applicable standard definitions and reporting timelines to be used and adhered to by the investigators.

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7.1 Definition

7.1.1 Adverse Event

An Adverse Event (AE) is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, in the context of a clinical investigation, whether or not related to the investigational medical device.

As part of ISO14155 Section 3.2, the Adverse Event definition has the following notes:

Note 1: This definition includes events related to the investigational medical device or the comparator.

Note 2: This definition includes events related to the procedures involved.

Note 3: For users or other persons, this definition is restricted to events related to the use of investigational medical devices or comparators.

7.1.2 Serious Adverse Event

Serious Adverse Event (SAE) is an AE that led to any of the following:

a) death,
b) serious deterioration in the health of the subject, that resulted in any of the following:
    1. life-threatening illness or injury,
    2. permanent impairment of a body structure or a body function,
    3. hospitalization or prolongation of patient hospitalization,
    4. medical or surgical intervention to prevent life threatening illness or injury or permanent impairment to a body structure or a body function.
    5. chronic disease
c) fetal distress, fetal death or a congenital physical or mental impairment or birth defect.

Note: A planned hospitalization for a pre-existing condition, or a procedure required by the CIP without a serious deterioration in health, is not considered a SAE.

7.2 Device Relationship

Determination of whether there is a reasonable possibility that an investigational product or device under investigation caused or contributed to an AE is to be **determined by the Investigator** and recorded on the appropriate CRF form. Determination should be based on the assessment of temporal relationships, evidence of alternative etiology, medical/biologic plausibility and patient condition (pre-existing condition).

7.3 Adverse Event Reporting

7.3.1 Adverse Event Reporting

<u>General Adverse Event Reporting</u>

[redacted]

Sites will collect information on **all procedure and device-related adverse events, whether serious or not, and all death** events and report to the Sponsor on an Adverse Event CRF. Sites should update the Adverse Event CRF with additional information regarding the event as the information becomes available.

Unchanged, chronic, non-worsening or pre-existing conditions are not AEs and should not be reported.

Serious Adverse Event Reporting

The investigator must report all **procedure and device-related SAEs** to the Sponsor as soon as possible.

Sites must record the date the site staff became aware that the event met the criteria of a reportable event as per this protocol in the source document. The Investigator will further report the applicable events to the local IRB/EC according to the institution's IRB/EC reporting requirements (if applicable).

7.3.2 Adverse Event Reporting to Country Regulatory Authorities by the Sponsor

The Sponsor will report the procedure or device-related SAEs to the country regulatory authority per local requirements.

8.0 STATISTICAL CONSIDERATIONS

The following section describes the statistical methods for the clinical investigation. Additional details on statistical analyses, including justification of clinical investigation design, sensitivity analyses, poolability analyses, subgroup analyses and analysis of descriptive endpoints, will be maintained in a separate Statistical Analysis Plan (SAP).

8.1 Analysis Populations

8.1.1 Enrolled Population

This analysis population will include enrolled subjects who have been attempted to implant for the Tendril™ STS 2088 lead in the LBBA.

8.1.2 Successfully Implanted Population

The successfully implanted population includes enrolled subjects who are successfully implanted with the Tendril STS 2088 lead in the left bundle branch area (refer to Section 6.1.2).

8.2 Statistical Analyses

8.2.1 Primary Safety Endpoint Analysis

The primary safety endpoint evaluates freedom from LBBAP lead-related SADEs through 6 months post-implant attempt.

The hypothesis is formally expressed as:

[redacted]

H_0: Freedom from LBBAP lead related SADEs ≤ 81.2%
H_1: Freedom from LBBAP lead related SADEs > 81.2%

[redacted]

The primary safety endpoint will be estimated as a binomial proportion and the 97.5% lower confidence bound (LCB) will be calculated using the Clopper-Pearson exact method. The null hypothesis is rejected at the 2.5% significance level if the LCB is greater than the performance goal (PG) of 81.2%. The p-value from a one-sided exact test for the binomial proportion will also be calculated and compared to the 0.025 significance level.

This analysis will be performed on the enrolled population, and the primary safety analysis will use evaluable subjects (refer to Section 8.3.1).

8.2.2 Primary Effectiveness Endpoint Analysis

The primary effectiveness endpoint evaluates the composite success rate of acceptable capture thresholds and sense amplitudes for LBBAP at 6 months post-implant.

