Physiologic Pacing Registry

Version Number: C
Date: June 9, 2020
NCT Number: NCT03719040
Sponsor: Abbott

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Clinical Plan

Clinical Plan Number
[redacted]

Version Number	[redacted]
Date	[redacted]
Planned Number of Sites and Region(s)	[redacted]
Clinical Investigation Type	The Physiologic Pacing Registry is a prospective, observational, multi-center registry.
Abbott Medical Expert	[redacted]
Sponsor	Abbott [redacted]
CIP Author of Current Version:	[redacted]

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COMPLIANCE STATEMENT:

This registry will be conducted in accordance with this Clinical Plan, the Declaration of Helsinki, applicable Good Clinical Practices and regulations (e.g. US 21 CFR Part 50, 21 CFR Part 56, and OUS ISO14155:2011) and the appropriate local legislation(s). The most stringent requirements, guidelines or regulations must always be followed. The conduct of the registry will be approved by the appropriate Institutional Review Board (IRB)/Ethics Committee (EC) of the respective clinical site and by any applicable regulatory authorities.

1.0 INTRODUCTION

The Physiologic Pacing Registry is a prospective, observational, multi-center registry performed to gain a broader understanding of 1) physiologic pacing implant and follow-up workflows, including pacing and sensing measurements and 2) the clinical utility in creating a 3-dimensional electro-anatomical map of cardiac structures prior to physiologic pacing device implants based on the clinical site's routine care. The registry will include patients undergoing implantation of an Abbott pacemaker, defibrillator, or a cardiac resynchronization therapy (CRT) pacemaker (CRT-P) or CRT defibrillator (CRT-D) according to the clinical site's routine care. Only patients scheduled to receive an Abbott device may be enrolled to ensure proper device data collection for future software and other physiologic pacing product development. The decision to provide physiologic pacing therapy and selection of devices for implant are at the discretion of the implanting physician. Abbott will collect data on the use of all commercially available leads and associated implant tools based on the physician's discretion as part of routine clinical practice within the registry.

This registry will be conducted in accordance with this Clinical Plan. All investigators involved in the conduct of the registry 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 and/or sinus node dysfunction, 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) apical pacing,[1,2,3] leading to accelerated progression of 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 dyssynchrony causing further cardiac disease progression into heart failure with impaired left ventricular function.[6] The standard of care treatment for patients with ventricular dyssynchrony is implantation of a CRT system to activate the left ventricle and resynchronize the electrical conduction within the heart. However, CRT is not always feasible due to difficulty in placing the left ventricular lead. Furthermore, the percentage of CRT non-responders remains high, up to 30-40%.[7,8]

An alternative and potentially more effective pacing strategy for patients with electrical conduction abnormalities is physiologic pacing. Physiologic pacing is achieved by delivering a pacing stimulus to a cardiac conduction structure, such as the bundle of His or left bundle branch (LBB) of the His-Purkinje system, with a permanent lead. Physiologic pacing activates the heart through the native His-Purkinje conduction system, thus offering the most

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physiologic pacing approach to correct electrical dyssynchrony. Physiologic pacing has emerged as a feasible and safe alternative to pacemaker therapy and CRT with clinical and electrophysiological advantages.

On such example of physiologic pacing includes activation of the His bundle. The concept of His bundle pacing (HBP) was first described by Scherlag et al based on recruiting the heart's native His-Purkinje system via pacing in both dogs and humans.[9] Follow-up clinical studies demonstrated a more thorough understanding of the His bundle conduction system demonstrating that pacing distal to the site of conduction delay could recruit fibers predestined to be the bundle branches and thereby narrow the QRS duration in patients with bundle branch block.[10,11,12] The next step of proving the viability of permanent HBP as a potential therapy was demonstrated in 2000 by Deshmukh et al. [13] in patients with normal His-Purkinje activation. This first study of permanent HBP showed implant success in 12 of 18 patients (67%) with chronic atrial fibrillation after ablation of the atrioventricular junction.[14,15] A subsequent study of permanent HBP several years later demonstrated a success rate of 65% in patients with AV block using standard pacing leads with retractable screws and manually shaped stylets.[16] Likewise, early feasibility studies of HBP in patients meeting CRT indications have shown that patients have narrower paced QRS, (as compared to intrinsic or CRT paced), shorter implant times, improved quality of life, improved left ventricular ejection fraction (LVEF), and improved New York Heart Association (NYHA) classification [17,18,19] in lieu of a left ventricular lead.[20] From these early studies, researchers found that QRS changes occur with different morphologies when undergoing permanent HBP [21,22, 23] and the morphology presentation is dependent upon: 1) the voltage output of the pulse generator 2) the anatomical position of the HBP lead and 3) the anatomical structure of the His bundle region. Identification of the HBP morphology is important to locate the optimal lead implant location and pacing configuration. These three characteristics also play a key role in the degree of electrical capture during HBP, resulting in either selective (pure His-bundle capture) or non-selective (surrounding fibrous tissue also recruited along with His-bundle) pacing.

Another example of physiologic pacing is direct stimulation of the left bundle branch (left bundle branch pacing – LBBP). Indirect stimulation of the left bundle branch was first demonstrated by El-Sherif et al [12] in CRT-indicated patients by using HBP and increasing the pacing output, thereby correcting left bundle branch block (LBBB). Direct LBBP was first reported by Huang et al [26, 27] during implant of a pacemaker in a patient with heart failure and LBBB. In this case, HBP with a high pacing output did not correct the LBBB but advancing the tip of the pacing lead to a more distal position did correct the LBBB at a lower pacing output. This resulted in a normalized QRS duration with prolonged AV delay, indicating synchronous LBBP with intrinsic RV stimulation was achieved. Similar to the reported effects of HBP, this patient saw significant improvement in their LVEF and significant reduction in heart failure symptoms. Based on these results, Huang et al proposed LBBP by stimulating distal to the diseased region for patients with heart failure and LBBB. Several subsequent studies have shown LBBP to be a safe and feasible pacing method not only for this patient population but also for patients with bradycardia. [28 - 36] Similar to HBP, LBBP capture can be either selective or non-selective. Confirmation of LBB capture is typically verified by QRS morphology changes from LBB pacing, identification of the LBB potential recorded from the pacing lead, selective capture with specific ECG changes and EGM component, and evaluation of the time from pacing stimulus to LV activation. [38, 39] Other methods of activating the left bundle branch through indirect stimulation are emerging and may be assessed through this registry as well.

One major goal of physiologic pacing is to provide a consistent reduction in QRS duration. Physiologic pacing provides an opportunity to ensure the normalization of the QRS; however, many technical challenges remain, including: lead delivery, accurate His-Purkinje capture (selective vs. non-selective), and maintenance of stable pacing thresholds over time. The data collected from this registry will offer further evidence on the utility of physiologic pacing implants and currently available tools, as well as the potential advantages of enhanced localization of physiologic pacing structures using a 3-dimensional mapping system.

