1.Cover Page

Medtronic

Clinical Investigation Plan Title	Tachy Prediction Download (TPD) Study	
Clinical Investigation Plan Identifier	MDT16067	
Study Product	EveraMRI Tachy Prediction Download Algorithm CareLink Monitor	
ClinicalTrials.gov Identifier	NCT03402126	
Sponsor/Local Sponsor	Medtronic, Inc. Cardiac Rhythm and Heart Failure Clinical Research 8200 Coral Sea Street NE Mounds View, MN 55112 1-800-328-2518	Medtronic Hong Kong Medical Limited 1104-11, 11/F, Tower 1 The Gateway, Harbour City, Tsim Sha Tsui, Kowloon (+852)-2919-1300 Medtronic, Bakken Research Center B.V. Endepolsdomein 5 6229 GW Maastricht The Netherlands (+31)-43-35-66-566
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Medtronic

Clinical Investigation Plan

Clinical Investigation Plan/Study Title	Tachy Prediction Download (TPD) Study
Clinical Investigation Plan Identifier	Not Yet Assigned
Study Product Name	EveraMRI Tachy Prediction Download Algorithm CareLink Monitor
Sponsor/Local Sponsor	Medtronic, Inc. Cardiac Rhythm and Heart Failure Clinical Research 8200 Coral Sea Street NE, MS: MVS33 Mounds View, MN 55112 1-800-328-2518 Medtronic Hong Kong Medical Limited 1104-11, 11/F, Tower 1, The Gateway, Harbour City, Tsim Sha Tsui, Kowloon (+852)-2919-1300 Medtronic, Bakken Research Center B.V. Endepolsdomein 5 6229 GW Maastricht The Netherlands (+31)-43-35-66-566
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Confidentiality Statement

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1. Glossary

Term	Definition
AE	Adverse Event
CIP	Clinical Investigation Plan
CRT	Cardiac Resynchronization Therapy
CTA	Clinical Trial Agreement
Data Protection authorization	Authorization to Use and Disclose Personal Health Information/Research Authorization/other privacy language
DD	Device Deficiency
DM	Data Management
eCRF	Electronic Case Report Form
EC	Ethics Committee
EGM	Electrogram
FCE	Field Clinical Engineer
FDA	Food and Drug Administration

Term	Definition
GCP	Good Clinical Practice
IC	Informed Consent
ICD	Implantable Cardioverter-Defibrillator
IDE	Investigational Device Exemption
IRB	Institutional Review Board
NSR	Non-Significant Risk
PI	Principal Investigator
PVC Density	Number of Pre-Ventricular Contractions per unit time
RR Interval	Time between successive R-waves
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SDN	Software Distribution Network
TPD	Tachy Prediction Download
UADE	Unanticipated Adverse Device Effect
USB	Universal Serial Bus
VT	Ventricular Tachycardia
VF	Ventricular Fibrillation
WO	Work Order

2. Synopsis

Title	Tachy Prediction Download (TPD) Study
Clinical Study Type	The TPD study is a prospective, non-randomized, non-interventional, multi-site passive data collection study. The data collected will be used to evaluate the feasibility of new algorithms to predict the imminent onset of ventricular arrhythmias. In the United States, this study will be executed as a non-significant risk investigational device exemption (NSR IDE)
Product Name	Evera MRI ICDs (with TPD investigational RAMware) Medtronic CareLink Monitor Medtronic 2090 Programmer (with TPD investigational software application)
Sponsor	Medtronic Inc.
Local Sponsor	Medtronic, Inc. Cardiac Rhythm and Heart Failure Clinical Research 8200 Coral Sea Street NE, MS: MVS33 Mounds View, MN 55112 1-800-328-2518 Medtronic Hong Kong Medical Limited 1104-11, 11/F, Tower 1, The Gateway, Harbour City, Tsim Sha Tsui, Kowloon (+852)-2919-1300 Medtronic, Bakken Research Center B.V. Endepolsdomein 5 6229 GW Maastricht The Netherlands (+31)-43-35-66-566
Indication under investigation	The study data is collected from ICD indicated patients. No new indications are being explored in this study.
Investigation Purpose	The purpose of the Medtronic Tachy Prediction Download (TPD) study is to collect data from an implantable cardiac defibrillator (ICD) device that will be used to identify markers for imminent onset of ventricular arrhythmias.
Product Status	All hardware used in the TPD study is market released, however investigational TPD RAMware will be installed on the Evera MRI ICDs and the TPD investigational software application will be loaded onto the 2090 programmer. The Evera MRI ICD will therefore be considered investigational while the TPD is present on the ICD and the 2090