The hypothesis is formally expressed as:

H_0: Composite success rate ≤ 80%
H_1: Composite success rate > 80%

Parameter	Acceptable values
Pacing voltage	Pacing threshold ≤ 2.0V
Sense amplitude	LBBA sense amplitude ≥ 5.0 mV or ≥ value at implant

Success Criteria: A subject will be considered to have met the primary effectiveness endpoint if: the pacing threshold voltage ≤ 2.0 V and LBBA sense amplitude is ≥ 5.0 mV or ≥ value at implant at 6 months. For subjects that do not have LBBA amplitude measured due to active tachyarrhythmias or any other heart rhythm conditions or procedures which prevent sense amplitude from being measured, success will be determined from the pacing threshold only. For subjects that do not have pacing threshold measured, due to active tachyarrhythmias or any other heart rhythm conditions or procedures which prevent pacing threshold from being measured, success will be determined from LBBA sense amplitude only. Subjects that do not have LBBA sense amplitude and pacing voltage, both of which are unobtainable due to active tachyarrhythmias or any other heart rhythm conditions or procedures which prevent pacing threshold from being measured, will be excluded from the analysis.

[redacted]

The success rate will be estimated as a binomial proportion and the 97.5% LCB of the rate will be calculated using the Clopper-Pearson exact method. The null hypothesis is rejected as the 2.5% significance level if the LCB exceeds the PG of 80%. The p-value from a one-sided exact test for the binomial proportion will also be calculated and compared to the 0.025 significance level.

[redacted]

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This analysis will be performed on the successfully implanted population, and the primary effectiveness analysis will use last observation carried forward (LOCF) method. Sensitivity analysis will be performed using multiple imputation.

8.2.3 Descriptive Endpoints Analyses

Summary statistics and no hypothesis tests will be provided for the following variables.

- Demographics (if provided): sex at birth, age range
- Indication for pacemaker or CRT-P/D implant
- Cardiovascular (CV) history and other significant medical conditions
- Procedure and device-related adverse events
- Implant success or failure for an LBBAP lead and if not successful, reasons for unsuccessful implant
- Number of repositioning attempts at implant
- Overall procedure time: skin-to-skin
- Implant procedure time: vascular access to lead fixation
- Fluoroscopy time and radiation dose
- Implant tools used (i.e., catheter, stylet, etc.): manufacturer, model#
- Capture threshold, pulse width, sense amplitude, and pacing impedance at all follow-up visits
- Mortality
- QRS duration and morphology (if available)
- NYHA classification (if available)
- LVEF, LVEDV, LVESV (if available)

8.3 Sample Size Calculation

8.3.1 Primary Safety Endpoint

[redacted] The minimum sample size to reject the null hypothesis is 165 evaluable subjects with 85% power at 2.5% one-sided significance level.

[redacted]

8.3.2 Primary Effectiveness Endpoint

[redacted] The minimum sample size to reject the null hypothesis is 190 evaluable subjects with 85% power at 2.5% one-sided significance level.

[redacted]

8.4 Timing of Analysis

The Sponsor will conduct the primary endpoint analyses when required data collection is complete.

8.5 Subgroup Analysis

Subgroup analyses may be performed on an ad hoc basis to understand outcomes for specific indications and patient populations.

8.6 Procedures for Accounting for Missing Data

The primary safety endpoint analysis will include evaluable subjects only. The primary effectiveness endpoint analysis will use LOCF method to impute missing 6-month data and sensitivity analyses will be performed using multiple imputation. All other outcome measures will be based on the available data, with no imputation for missing values.

8.7 Planned Interim Analysis

No interim analyses are planned for this registry.

8.8 Deviations from Statistical Plan

The Sponsor will document any major changes to the statistical plan in an amendment to the statistical plan and any less significant changes to the planned analyses in the final report.

9.0 DIRECT ACCESS TO SOURCE DATA/DOCUMENTS

The data collection for this clinical investigation will be performed by personnel at the investigating institution.

The investigator/institution will permit direct access to source data/documents for performing clinical investigation-related monitoring, audits, IRB/EC review, and regulatory inspections.

10.0 QUALITY CONTROL AND QUALITY ASSURANCE

10.1 Selection of Clinical Sites and Investigators

The Sponsor will select investigators qualified by training and experience to participate in the clinical investigation.

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10.2 Site Principal Investigator Responsibilities

The role of the Site Principal Investigator is to implement, oversee the management of the day-to-day conduct of the clinical investigation as well as ensure data integrity and the rights, safety and well-being of the subjects involved in the clinical investigation. The principal investigator shall support monitoring and reporting to IRB/EC and local competent authorities as necessary, throughout the conduct of the clinical investigation.