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1.1.2 Rationale for Conducting this Clinical Registry

In the recent recommendations from the His Bundle Pacing Collaborative Working group[24], the authors suggested that technical challenges of achieving permanent HBP has been an obstacle to its reliable application in routine clinical practice. These technical challenges include difficulty in locating and placing a pacing lead at the appropriate His bundle location due to its small size and the surrounding fibrous tissue. There are additional concerns related to maintaining chronic pacing due to high thresholds and lead dislodgement. Pacing the LBB as known today has similar challenges in locating and navigating the pacing lead to a small target.

The Physiologic Pacing Registry will be conducted to gain a deeper understanding of device implants for physiologic pacing and follow-up workflows, including the use of any lead delivery tools, to help inform Abbott's product and clinical data development efforts. Additionally, the registry will provide a broader understanding of the clinical utility in mapping cardiac conduction structures, such as the bundle of His and Left Bundle Branch, with the use of Abbott's EnSite Cardiac Mapping System with an electrophysiology catheter prior to device implants for those institutions where mapping is routine care prior to a physiologic pacing device implant.

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2.0 CLINICAL REGISTRY OVERVIEW

2.1 Objectives

2.1.1 Primary objective

The Physiologic Pacing Registry will characterize implant and follow-up measures associated with physiologic pacing device implants. The registry will also compare implant and follow-up characteristics for these device implants with and without utilizing the EnSite Cardiac Mapping System, based on the site's routine care. Data on all tools used as chosen by the physician as part of their standard practice will be collected. Abbott will collect data on the following characteristics at implant and follow-up:

Implant Characteristics:

- Fluoroscopy time and radiation dose
- Overall procedure time: skin-to-skin
- Implant procedure time: vascular access to lead fixation
- All implant tools used
- Implant-related workflow
- Final implanted hardware
- Final post-procedure device programming
- Procedure- and device-related adverse events and device deficiencies
- Implant success
- All types of physiologic pacing capture observed such as selective and non-selective
- Physiologic pacing capture and sensing thresholds
- Pacing output necessary to correct bundle branch block using 12-lead ECG (if applicable)
- Presenting QRS duration at baseline using 12-lead ECG
- QRS duration for all types of physiologic pacing captures observed using 12-lead ECG
- For His placement only: Measured H wave using device intracardiac electrogram (IEGM)
- Measured R wave using device IEGMs through the lead implanted for physiologic pacing

Follow-up Characteristics:

- Follow-up related workflow
- Physiologic pacing capture and sensing thresholds
- For His placement only: Measured H wave using device IEGM
- Measured R wave using device IEGMs through the lead implanted for physiologic pacing
- Presenting PR interval and QRS duration using 12-lead ECG
- QRS duration for all types of physiologic pacing captures observed using 12-lead ECG
- Incidence of increase in capture threshold of > 1V in leads implanted for physiologic pacing or RV pacing leads

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- Far-field atrial oversensing and ventricular oversensing and/or any interventions – including programming – required to address these issues
- NYHA Classification
- LVEF, Left Ventricular End Diastolic Volume (LVEDV), Left Ventricular End Systolic Volume (LVESV) (if available)
- Tricuspid and mitral regurgitation severity by echocardiogram (if available)
- Device estimated battery longevity via device session records
- Frequency/burden of detected atrial and ventricular arrhythmias via device session records
- Procedure and device-related adverse events and device deficiencies

2.2 Device(s) To Be Used in the Clinical Registry

2.2.1 Name of the Device(s)

Table 1 outlines the devices that will be used. The devices selected for use will be at the discretion of the implanting physician.

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	St. Jude Medical	All geographies	Market released
Any market-approved pacing, defibrillation, and/or CRT lead(s)	Any market-approved models	All	All geographies	Market released
EnSite Cardiac Mapping System (optional)	Any market-approved models	St. Jude Medical	All geographies	Market released
Merlin Patient Care System	v19.1.1 or later	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 Intended Indication for Use

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

2.2.3 Description of the Device(s)

Please refer to the Indications for Use for additional information regarding the devices used in this registry.

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3.0 REGISTRY DESIGN

The Physiologic Pacing Registry is a prospective, observational, multi-center registry designed to characterize device data at implant and follow-up in patients with a permanent physiologic pacing lead and an Abbott pacemaker, defibrillator, or CRT-P/D. The devices selected for use will be at the discretion of the implanting physician.

[redacted]

3.1 Overall Flow of the Clinical Registry and Follow-up Schedule

The Physiologic Pacing Registry will evaluate subjects at baseline (before implant, Figure 1), implant, and at 1 month and 6 months post-implant. If part of their routine clinical practice in physiologic pacing implants, physicians may create a 3-dimensional map of cardiac structures utilizing the EnSite Cardiac Mapping System prior to implanting an Abbott device with any market available lead and associated implant tools. Only patients scheduled to receive an Abbott device may be enrolled to ensure proper device data collection for future software and other physiologic pacing product development.

Note: The site must receive approval from the Sponsor and EC/IRB prior to beginning registry enrollment. A patient is considered enrolled once the informed consent form has been signed (Figure 1).

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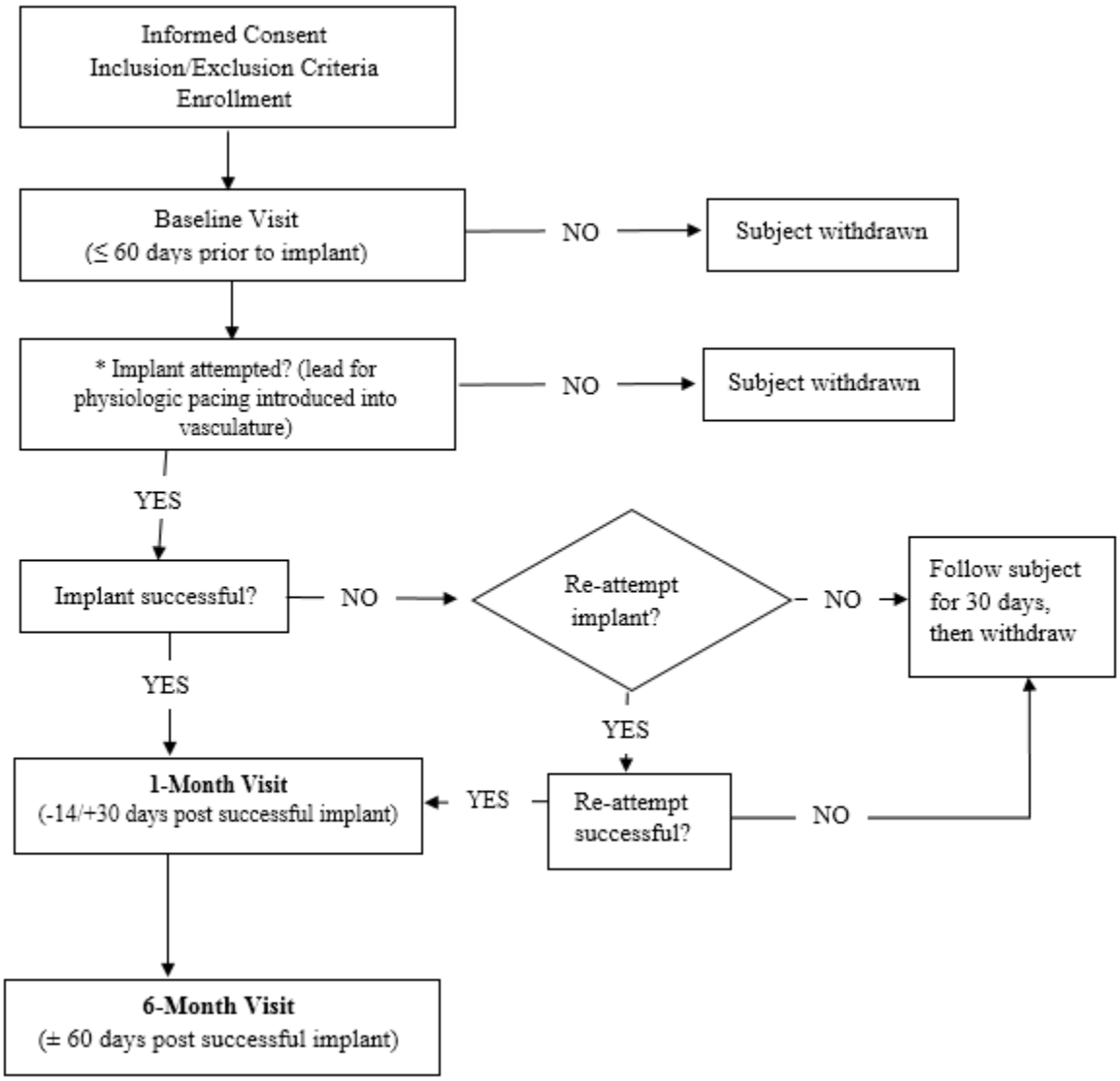