	programmer will be considered investigational when the TPD software application is active.
Primary Objective(s)	The primary objective of this study is to collect data that can be used to predict the imminent onset of ventricular arrhythmias.
Study Design	The TPD Study is a prospective, non-randomized, non-interventional, multi-site data collection clinical study to collect ICD longitudinal data that may be used to develop a VT/VF prediction algorithm. The study subjects will include patients currently implanted, or who will be implanted with a market-approved Medtronic Evera MRI® ICD. The expected study duration is 3 years, with an enrollment period of approximately 2 years and a follow-up period of approximately 1 year.
Sample Size	Up to 300 subjects at up to 20 sites in the US and Hong Kong may participate in this study.

Inclusion/Exclusion Criteria	**Inclusion Criteria**
	• Subject is implanted or will be implanted, with an Evera MRI device with properly functioning Medtronic tachycardia lead placed in the right ventricle (with or without atrial lead) with remaining device longevity of 4 years or more for:
	  ○ Secondary Prevention or,
	  ○ Primary Prevention and has had a device treated VT/VF or a device recorded episode of sustained VT/VF
	• Subject is ≥ 18 years old
	• Subject has previously documented history of VT/VF
	• Subject must be willing and able to use Medtronic CareLink network monitoring system
	• Subject provides signed and dated authorization and/or consent per institution and local requirements
	• Subject is willing and able to comply with the protocol
	Exclusion Criteria
	• Subject who received device for Primary Prevention indication and who has not had either a device treated VT/VF episode or a device recorded episode of sustained VT/VF
	• Subject is enrolled in a concurrent study that may confound the results of this study, without documented pre-approval from a Medtronic study manager
	• Subject has chronic AF
	• Subject has inherited disorders of ion transport mechanisms that predispose the subject to sudden death (“Channelopathies”): Long QT and Brugada Syndromes
	• Subject with multiple implanted active devices that may cause an interruption of a transmission of device data to CareLink

	• Subject has active electronic medical device other than an ICD • Subject requires more than 25% atrial or ventricular pacing • Subject has medical conditions that would limit study participation (per investigator judgment) • Subject has projected life expectancy of less than 1 year • Subject is pregnant or plans to be pregnant over the next year (females of child-bearing potential must have a negative pregnancy test within one week of enrollment and must practice a reliable form of birth control while enrolled in the study) Subject meets exclusion criteria required by local law (e.g. age, breastfeeding, etc.)
Study Procedures and Assessments	• The TPD study requires a baseline visit and a follow up visit. At the baseline visit, baseline characteristics will be recorded and the TPD investigational RAMware will be installed onto the Evera MRI ICD. At the follow up visit (ideally 365-400 days later) the TPD RAMware will be removed from the ICD and the device programming will be evaluated and adjusted as needed. Required study data will be transmitted over the CareLink Network as it is collected. At any visit not required by the study occurring between baseline and follow up, it is recommended to confirm that the TPD RAMware is installed on the device and that the parameters are appropriately configured.
Safety Assessments	No significant risks have been identified in this study design.