The principal investigator is responsible for ensuring adequate training and qualification of the investigation site team and for maintaining oversight of their activities. The principal investigator may delegate tasks to members of the investigation site team but retains responsibility for the clinical investigation. This also applies when activities are outsourced to an external organization by the principal investigator in which case he/she shall exercise oversight to ensure the integrity of all tasks performed and any data generated by this external organization.

10.3 Clinical Investigation Finances and Agreements

Abbott will finance the clinical investigation and will compensate investigational sites for participation in the clinical investigation per the conditions of agreement between Abbott and the investigational site.

10.4 CIP Amendments

The Sponsor will provide approved CIP amendments to the Investigators prior to implementing the amendment. The Principal Investigator is responsible for notifying the IRB/EC or equivalent committee of the CIP amendment (administrative changes) or obtaining IRB's/EC's approval of the CIP amendment (changes in subject care or safety), according to the instructions provided by the Sponsor with the CIP amendment.

Sites must document in writing acknowledgement/approval of the CIP amendment by the IRB/EC prior to implementation of the CIP amendment. Sites must also provide copies of this documentation to the Sponsor.

10.5 Training

10.5.1 Site Training

All Investigators and clinical investigation personnel are required to attend Sponsor training sessions, which may be conducted at an Investigator's meeting, a site initiation visit, or other appropriate training sessions. Over-the-phone or self-training may take place as required. Training of Investigators and clinical investigation personnel will include, but is not limited to, the CIP requirements, electronic case report form completion, and clinical investigation personnel responsibilities. All Investigators and clinical investigation personnel that are trained must sign a training log (or an equivalent) upon completion of the training. Prior to signing the training log, Investigators and clinical investigation personnel must not perform any CIP-related activities that are not considered standard of care at the site.

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10.6 Monitoring

Sponsor and/or designee will monitor the clinical investigation over its duration according to the CIP-specific monitoring plan which will include the planned extent of source data verification.

Prior to initiating any procedure, the Sponsor monitor (or delegate) will ensure that the following criteria are met:

- The investigator understands and accepts the obligation to conduct the clinical investigation according to the CIP and applicable regulations and has signed the Investigator Agreement or the Clinical Trial Agreement.
- The Investigator and his/her staff should have sufficient time and facilities to conduct the clinical investigation and should have access to an adequate number of appropriate subjects to conduct the clinical investigation.
- Sites must have source documentation (including original medical records) to substantiate proper informed consent procedures (if required), adherence to CIP procedures, adequate reporting and follow-up of adverse events, accuracy of data collected on case report forms, and device information.
- The Investigator/site will permit access to such records and will maintain a monitoring visit sign-in log at the site. The Investigator will agree to dedicate an adequate amount of time to the monitoring process. The Investigator and/or research coordinator will be available for monitoring visits. It is expected that the Investigator will provide the monitor with a suitable working environment for review of clinical investigation-related documents.

10.7 Deviations from CIP

The Investigator should not deviate from the CIP for any reason

The Sponsor will not grant any waivers for CIP deviations. Sites must report all deviations to the Sponsor using the Deviation CRF. The Sponsor will monitor the occurrence of CIP for evaluation of investigator compliance to the CIP and regulatory requirements and handle according to written procedures. Investigators will determine the cause of deviations, implement corrective actions and inform their IRB/EC or equivalent committee of CIP deviations in accordance with their specific IRB/EC or equivalent committee reporting policies and procedures.

In the event of repeated non-compliance, as determined by the Sponsor, a Sponsor's monitor or company representative will attempt to secure compliance by one or more of the following (and not limited to):

- Visiting the investigator and/or delegate
- Telephoning the investigator and/or delegate
- Corresponding with the investigator and/or delegate

Repeated non-compliance with the signed agreement, the CIP, or any other conditions of the clinical investigation may result in further escalation in accordance with the Sponsor's written procedures,

including securing compliance or, at its sole discretion, the Sponsor may terminate the investigator's participation in the clinical investigation.

10.8 Quality Assurance Audit

A Sponsor representative or designee may request access to all clinical investigation records, including source documentation, for inspection during a Quality Assurance audit.