Figure 1: Clinical Registry Flow Chart

3.2 Suspension or Early Termination of the Clinical Registry

No formal statistical rule for early termination of the registry is defined.

The Sponsor reserves the right to discontinue the registry 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:

- Subject safety
- Further product development cancelled

If the registry is discontinued by the Sponsor, subjects will be followed per routine hospital practice with device-related adverse events reported to the Sponsor as per vigilance/commercial reporting requirements.

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Should this occur, the investigator shall return all unused registry materials to the Sponsor and provide a written statement as to why the premature termination has taken place to the EC/IRB (if applicable). All applicable registry documents shall be subject to the same retention policy as detailed in Section 11.0.

A Principal Investigator, EC/IRB, or regulatory authority may suspend or prematurely terminate participation in this registry at the clinical sites for which they are responsible. The investigators will follow the requirements specified in the Clinical Trial Agreement.

If the Sponsor suspends or prematurely terminates the registry 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 Clinical Plan and existing agreements for following the subjects enrolled in the registry, and the Principal Investigator or authorized designee will promptly inform the enrolled subjects at his/her site, if appropriate.

4.0 ENDPOINTS

4.1 Registry Outcome Measures

The Physiologic Pacing Registry will collect data on the following measures as recommended by the His Bundle Pacing Collaborative Working group[17] to characterize the workflow associated with physiologic pacing device implants and follow-up, and to quantify the clinical utility of mapping the cardiac structures prior to physiologic pacing device implants according to sites' routine care. Implant and follow-up characteristics will be compared with and without utilizing the EnSite Cardiac Mapping System during device implants.

Implant Characteristics:

- Fluoroscopy time and radiation dose
- Overall procedure time: skin-to-skin
- Implant procedure time: vascular access to lead fixation
- All implant tools used
- Implant-related workflow
- Final implanted hardware
- Final post-procedure device programming
- Procedure- and device-related adverse events and device deficiencies
- Implant success
- All types of physiologic pacing capture observed such as selective and non-selective
- Physiologic pacing capture and sensing thresholds
- Pacing output necessary to correct bundle branch block using 12-lead ECG (if applicable)
- QRS duration at baseline and following implant using 12-lead ECG
- QRS duration for all types of physiologic pacing captures observed using 12-lead ECG

- For His placement only: Measured H wave using device IEGM
- Measured R wave using device IEGMs through the lead implanted for physiologic pacing

Follow-up Characteristics:

- Follow-up related workflow
- Physiologic pacing capture and sensing thresholds
- For His placement only: Measured H wave using device IEGM
- Measured R wave using device IEGMs through the lead implanted for physiologic pacing
- Presenting PR interval and QRS duration using 12-lead ECG
- QRS duration for all types of physiologic pacing captures observed using 12-lead ECG
- Incidence of increase in capture threshold of > 1V in leads implanted for physiologic pacing or RV pacing leads
- Far-field atrial oversensing and ventricular oversensing and/or any interventions – including programming – required to address these issues
- NYHA Classification
- LVEF, LVEDV, LVESV (if available)
- Tricuspid and mitral regurgitation severity by echocardiogram (if available)
- Device estimated battery longevity via device session records
- Frequency/burden of detected atrial and ventricular arrhythmias via device session records
- Procedure and device-related adverse events

5.0 SUBJECT SELECTION AND WITHDRAWAL

5.1 Subject Population

The patient population for this registry is potential subjects undergoing implantation of an Abbott pacemaker, defibrillator, or CRT-P/D with any market released pacing lead as part of a physiologic pacing procedure according to the clinical site's routine care. The decision to provide physiologic pacing therapy and selection of devices for implant are at the discretion of the implanting physician.

This registry will consecutively approach patients scheduled to receive an Abbott device to enroll male and female subjects who are eligible for the above-mentioned device implant. Subjects must meet all eligibility criteria and provide written informed consent prior to conducting any registry-specific procedures not considered standard of care.

5.2 Subject Screening and Informed Consent

5.2.1 Subject Screening

Members of the site's research team (physician and/or research coordinator, or other delegated and qualified personnel) previously trained to this Clinical Plan must screen potential patients for eligibility and should document screening efforts onto a site-specific screening log. Patients who meet the inclusion criteria and none of the exclusion criteria may participate in this registry.

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Potential patients meeting inclusion criteria and no exclusion criteria will be fully informed about the registry, following the established informed consent process (described in Section 5.2.2). They will be asked to sign an Informed Consent form if they wish to participate in the registry. These patients should also be entered onto the site-specific screening log.

Once a duly dated and signed Informed Consent form is obtained, the registry-specific screening procedures may begin.

The following assessments are performed as part of the screening process:

- Medical History
- Cardiovascular Baseline Measures

Subject data will be collected following enrollment into the registry.

5.2.2 Informed Consent

The Patient Informed Consent form must receive approval from the Sponsor and EC/IRB prior to beginning registry enrollment.

The Investigator or his/her authorized designee will conduct the Informed Consent process, as required by applicable regulations and the center's EC/IRB. This process will include a verbal discussion with the patient on all aspects of the registry that are relevant to the patient's decision to participate, such as details of registry procedures, anticipated benefits, and potential risks of registry participation. Patients must be informed about their right to withdraw from the registry at any time and for any reason without sanction, penalty or loss of benefits to which the patient is otherwise entitled. Withdrawal from the registry will not jeopardize their future medical care or relationship with the investigator.