3. Introduction

3.1. Background

Clinical studies demonstrate that ICDs can reduce mortality in selected patient populations by treatment of ventricular tachyarrhythmia by defibrillation. However, defibrillation shock therapy is applied after the development of VF (or fast VT) and may not prevent the morbidity of syncope during the event nor the pain and potential injury of the shock itself. Significant effort has been focused on reducing the need for defibrillation with ICDs by reducing inappropriate shocks and applying anti-tachycardia pacing (ATP) to prevent a slow ventricular tachycardia from developing into FVT or VF. Although these clinical studies were successful and shock rates were reduced, the need for defibrillation still exists. One strategy to reduce the need for shock therapy further is to prevent monomorphic ventricular arrhythmias (which can develop into VF) or idiopathic VF from developing. This might be accomplished by monitoring a marker in real time to predict the imminent onset of VT/VF in the seconds to minutes before it starts and inhibiting the arrhythmia by applying an intervention. Alternatively, if the arrhythmia cannot be successfully prevented from initiating, the patient might be warned that an arrhythmia is imminent to avoid injury from syncope or to provide time for medical intervention.

In a Medtronic internal research report entitled "Prediction and Prevention of Imminent Ventricular Arrhythmias-Review" compiled by Scheiner, Musley, and Kornet. (2016), the following recommendations were made, based on the literature search: All previous research has been population based. Because there are large variations in the underlying mechanism and trigger for VT/VF from patient to patient, none of the studies has shown high enough accuracy of prediction to use for imminent patient or caregiver interdiction. We should, therefore, consider studying individual patients who have serial arrhythmias to identify markers specific to a patient. Using that dataset, develop an algorithm to identify which repolarization markers of impending arrhythmias are most accurate predictors in an individual patient. It may be possible to identify marker changes that have useful prognostic value in individual patients, even though they fail to accurately correlate with initiation of an event on a population level. The research study would consist of:

1. Taking serial ECG or EGM measurements for multiple VT/VF episodes in multiple patients of a certain patient group.
2. Evaluating parameters that are known to have some predictive value for VT/VF in a time period of several hours before the VT/VF episode. Determine if there is a consistent change for any of the parameters before a VT/VF episode in each particular patient for this specific patient group.
3. Determining if the next episode can be predicted using the identified parameter(s) or combination of parameters for a particular patient?
4. Determining if exogenous factors may contribute to arrhythmia risk and trigger and if they can be used to identify subgroups of patients in which prediction is more accurate

3.2. Purpose

The purpose of the Medtronic Tachy Prediction Download (TPD) study is to collect data that can be used to determine if an ICD device algorithm can be developed to predict the imminent onset of ventricular arrhythmias.

4. Objectives and Endpoints

4.1. Objectives

4.1.1. Primary Objective

The primary objective of this study is to collect data that can be used to predict the imminent onset of ventricular arrhythmias. These data will include pre-storage device EGMs, RR intervals, PVC density, activity and other physiologic variables before these ventricular arrhythmias, and matching control data.

4.1.2. Endpoint

Due to the feasibility nature of this trial, there is no sample size requirement for this objective. Up to 300 subjects will be enrolled in the study to ensure sufficient data sets (at least 50 VT/VF events collected from unique subjects) are collected for analysis.

5. Study Design

The TPD Study is a prospective, non-randomized, non-interventional, multi-site data collection clinical study to collect ICD longitudinal data that may be used to develop a VT/VF prediction algorithm. The study subjects will include patients currently implanted, or who will be implanted with a market-approved Medtronic Evera MRI® ICD. Up to 300 subjects at up to 20 sites in the US and Hong Kong may participate in this study.

5.1. Duration

It is expected that study subjects will remain in the study for 12 months, then be seen in-office for follow-up and study exit. Study data will be collected from enrollment until exit via CareLink® such that study involvement will not affect the normal follow-up practice or schedule.