If an investigator is contacted by a Regulatory Agency in relation to this clinical investigation, the Investigator will notify Sponsor immediately. The Investigator and Research Coordinator must be available to respond to reasonable requests and audit queries made during the audit process. The Investigator must provide the Sponsor with copies of all correspondence that may affect the review of the current clinical investigation (e.g., Form FDA 483, Inspectional Observations, Warning Letters, Inspection Reports, etc.). The Sponsor may provide any needed assistance in responding to regulatory audits.

10.9 Sponsor Auditing

Sponsor audits may be performed for other clinical investigations as required by the design and/or regulatory impact of the investigation.

1. The Sponsor shall prepare an audit plan as well as the operating procedures for the related duties and conduct audits in accordance with the audit plan and the operating procedures.
2. Individuals engaged in auditing (hereinafter referred to as "auditor") shall be different than those in charge of medical device development or monitoring.
3. The auditor shall prepare an audit report documenting the matters confirmed in the audit to certify and verify that the audit has been conducted and submit them to the Sponsor.

11.0 DATA HANDLING AND RECORD KEEPING

Sponsor and/or its affiliates will maintain documentation of the systems and procedures used in data collection for the duration of the clinical investigation.

CRF data collection will be performed through a secure web portal and only authorized personnel will access the EDC system using a unique username and password to enter, review or correct data. Passwords and electronic signatures will be strictly confidential.

The data will be subjected to consistency and validation checks within the EDC system and supplemental review by the Sponsor.

At the end of the clinical investigation, completed CRF images with the date-and-time stamped electronic audit trail indicating the user, the data entered, and any reason for change (if applicable) will be provided to the investigational sites, if requested.

For the duration of the clinical investigation, the Investigator will maintain complete and accurate documentation including, but not limited to, medical records, clinical investigation progress records, laboratory reports, CRFs, signed ICFs/data collection notifications (if applicable), device accountability

records (if applicable), correspondence with the IRB/EC and clinical investigation monitor/Sponsor, adverse event reports, and information regarding subject completion of the clinical investigation.

11.1 Protection of Personally Identifiable Information

The Sponsor respects and protects personally identifiable information collected or maintained for this clinical investigation.

The Sponsor implements technical and physical access controls to ensure that Personal Information is accessible only to and processed only on a 'need to know' basis, including periodic review of access rights, and revocation of access when an individual's employment is terminated or the individual transitions to a role that does not require access to Personal Information, and appropriate restrictions on physical access to premises, facilities, equipment, and records containing Personal Information.

The Sponsor requires the investigational sites to enter only pseudonymous Personal Information (key-coded) necessary to conduct the clinical investigation, such as the patient's medical condition, treatment, dates of treatment, etc., into Sponsor's data management systems. The Sponsor discloses as part of the clinical investigation informed consent/data transfer notification process that some Sponsor representatives still may see Personal Information at the participating sites for monitoring and quality control purposes. All parties will observe confidentiality of Personal Information always throughout the clinical investigation. All reports and data publications will preserve the privacy of each subject and confidentiality of his/her information.

The Sponsor data management systems and processes were designed, developed, and tested according to industry standards to appropriately safeguard Confidential Information (including any Personal Information) against unauthorized access and/or interference by third parties, intrusion, theft, destruction, loss or alteration. Clinical Investigation data are encrypted in transit and at rest.

The Sponsor maintains a Privacy Incident procedure that complies in all respects with Applicable Law and industry best practices.

11.2 Data Management Plan

A Data Management Plan (DMP) will describe procedures used for data review, data cleaning, issuing and resolving data discrepancies, and database locking. If appropriate, the Sponsor may update the DMP throughout the duration of the clinical investigation. The Sponsor will track and document control all revisions.

11.3 Source Documentation

Regulations and GCP require the Investigator to maintain information in the subject's original medical records that corroborates data collected on the CRFs. To comply with these regulatory requirements/GCP, sites should include the following information in the subject record at a minimum and if applicable to the clinical investigation:

- Medical history/physical condition of the subject before involvement in the clinical investigation sufficient to verify CIP entry criteria

- Dated and signed notes on the day of entry into the clinical investigation referencing the Sponsor, CIP number, subject ID number, and a statement that informed consent was obtained (if applicable)
- Dated and signed notes from each subject visit (for specific results of procedures and exams)
- AEs reported and their resolution, including supporting documents, such as discharge summaries, catheterization laboratory reports, ECGs, and lab results including documentation of site awareness of SAEs and of investigator assessment of device relationship for SAEs.
- CIP-required laboratory reports and 12-lead ECGs, reviewed and annotated for clinical significance of out of range results (if applicable).
- Notes regarding prescription medications taken at baseline
- Subject's condition upon completion of the clinical investigation
- Any other data required to substantiate data entered into the CRF

11.4 Case Report Form Completion

Site research personnel trained on the CIP and CRF completion will perform the primary data collection clearly and accurately based on source-documented hospital and/or clinic chart reviews. The investigator will ensure accuracy, completeness, legibility, and timeliness of the data reported to the Sponsor on the CRFs and in all required reports.