During the discussion, the Principal Investigator or his/her authorized designee will avoid any improper influence on the patient and will respect the patient's legal rights. The patient shall be provided with the Informed Consent form written in a language that is understandable to the patient and has been approved by the center's EC/IRB. The patient shall have adequate time to review, ask questions and consider participation. If the patient agrees to participate, the Informed Consent form must be signed and dated by the patient and thereafter by the person obtaining the consent prior to any registry-specific procedures. The signed original will be filed in the subject's hospital or research charts, and a copy will be provided to the subject.

In addition, an authorization for use and disclosure of the subject's protected health information, in accordance with the Health Insurance Portability and Accountability Act (HIPAA), must be obtained from the subjects or their legal representative.

Failure to obtain informed consent from a subject prior to enrollment should be reported to the Sponsor within 5 working days and to the reviewing center's EC/IRB according to the EC/IRB's reporting requirements.

If, during the registry, new information becomes available that can significantly affect a subject's future health and medical care, the Principal Investigator or his/her authorized designee will provide this information to the subject. If relevant, the subject will be asked to confirm their continuing informed consent in writing.

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Vulnerable Populations

Vulnerable populations will not be enrolled in the Physiologic Pacing Registry.

5.3 Eligibility Criteria

5.3.1 General Eligibility Criteria

Assessment for general eligibility criteria is based on medical records of the site and interview with a candidate patient. If some of the clinical and laboratory tests are not included in the site's standard tests, they must be done after written informed consent is obtained. Patients must meet ALL the inclusion criteria to be considered for the registry. If ANY of the exclusion criteria are met, the patient is excluded from the registry and cannot be enrolled.

5.3.2 Inclusion Criteria

5.3.2.1 General Inclusion Criteria

Subjects must meet all the following inclusion criteria for enrollment in the registry.

1. Scheduled for implantation of an Abbott pacemaker, defibrillator, or CRT-P/D device with any commercially available pacing lead as part of a physiologic pacing procedure according to the clinical site's routine care.
2. At least 18 years of age.
3. Willing and able to comply with the prescribed follow-up tests and schedule of evaluations.
4. Provided written informed consent prior to any registry-related procedures.

5.3.3 Exclusion Criteria

5.3.3.1 General Exclusion Criteria

Subjects will be excluded from enrollment if any of the exclusion criteria is met below.

1. History of tricuspid valve repair or replacement.
2. Currently participating in another clinical study with an active treatment arm and belong to the active arm
3. Presence of other anatomic or comorbid conditions, or other medical, social, or psychological conditions that, in the investigator's opinion, could limit the subject's ability to participate in the registry or to comply with follow-up requirements, or impact the scientific soundness of the registry results.
4. Chronic physiologic pacing lead implanted
5. Life expectancy of < 6 months.
6. Known contraindication for physiologic pacing therapy/implant (i.e. ongoing infection, known occlusion of the subclavian vein, etc.).

5.4 Subject Enrollment

A patient is considered enrolled in the registry once he/she meets eligibility requirements and has signed the informed consent form. Subjects who have a successful implant and are later found to have met exclusion criteria

or not all inclusion criteria will continue follow-up in the registry and will be included in the enrolled population; a protocol deviation will be completed for these subjects.

5.5 Subject Withdrawal

Each enrolled subject shall remain in the registry until completion of the required follow-up period; however, a subject's participation in any registry is voluntary and the subject has the right to withdraw at any time without penalty or loss of benefit. Conceivable reasons for discontinuation may include, but not be limited to, the following:

- Subject death
- Subject voluntary withdrawal
- Subject withdrawal by physician as clinically-indicated
- Subject lost-to follow-up as described below

The Sponsor must be notified of the reason(s) for subject discontinuation. The site will provide this information to the Sponsor. Investigators must also report this to their respective EC/IRB as defined by their institution's procedure(s). No additional follow–up will be required or data recorded from subjects once withdrawn from the registry. The status of the subject's condition should be documented at the time of withdrawal.

Before the subject is withdrawn from the registry the site should make attempts to schedule the subject for a final registry follow-up visit. At this final follow-up visit, the subject will undergo the following assessments with documentation completed on the unscheduled follow-up form:

- Follow-up related workflow
- Physiologic pacing capture and sensing thresholds
- For His placement only - Measured H wave using device IEGM
- Measured R wave using device IEGMs through the lead implanted for physiologic pacing
- QRS duration for all physiologic pacing captures observed using 12-lead ECG
- PR interval using 12-lead ECG
- Incidence of increase in capture threshold of > 1V in the lead implanted for physiologic pacing or RV pacing leads
- Far-field atrial oversensing and ventricular oversensing and/or any interventions – including programming – required to address these issues
- NYHA Classification
- LVEF, LVEDV, LVESV (if available)
- Tricuspid and mitral regurgitation severity by echocardiogram (if available)
- Device estimated battery longevity via device session records
- Frequency/burden of detected atrial and ventricular arrhythmias via device session records
- Procedure and device-related adverse events and device deficiencies

<u>Lost-to-Follow-up</u>

If the subject misses the scheduled 1-month follow-up time point and the attempts at contacting the subject detailed below are unsuccessful, then the subject is considered lost-to-follow-up. Site personnel shall make all reasonable

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efforts to locate and communicate with the subject (and document these efforts in the source documents), including the following, at each contact time point:

- A minimum of two telephone calls on different days over the specified follow-up windows to contact the subject should be recorded in the source documentation, including date, time and initials of site personnel trying to make contact.
- If these attempts are unsuccessful, a letter (certified if applicable) should be sent to the subject.
- If a subject misses the 1-month follow-up contact time point, it will be considered a missed visit. The subject may then return for the 6-month follow-up visit. If the subject misses the 1-month follow-up visit and the above-mentioned attempts at communicating with the subject are unsuccessful, the subject will be considered lost-to-follow-up.

Note: Telephone contact with a General Practitioner, non-registry Cardiologist or relative without the presence of the subject or indirect documentation obtained via discharge letters will not be considered as subject contact.

5.6 Total Expected Duration of the Clinical Registry

Sites will follow enrolled subjects who receive physiologic pacing therapy for 6 months. The total expected duration of the registry is approximately 4 years, including enrollment, implant procedure, follow-up visits, and registry closure.

5.7 Expected Duration of Each Subject's Participation

The total expected duration of each subject's participation in the registry is approximately 6 months post implant of the device.

5.8 Number of Subjects Required for Inclusion in the Clinical Registry

The Physiologic Pacing Registry will have no formal power analysis and sample size calculation; the registry needs to enroll enough subjects from a comprehensive patient population to characterize the workflow associated with physiologic pacing device implants and to quantify the clinical utility of mapping physiologic pacing structures prior to device implants based on sites' routine care using the EnSite Cardiac Mapping System. The data from this registry will also be used to help inform Abbott's future product and clinical data development efforts and therefore must contain information from a wide variety of sites and subjects. [redacted]

5.9 Estimated Time Needed to Select Required Number of Subjects

[redacted]

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6.0 TREATMENT AND EVALUATION OF ENDPOINTS

6.1 Baseline Clinical Assessments

Patients will undergo screening evaluations as outlined by the inclusion/exclusion criteria. The Principal Investigator (PI) or delegated research personnel are responsible for screening all potential patients to determine eligibility for the registry. All patients will complete a Baseline visit within 60 days prior to implant. During this visit, eligible patients will sign an EC/IRB-approved Informed Consent form. Once informed consent has been obtained, sites will collect the following data at the Baseline visit:

- Subject demographics
- Subject medical history
- Physical examination
- Cardiovascular history
- Indications for device implant
- LVEF, LVEDV, LVESV (if available)
- Tricuspid valve regurgitation and Mitral valve regurgitation severity by echo (if available)
- Intrinsic QRS duration using 12-lead ECG
- PR interval using 12-lead ECG
- Baseline conduction pattern using 12-lead ECG
- NYHA Classification

Sites must complete and submit the associated Baseline Visit Case Report Forms (CRFs) to Abbott using the electronic data capture (EDC) system.

6.2 Implant Procedure

Investigators should follow their standard implant technique and workflow for physiologic pacing procedures and the associated devices indications for use. The decision to provide physiologic pacing therapy and selection of devices for implant are at the discretion of the implanting physician. Only subjects scheduled to receive an Abbott device may be enrolled to ensure proper device data collection for future software and other physiologic pacing product development; however, the investigator may use any market-approved lead and associated implant tools. If part of their routine clinical practice in physiologic pacing implants, physicians may create a 3-dimensional map of cardiac structures using any diagnostic mapping catheter with the EnSite Cardiac Mapping System.

Sites will collect the following data during the implant procedure:

- Fluoroscopy time and radiation dose
- Overall procedure time: skin-to-skin
- Implant procedure time: vascular access to lead fixation
- All Implant tools used
- Implant-related workflow
- Final implanted hardware

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- Final post-procedure device programming
- Procedure- and device-related adverse events and device deficiencies
- Implant success
- All types of physiologic pacing capture observed such as selective and non-selective
- Physiologic pacing capture and sensing thresholds
- Pacing output necessary to correct bundle branch block using 12-lead ECG (if applicable)
- QRS duration for all types of physiologic pacing captures observed using 12-lead ECG
- For His placement only: Measured H wave using device IEGM
- Measured R wave using device IEGMs through lead implanted for physiologic pacing

Investigators will program the implanted device based on their discretion. Sites must download the device session records and submit to Abbott using the EDC system. Sites must also submit a copy of the subject's physiologic pacing 12-lead ECG in digital format (if available). Sites must complete and submit the associated Implant visit CRFs to Abbott using the EDC system.

6.2.1 Unsuccessful Implants and Device Explants

Sites will follow subjects who have an unsuccessful implant of the lead implanted for physiologic pacing for a period of 30 days for procedure-related adverse events and then withdraw the subject from the registry, unless the physiologic pacing lead implant will be re-attempted. Sites should submit all available data for the attempted implant through what was completed during the procedure.

Sites will follow subjects who have their device or lead implanted for physiologic pacing explanted for a period of 30 days for procedure-related adverse events, and then withdraw the subject from the registry.

Sites will withdraw subjects from the registry if a lead implant for physiologic pacing was not attempted – no data collection at implant or following implant is required.

All explanted Abbott devices and Abbott leads should be returned to Abbott to the address below:

[redacted]

Sites must complete and submit a Product Out of Service CRF for any explanted devices to Abbott using the EDC system. After 30 days, if the investigator will not re-attempt implant of a lead for physiologic pacing, sites must complete and submit a Withdrawal CRF and Adverse Event CRF (if applicable) to Abbott using the EDC system.

The physician may re-attempt to implant a lead for physiologic pacing and/or Abbott device at their discretion within 30 days of the initial attempted implant. If the physician chooses to re-attempt the implant, site must complete and submit the associated Implant visit CRFs, an Adverse Event CRF (if applicable) and a Product Out of Service CRF (if applicable) to Abbott using the EDC system.

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6.3 Follow-up Assessments at 1 and 6 Months

The schedule of follow-up visits is based on the date of the successful implant of a lead for physiologic pacing with Abbott device implant. Table 2 outlines the time window permitted for each of the registry visits.

Table 2: Registry Time Interval Windows

1 Month	6 Months
-14 days/+30 days	± 60 days

Sites will follow all subjects at 1 month and 6 months after the date of successful HBP lead and Abbott device implant.

During each follow-up visit, the following data will be collected:

- Follow-up related workflow
- Physiologic pacing capture and sensing thresholds
- For His placement only: Measured H wave using device IEGM
- Measured R wave using device IEGMs through lead implanted for physiologic pacing
- Presenting QRS duration and PR interval from 12-lead ECG
- QRS duration for all types of physiologic pacing captures observed from 12-lead ECG
- Incidence of increase in capture threshold of > 1V in leads implanted for physiologic or RV pacing leads
- Far-field atrial oversensing and ventricular oversensing and/or any interventions – including programming – required to address these issues
- NYHA Classification
- LVEF, LVEDV, LVESV (if available)
- Tricuspid and mitral regurgitation severity by echocardiogram (if available)
- Device estimated battery longevity via device session records
- Frequency/burden of detected atrial and ventricular arrhythmias via device session records
- Procedure and device-related adverse events and device deficiencies

Sites must download the device session records and submit to Abbott using the EDC system. Sites must also submit copies of the subject's physiologic pacing 12-lead ECGs in digital format (if available). Sites must complete and submit the associated Follow-up visit CRFs to Abbott using the EDC system.

Sponsor Representatives may provide support during the follow-up procedures for device-related data collection.

6.3.1 Unscheduled Visits

An unscheduled visit is defined as a visit between two registry-required visits during which the clinical site performs a device interrogation and reprogramming. Sites should download device session records and 12-lead ECGs (if available) and submit to Abbott using the EDC system. Sites must complete and submit the associated Follow-up visit CRFs, and any other applicable CRFs to Abbott using the EDC system.

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6.3.2 Schedule of Events

Table 3: Schedule of Events

CIP Activity	Baseline (≤ 60 days prior to implant)	Implant	1-Month (-14/+30 days post successful implant)	6- Month (±60 days post successful implant)	Unscheduled
Informed Consent Process	X				
Demographics	X				
Physical Examination	X		X	X	X
Cardiovascular History	X				
Implant indication	X				
Medical History	X				
NYHA Class	X		X	X	X
Implant Data Collection (Section 6.2)		X			
System Information		X			
Device Interrogation		X	X	X	X
Device Programming		X	X	X	X
12-lead ECG	X	X*	X	X	X
For His placement only: Measured H wave using device IEGM		X	X	X	X
Measured R wave using device IEGMs through physiologic pacing lead		X	X	X	X
Electro-anatomical Mapping (optional)		(X)			
LVEF (if available)	X			X	
Follow-up Data Collection (Section 6.3)			X	X	
Device Session Records		X	X	X	X
Adverse Event	(X)	(X)	(X)	(X)	(X)
Device Deficiency		(X)	(X)	(X)	(X)
Deviation	(X)	(X)	(X)	(X)	(X)
Termination	(X)	(X)	(X)	(X)	(X)
Assessment for Hospitalization			X	X	X
Death	(X)	(X)	(X)	(X)	(X)
Product Out of Service			(X)	(X)	(X)

(X) if applicable; *If available

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7.0 ADVERSE EVENTS

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

7.1 Definition

7.1.1 Adverse Event

An adverse event is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the medical device under investigation.