Only authorized site personnel will be permitted to enter the CRF data through the EDC system deployed by the Sponsor. The Sponsor will use an electronic audit trail to track any subsequent changes of the entered data.

11.5 Record Retention

The Sponsor and Investigator/Site will archive and retain all documents pertaining to the clinical investigation as per the applicable regulatory record retention requirements. The Investigator must obtain permission from Sponsor in writing before destroying or transferring control of any clinical investigation records.

12.0 ETHICAL CONSIDERATION

12.1 Institutional Review Board/Medical Ethics Committee Review and Approval

The Principal Investigator at each investigational site will obtain IRB/EC approval for the CIP (if applicable) and ICF/data transfer notification provided to the patient (if applicable) prior to consenting (if applicable) and enrolling patients in this clinical investigation. The site must receive the approval letter prior to the start of this clinical investigation and provide a copy to the Sponsor.

Sites will submit any amendments to the CIP as well as associated ICF/data transfer notification changes (if applicable) to the IRB/EC and written approval obtained prior to implementation, according to each institution's IRB/EC requirements.

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No changes will be made to the CIP or ICF/data transfer notification (if applicable) or other written information provided to the patient (if applicable) without appropriate approvals, including IRB/EC, the Sponsor, and the regulatory agencies (if applicable).

Until the clinical investigation is completed, the Investigator will advise his/her IRB/EC of the progress of this clinical investigation, per IRB/EC requirements. Written approval must be obtained from the IRB/EC yearly to continue the clinical investigation, or according to each institution's IRB/EC requirements.

Sites will not perform any investigative procedures, other than those defined in this CIP, on the enrolled subjects without the written agreement of the IRB/EC and the Sponsor.

13.0 CLINICAL INVESTIGATION CONCLUSION

The clinical investigation will be concluded when:

- All sites are closed AND
- The final report has been provided to investigators or the Sponsor has provided formal documentation of clinical investigation closure.

The Sponsor will submit the clinical investigation report within one year of the end of the investigation to the investigational sites, competent authorities and reviewing IRBs and ECs.

14.0 PUBLICATION POLICY

The data and results from the clinical investigation are the sole property of the Sponsor. The Sponsor shall have the right to access and use all data and results generated during the clinical investigation. The Investigators will not use this clinical investigation-related data without the written consent of the Sponsor for any purpose other than for clinical investigation completion or for generation of publication materials, as referenced in the Clinical Trial Agreement. Single-center results are not allowed to be published or presented before the multi-center results. The Sponsor must review and approve any proposals for publications or presentations by the investigators in a timely manner in compliance with the Sponsor's publication policy set forth in the Clinical Trial Agreement.

The Sponsor will be responsible for registering this clinical investigation on ClinicalTrials.gov website, in accordance with the International Committee of Medical Journal Editors guidelines, or any other applicable guidelines. Sponsor shall be responsible for any such registration and results posting as required by the ClinicalTrials.gov website. Institution and/or Principal Investigator(s) shall not take any action to register the clinical investigation. A full report of the pre-specified outcomes, regardless of the results, will be made public through the ClinicalTrials.gov website no later than 12 months after clinical investigation completion, as required by section 801 of the FDA Amendments Act. If this clinical investigation is terminated early, the Sponsor will make every effort to hasten the release of the pre-specified outcomes through the ClinicalTrials.gov website.

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15.0 RISK ANALYSIS

This is a retrospective data collection registry; no clinical activities will be performed on any subjects. Therefore, there is no risk analysis required.

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APPENDIX I: ABBREVIATIONS AND ACRONYMS

Abbreviation	Term
AE	Adverse Event
CIP	Clinical Investigational Plan
DMP	Data Management Plan
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
IRB	Institutional Review Board
LBBAP	Left Bundle Branch Area Pacing
LVEF	Left Ventricular Ejection Fraction
LVEDV	Left Ventricular End Diastolic Volume
LVESV	Left Ventricular End Systolic Volume
NA	Not Applicable
RVP	Right Ventricular Pacing
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event

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APPENDIX II: SITE CONTACT INFORMATION

A list of Clinical Investigational sites will be kept under a separate cover and is available upon request.