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

7.1.2 Serious Adverse Event

If the adverse event meets any of the criteria below, it is regarded as a serious adverse event.

a) Led to a death,
b) Led to a serious deterioration in health of the subject, that either resulted in
    1. a life-threatening illness or injury, or
    2. a permanent impairment of a body structure or a body function, or
    3. in-patient hospitalization or prolongation of existing hospitalization, or
    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) Led to fetal distress, fetal death or a congenital abnormality or birth defect.

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

7.2 Procedure and/or Device Relationship

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

7.3 Adverse Event, Device Deficiency, and Complaint Reporting

7.3.1 Adverse Event Reporting

General Adverse Event Reporting

Safety surveillance and reporting starts as soon as the patient has an attempted implant in the registry. An attempted implant is defined as insertion of the physiologic pacing lead into vasculature. Safety surveillance and reporting will continue until the last follow-up visit has been performed, the subject is deceased, the subject concludes

participation in the registry, or the subject withdraws from the registry. Sites will collect all serious adverse events (including all deaths) and all adverse events related to the procedure and/or device, whether serious or not, throughout the time period defined above and will report to the Sponsor on a CRF. Additional information regarding an adverse event should be updated within the appropriate CRF.

Unchanged, chronic, non-worsening or pre-existing conditions are not adverse events and should not be reported. An off-line form will be made available to allow the investigator to report serious adverse events in the event the entry cannot be made in the EDC. This does not replace the EDC reporting system. All information must still be entered in the EDC system as soon as feasible.

Serious Adverse Event Reporting

The investigator will report all serious adverse events, including all deaths, to the Sponsor as soon as possible but no later than outlined below.

Clinical Site	Reporting timelines
All Sites	All serious adverse events must be reported to the Sponsor no later than 3 calendar days from the day the site personnel became aware of the event or as per the investigative site's local requirements, if the requirement is more stringent than those outlined.

The date the site staff became aware the event met the criteria of a serious adverse event must be recorded in the source document. The Investigator will further report the serious adverse event to the local EC/IRB according to the institution's EC/IRB reporting requirements.

7.3.2 Complaint Reporting

During the registry, the investigator will be responsible for reporting all complaints. A complaint is defined as any written, electronic or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness or performance of a device after it is released for distribution.

If the complaint does not involve an adverse event, the investigator must notify the Post-Market Surveillance Department by submitting the information on the device via email to [redacted] as soon as possible after becoming aware of the complaint. This information will not be collected on a CRF for the registry.

If the complaint involves an adverse event, the investigator must complete an Adverse Event CRF, including the information on the complaint and submit to the Sponsor as soon as possible.

7.3.3 Device Deficiency/Malfunction Reporting

Device deficiency is defined as an inadequacy of a medical device related to its identity, quality, durability, reliability, safety or performance, such as malfunction, misuse or use error and inadequate labeling. This includes the failure of the device to meet its performance specifications or otherwise perform as intended. Note: performance specifications include all claims made in the labeling of the device.

A device malfunction is the failure of a device to meet its performance specifications or otherwise perform as intended, when used in accordance with the instructions for use or CIP.

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Sites should report all device deficiencies/malfunctions for any Abbott product used to the Sponsor on the appropriate CRF form. The investigator must report all device deficiencies/malfunctions to the Sponsor as soon as possible but no later than outlined below.

Clinical Sites	Reporting timelines
All Sites	Device deficiencies/malfunctions for any Abbott product used must be reported to the Sponsor no later than 3 calendar days from the day the site personnel became aware of the event or as per the investigative site's local requirements, if the requirement is more stringent than those outlined.

Sites should return all devices to the Sponsor which are not implanted or not remaining in the subject. In addition, sites should report device deficiencies/malfunctions to the IRB/EC per the investigative site's local requirements.

The Sponsor will provide an offline form to allow the investigator to report device deficiencies/malfunctions if the entry cannot be made in the EDC system. This does not replace the EDC reporting system. Sites must continue to enter all information in the EDC system as soon as feasible.

7.3.4 Procedure for Recording and Reporting Subject Death

For all deaths, the investigator should record death information in the hospital records and immediately document the information on the Adverse Event CRF and submit to Sponsor.

The investigator should make all efforts to obtain details about the circumstances surrounding the subject death.

A subject's death is an early conclusion of the subject's participation in the registry. Therefore, the Investigator is required to complete the Withdrawal CRF.

Sites should report all death events as per the serious adverse event reporting requirements stated in the 'Adverse Event Reporting Requirements' section (7.3.1).

8.0 STATISTICAL CONSIDERATIONS

8.1 Analysis Populations

The analysis populations include:

1. Enrollment population: includes all subjects enrolled in the registry.
2. Implanted population: includes subjects enrolled in the registry, implanted with Abbott device, and have an active (programmed on) lead implanted for physiologic pacing post implant.

Additional analysis populations will be defined in a separate statistical analysis plan as appropriate.

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8.2 Statistical Analyses

Descriptive statistics for continuous variables will include the number of observations, means and standard deviations. Descriptive statistics for categorical variables will include subject counts and percentages/rates. Survival analysis may be performed to analyze time-to-event variables. Confidence intervals may be provided as appropriate. Statistical methodology and considerations will be documented in a separate Statistical Analysis Plan.

8.2.1 Primary Outcome Measures Analyses

[redacted]

8.3 Sample Size Calculation and Assumptions

[redacted]

8.4 Timing of Analysis

[redacted]

8.5 Subgroup Analysis

[redacted]

8.6 Multiplicity

[redacted]

8.7 Pooling Strategy

[redacted]

8.8 Procedures for Accounting for Missing Data

[redacted]

8.9 Planned Interim Analysis

[redacted]

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8.10 Statistical Criteria for Termination

[redacted]

8.11 Success Criteria

[redacted]

8.12 Labeling Claim

[redacted]

8.13 Deviations from Statistical Plan

Any major changes to the statistical plan will be documented in an amendment to the statistical plan. Minor changes to the planned analyses will be documented in the final report.

9.0 DIRECT ACCESS TO SOURCE DATA/DOCUMENTS

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

Subjects providing informed consent are agreeing to allow monitors or regulatory authorities to review, in confidence, any records identifying the subjects in this registry. This information may be shared with regulatory agencies; however, the Sponsor undertakes not to otherwise release the subject's personal and private information.

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 registry. Sites will be selected based upon review of a recent site assessment, if applicable, and the qualifications of the Principal Investigator or multidisciplinary team at the site.

10.2 Clinical Plan Amendments

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

Acknowledgement/approval by the EC/IRB of the Clinical Plan amendment must be documented in writing prior to implementation of the amendment. Copies of this documentation must also be provided to the Sponsor.

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10.3 Training

10.3.1 Site Training

All investigators and research personnel are required to attend Sponsor training sessions, which may be conducted at an Investigator's meeting, a site training visit, or other appropriate training sessions. Over-the-phone or self-training may take place as required. Training of investigators and research personnel will include, but is not limited to, the Clinical Plan requirements, electronic CRF completion, and research personnel responsibilities. All investigators and research 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 research personnel must not perform any registry-related activities that are not considered standard of care at the site.

10.4 Deviations from the Clinical Plan

The Investigator should not deviate from the Clinical Plan for any reason except in cases of medical emergencies when the deviation is necessary to protect the rights, safety and well-being of the subject or eliminate an apparent immediate hazard to the subject. In that event, the Investigator will notify the Sponsor immediately by phone or in writing.

No waivers for protocol deviations will be granted by the Sponsor. All protocol deviations must be reported to the Sponsor using the Deviation CRF. The occurrence of deviations will be monitored by the Sponsor for evaluation of investigator compliance to the Clinical Plan and regulatory requirements and dealt with according to written procedures. Investigators will inform their EC/IRB or equivalent committee of all deviations in accordance with their specific EC/IRB 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 Clinical Plan or any other conditions of the registry 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 registry.

10.5 Monitoring

The Sponsor and/or designee will monitor the registry using a risk-based strategy according to the study-specific monitoring plan which will include the extent of source data verification.

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

- The Investigator understands and accepts the obligation to conduct the registry according to the Clinical Plan and applicable regulations and has signed the Investigator Agreement.
- The Investigator and his/her staff should have sufficient time and facilities to conduct the registry and should have access to an adequate number of appropriate subjects to conduct the registry.

- Source documentation (including original medical records) must be available to substantiate proper informed consent procedures, adherence to Clinical Plan 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. A monitoring visit sign-in log will be maintained 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 Plan-related documents.

10.6 Quality Assurance Audit

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

In the event an Investigator is contacted by a Regulatory Agency in relation to this registry, the Investigator will notify the 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 registry (e.g., Form FDA 483, Inspectional Observations, Warning Letters, Inspection Reports, etc.). The Sponsor may provide any needed assistance in responding to regulatory audits.

11.0 DATA HANDLING AND RECORD KEEPING

The Sponsor and/or its affiliates will include documentation of the systems and procedures used in data collection for the duration of the registry.

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 conclusion of the registry, 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 clinical sites, if requested.

For the duration of the registry, the Investigator will maintain complete and accurate documentation including, but not limited to, medical records, registry progress records, laboratory reports, electronic CRFs, signed Informed Consent forms, correspondence with the EC/IRB and Sponsor, adverse event reports, and information regarding subject discontinuation or completion of the registry.

11.1 Protection of Personally Identifiable Information

The Sponsor respects and protects personally identifiable information collected or maintained for this registry. The privacy of each subject and confidentiality of his/her information will be preserved in reports and when publishing

any data. Confidentiality of data will be observed by all parties involved at all times throughout the registry. All data will be secured against unauthorized access.

11.2 Data Management Plan

A Data Management Plan will describe procedures used for data review, database cleaning, and issuing and resolving data queries. If appropriate, the Data Management Plan may be updated throughout the duration of the registry. All revisions will be tracked and document controlled.

11.3 Source Documentation

Regulations and Good Clinical Practice require the Investigator to maintain information in the subject's original medical records that corroborates data collected on the CRFs. In order to comply with these regulatory requirements/Good Clinical Practice, the following information should be included in the subject record at a minimum:

- Medical history/physical condition of the subject before involvement in the registry sufficient to verify the Clinical Plan entry criteria
- Dated and signed notes on the day of entry into the registry referencing the Sponsor, Clinical Plan number, subject ID number and a statement that informed consent was obtained
- Dated and signed notes from each subject visit (for specific results of procedures and exams)
- Procedure and device-related adverse events reported and their resolution, including supporting documents, such as discharge summaries, catheterization laboratory reports, ECGs, and lab results including documentation of site awareness of serious adverse events and of investigator assessment of device relationship for serious adverse events.
- Device session records
- Subject's condition upon completion of or withdrawal from the registry
- Any other data required to substantiate data entered into the CRF

11.4 Electronic Case Report Form Completion

Primary data collection based on source-documented hospital and/or clinic chart reviews will be performed clearly and accurately by site personnel trained on the Clinical Plan and electronic CRF completion. Data from electronic CRFs will be collected for all subjects enrolled into the registry. 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. An electronic audit trail will be used 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 registry as per the applicable regulatory record retention requirements. The Investigator must obtain permission from Sponsor in writing before destroying or transferring control of any registry records.

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12.0 ETHICAL CONSIDERATION

12.1 Institutional Review Board Review Approval

EC/IRB approval for the Clinical Plan and Informed Consent form/other written information provided to the patient will be obtained by the Principal Investigator at each clinical site prior to consenting and enrolling patients in this registry. The approval letter must be received prior to the start of this registry and a copy must be provided to the Sponsor.

Any amendments to the Clinical Plan as well as associated Informed Consent form changes will be submitted to the EC/IRB and written approval obtained prior to implementation, according to each institution's EC/IRB requirements.

No changes will be made to the Clinical Plan or Informed Consent form or other written information provided to the patient without appropriate approvals, including EC/IRB, the Sponsor, and the regulatory agencies (if applicable).

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

No investigative procedures other than those defined in this Clinical Plan will be undertaken on the enrolled subjects without the written agreement of the EC/IRB and the Sponsor.

13.0 REGISTRY CONCLUSION

The registry will conclude when:

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

14.0 PUBLICATION POLICY

The data and results from the registry are the sole property of the Sponsor. The Sponsor shall have the right to access and use all data and results generated during the registry. The investigators will not use this registry-related data without the written consent of the Sponsor for any purpose other than for registry 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. Any proposals for publications or presentations by the investigators must be reviewed and approved by the Sponsor in a timely manner to enable Sponsor review in compliance with the Sponsor's publication policy set forth in the Clinical Trial Agreement.

The Sponsor will register the study on www.clinicaltrials.gov and will be responsible for posting results as required by the ClinicalTrials.gov website.

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15.0 RISK ANALYSIS

Patients participating in this registry are indicated for a pacemaker, defibrillator, or CRT device as part of their standard medical management and are subject to the risks associated with these devices. Risks associated with the specified device and procedure, together with their likely incidence, are described in the individual device Indications for Use. There may be risks related to the devices used in the registry that are unknown at present. Likewise, the exact frequency of the risk may be unknown.

15.1 Anticipated Clinical Benefits from Participating in this Clinical Registry

Patients participating in this registry have the same clinical benefit as any patient receiving a pacemaker, defibrillator, or CRT device. Participation in this registry is not required in order for a patient to receive physiological pacing therapy.

Data collected in this study will help to understand device use and implantation procedures for physiologic pacing therapy. Data collected will also be used to inform future Abbott product development.

15.2 Risks Associated with Participation in this Clinical Registry

All procedures required by this registry are standard of care according to each individual clinical site's practice. There are no anticipated risks associated with participation in this registry or any risks beyond those identified in the individual device Indication for Use.