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APPENDIX III: LABELS

IFU documents will be kept under a separate cover and are available upon request.

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APPENDIX IV: CASE REPORT FORMS

Case Report Forms will be kept under a separate cover and are available upon request.

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APPENDIX V: MONITORING PLAN

A copy of the Monitoring Plan can be obtained upon request from the Sponsor Clinical Project Manager for the clinical investigation.

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APPENDIX VI: REVISION HISTORY

[redacted]

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APPENDIX VII: CIP SUMMARY

Clinical Investigation Name and Number	LBBAP Data Collection Registry
Title	Left Bundle Branch Area Pacing (LBBAP) Data Collection Registry
Objective(s)	The LBBAP data collection registry will be conducted to support an indication expansion of the Tendril™ STS 2088 lead to include pacing/sensing in the left bundle branch area.
Device Under Investigation	Tendril™ STS 2088 lead
Number of Subjects Required for Inclusion in Clinical Investigation	Data on a minimum of 220 attempted subjects will be included in order to have 190 evaluable subjects in this registry. The chart review will be conducted at up to 20 centers worldwide.
Clinical Investigation Design	Retrospective, observational, non-randomized, multi-center registry • This registry will retrospectively collect data on LBBAP implants already attempted in patients using the Tendril STS 2088 lead. • Sites should make every effort to enroll consecutive subjects with an attempted LBBAP implant • Sites will retain an enrollment log which links the subject ID and identifiable information for traceability purposes in order to address inquiries from regulatory agencies, as needed. • Sites will review patient medical records (i.e., electronic health records) and submit only de-identified data through Case Report Forms (CRFs) • Sites should make all the effort to collect both successful and unsuccessful LBBAP implantation attempts for the time being applicable to the purpose of this registry by utilizing a device inventory list and/or sales data relevant to the usage of the Tendril™ STS 2088 lead. • Data will be collected from previously occurring visits at baseline (required), implant (required), 6 months (± 3 months, required), and 12 months (-2, +4 months, optional). • Monitoring by the sponsor will be conducted using a risk-based approach to maintain the reliability and data integrity of the data included in this registry.
Waiver of Informed Consent	Waiver of patient informed consent will be requested at each site's governing IRB/EC since this registry involves no more than minimal risk and a requirement of individual informed consent would make the conduct of the research impracticable[1]

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	• No more than minimal risk: The only risk to patients are related to the safeguarding of patient information. The registry design mitigates this risk by including controls to ensure there is minimal risk to patients by collecting only de-identified data and reporting pooled results with no direct identification of any individual patient or study center. • Impracticable to require individual informed consent: A requirement of informed consent could introduce sampling bias into the findings since the subset of patients who respond to the solicitation for this registry and who provide informed consent may not be representative of the registry population [1]Council for International Organizations of Medical S. International ethical guidelines for biomedical research involving human subjects. Bull Med Ethics. 2002(182):17-23.
Primary Endpoints	The primary safety endpoint evaluates freedom from LBBAP lead related serious adverse device effects (SADEs) through 6 months post-implant attempt. The primary effectiveness endpoint evaluates the composite success rate of acceptable capture thresholds and sense amplitudes for LBBAP at 6 months after successful implantation.
Subject Follow-up	• Follow-up office visits as noted in subject's medical records at the following scheduled interval: Implant (required), 6 months (± 3 months, required), and 12 months (-2, +4 months, optional) post-implant attempt • Any visits that occur between this visit schedule will be collected and reported as unscheduled visits.
Inclusion Criteria	1) Subject has a de novo attempted implant of the Tendril™ STS 2088 lead in the Left Bundle Branch Area on or before January 31 2023 and Subject's medical records contain data through at least 6 months (± 3 months) after LBBAP implant attempt 2) Subject is ≥ 18 years of age or the legal age, whichever age is greater 3) For sites where the governing IRB/EC has not granted a waiver of informed consent, subject has either been informed of the nature of the clinical investigation using a privacy notice or has provided a signed written informed consent, as approved by the IRB/EC (Note: This inclusion criterion is not applicable for sites where the governing IRB/EC or applicable regulation has granted a waiver of patient consent)
Exclusion Criteria	1) Subject was enrolled in another clinical trial during this data collection period that might impact the outcomes of the present registry

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APPENDIX VIII: REFERENCES

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