15.3 Steps Taken to Control or Mitigate Risks

Physicians participating in this registry will be selected based on their education, training, or experience in performing physiologic pacing procedures. Therefore, physicians are expected to be aware of the known and foreseeable safety risks associated with the use of the devices, including the surgical and/or non-surgical treatment of these conditions. The procedures outlined in this Clinical Plan are all standard of care according to the individual clinical site's practice. Additionally, clinical sites will report all procedure and device-related adverse events to the Sponsor – all adverse events will be monitored internally for safety surveillance purposes.

15.4 Risk to Benefit Rationale of Treatment Under Study

The risks associated with the registry are in line with the risks associated with a standard of care implant of a cardiac pacemaker, defibrillator, or CRT device. There are potential unknown risks of physiologic pacing associated with the lead implant procedure and long-term follow-up. Patients are indicated for an implant of a cardiac device and will undergo the implant based on the clinical site's standard of care. As such, patients participating in this registry have the same clinical benefit as those patients receiving a pacemaker, defibrillator, or CRT device. There are potential benefits from receiving physiologic pacing. These benefits include the potential for sustained or improved ventricular function, as well as the potential benefits gained by the enhanced visualization and localization of cardiac conduction structures prior to implant of a permanent lead for physiologic pacing. Based on this information, the Sponsor believes the benefits outweigh the risks associated with participation in the registry.

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APPENDIX I: ABBREVIATIONS AND ACRONYMS

AE: Adverse Event

AV: Atrioventricular

CRT: Cardiac Resynchronization Therapy

CRT-D: Cardiac Resynchronization Therapy Defibrillator

CRT-P: Cardiac Resynchronization Therapy Pacemaker

CRF: Case Report Form

EC: Ethics Committee

ECG: Electrocardiogram

EDC: Electronic Data Capture

FDA: Food and Drug Administration

HBP: His Bundle Pacing

HIPAA: Health Insurance Portability and Accountability Act

IEGM: Intracardiac Electrogram

IRB: Institutional Review Board

LBBP: Left Bundle Branch Pacing

LVEF: Left Ventricular Ejection Fraction

LVESV: Left Ventricular End Systolic Volume

LVEDV: Left Ventricular End Diastolic Volume

NYHA: New York Heart Association

PI: Principal Investigator

RV: Right Ventricular

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APPENDIX II: SITE CONTACT INFORMATION

Available separately by contacting Abbott at:

[redacted]

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APPENDIX III: REVISION HISTORY

This Clinical Plan may be amended as appropriate by the Sponsor. Rationale will be included with each amended version in the revision history Table below. The version number and date of amendments will be documented.

EC/IRB and relevant Regulatory Authorities, if applicable, will be notified of amendments to the Clinical Plan.

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APPENDIX IV: SUMMARY

Registry Name	Physiologic Pacing Registry
Title	Physiologic Pacing – Post Market Registry
Purpose	The Physiologic Pacing Registry will be conducted to gain a deeper understanding of physiologic pacing device implants and follow-up workflows, including device and programmer measurements to help inform Abbott's product and clinical data development efforts. Additionally, the registry will provide a broader understanding of the clinical utility in mapping physiologic pacing structures with the use of Abbott's EnSite Cardiac Mapping System with an electrophysiology catheter prior to device implants for those institutions where mapping is routine care prior to physiologic pacing device implant.
Objective(s)	The Physiologic Pacing Registry will characterize implant and follow-up measures associated with physiologic pacing device implants. The registry will also compare implant and follow-up characteristics for implants performed with and without utilizing the EnSite Cardiac Mapping System.
Devices Included in Registry	Any market-approved Abbott pacemaker, defibrillator, or CRT device Any market-approved implant tools EnSite Cardiac Mapping System (optional)
Number of Subjects Required	[redacted]
Registry Design	This registry is designed as a prospective, non-randomized, multi-center registry. The registry will enroll patients scheduled for implant with an Abbott device with any available lead and associated implant tools – this is to ensure proper device data collection for future software and other physiologic pacing product development. Prior to device implant, investigators may perform a comprehensive electrophysiology study and/or create a 3-dimensional electro-anatomical map of physiologic pacing structures based on their site's routine care using any diagnostic mapping catheter with the EnSite Cardiac Mapping System.

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Primary Outcomes Measure(s)	The Physiologic Pacing Registry will collect data on the following measures to characterize the workflow associated with physiologic pacing device implants and follow-up, and to quantify the clinical utility of mapping the physiologic pacing structures prior to implants according to sites' routine care. Implant and follow-up characteristics will be compared with and without utilizing the EnSite Cardiac Mapping System during device implants. Implant Characteristics: • Fluoroscopy time and radiation dose • Overall procedure time: skin-to-skin • Implant procedure time: vascular access to lead fixation • All implant tools used • Implant-related workflow • Final implanted hardware • Final post-procedure device programming • Procedure- and device-related adverse events, and device deficiencies • Implant success • All types of physiologic pacing capture observed such as selective and non-selective • Physiologic pacing capture and sensing thresholds • Pacing output necessary to correct bundle branch block using 12-lead ECG (if applicable) • QRS duration for all types of physiologic pacing captures observed using 12-lead ECG • For His placement only: Measured H wave using device intracardiac electrogram (IEGM) • Measured R wave using device IEGMs through physiologic pacing lead Follow-up Characteristics: • Follow-up related workflow • Physiologic pacing capture and sensing thresholds • For His placement only: Measured H wave using device IEGM • Measured R wave using device IEGMs through physiologic pacing lead • QRS duration for all types of physiologic pacing captures observed using 12-lead ECG • Presenting QRS Duration and PR interval using 12-lead ECG • Incidence of increase in capture threshold of > 1V in physiologic or RV pacing leads

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	• Far-field atrial oversensing and ventricular oversensing and/or any interventions – including programming – required to address these issues • NYHA Classification • LVEF, LVEDV, LVESV (if available) • Tricuspid and mitral regurgitation severity by echocardiogram (if available) • Device estimated battery longevity via device session records • Frequency/burden of detected atrial and ventricular arrhythmias via device session records • Procedure and device-related adverse events, and device deficiencies
Subject Follow-up	The subjects will be followed in-clinic at baseline (before implant), implant, and at 1 month and 6 months after the date of successful implant.

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Inclusion Criteria	• Scheduled for implantation of an Abbott pacemaker, defibrillator, or CRT-P/D device with a pacing lead located at a physiologic pacing structure according to the clinical site's standard of care • At least 18 years of age • Willing and able to comply with the prescribed follow-up tests and schedule of evaluations • Provided written informed consent prior to any registry-related procedure
Exclusion Criteria	• History of tricuspid valve repair or replacement • Currently participating in another clinical study with an active treatment arm and belong to the active arm • Presence of other anatomic or comorbid conditions, or other medical, social, or psychological conditions that, in the investigator's opinion, could limit the subject's ability to participate in the registry or to comply with follow-up requirements, or impact the scientific soundness of the registry results • Chronic physiologic pacing lead implanted • Life expectancy of < 6 months • Known contraindication for a physiologic pacing implant (i.e. ongoing infection, known occlusion of the subclavian vein, etc.)

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APPENDIX V: REFERENCES

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