5.2. Rationale

Sparse long-term pre-VT/VF onset EGM, RR interval, activity, and PVC density data exists because it is hard to collect. Ideally, Holter recordings could provide this data without altering the function of the ICD under investigation. Unfortunately, the yield of spontaneous VT/VF events on Holter recording is minuscule due to the relatively short-term monitoring provided by Holter and the scarcity of VT/VF events in most patients. The best method for collecting periodic and longer pre-onset data is to modify an ICD's RAMware to allow it to collect the desired EGM, RR interval, and other data prior to VT/VF and HF events. This can be done without affecting device therapy. The data will later be used to determine if there are algorithmic indications that can predict imminent VT/VF.

6. Product Description

6.1. General

Market-released Medtronic Evera MRI™ ICD, Medtronic CareLink Programmer, CareLink® Network and the CareLink Monitor will be used. These components are described in the following sections. Please note, each ICD may only be used in the geographies in which it is market released.

Table 1 System Component Information

Component	Model Number	Investigational or Market released
Evera MRI™ XT DR SureScan™ ICD	DDMB1D4, DDMB1D1, DDMB2D4*, DDMB2D1^	Market Released
Evera MRI™ XT VR SureScan™ ICD	DVMB1D4, DVMB2D4^	Market Released
Evera MRI™ S DR ICD	DDMC3D4, DDMC3D1	Market Released
Evera MRI™ S VR ICD	DVMC3D4, DVMC3D1	Market Released
Medtronic CareLink Programmer	2090	Market Released
Medtronic CareLink Monitor	2020A/B 2490C 24950 Virtual Express	Market Released
Medtronic CareLink Network	___	Market Released
TPD Software	___	Investigational
TPD RAMware	___	Investigational

* Included to support Hong Kong inclusion in the study

^ These models are currently not in the scope of the study geography, however being included for the potential study expansion.

6.1.1. Evera MRI™ ICD

The Evera MRI™ VR (single chamber) and DR (dual chamber) devices are multi-programmable, DF4 or DF1 ICDs which monitor and regulate the patient's heart rate by providing ventricular tachyarrhythmia therapies and rate responsive bradycardia pacing, when needed. The Evera MRI™ ICD includes Medtronic's most advanced features, such as SmartShock™ Technology, Advanced T-wave, Lead Integrity Alert, Atrial Therapies and Interventions (DR device only), Rate Drop Response, and Full Automaticity (e.g., Atrial and Ventricular Capture Management). Additionally, this device contains Medtronic's exclusive SureScan® technology.

6.1.2. Market-Released Medtronic CareLink Monitor and Medtronic CareLink Network

The Medtronic CareLink Monitor and the Medtronic CareLink Network are indicated for use in the transfer of patient data from some Medtronic implantable cardiac devices based on physician instructions and as described in the product manual. These products are not a substitute for appropriate medical attention in the event of an emergency and should only be used as directed by a physician.

The Medtronic CareLink Network enables subjects to remotely transfer data from their device to the clinic. Subjects may be requested to use the Medtronic CareLink Monitor to send their device data to the clinic. Study site personnel can access the data by logging onto the CareLink website via the internet.

6.1.3. Market-Released Medtronic CareLink Programmer

Medtronic's market-released Model 2090 CareLink Programmer must be available at each site to support study visits. Programmers will be used to interrogate devices, collect lead electrical data, program devices, and save device data. They will also be used to install the RAMware into the ICD.

6.1.4. TPD Software

Investigational TPD Software will be distributed via Medtronic's Software Distribution Network (SDN) to the 2090 programmer. Further details on this process can be found in the TPD User Manual. Investigational device tracking is covered in Section 6.5.

6.1.5. RAMware

Investigational RAMware enables the Evera MRI device to save the following data continuously and, when triggered, to transmit data to CareLink. RAMware usage is controlled by a Medtronic provided access key derived from the ICD serial number.

Expanded EGM data

Minimum 30 seconds of EGM data from 2 EGM channels for one and six hour data

Minimum duration of 2 minutes, 20 seconds of EGM data from 2 EGM channels for event trigger stored data

Expanded Interval and EGM amplitude data

Minimum of 5 minutes of data from immediately prior to the data storage time

PVC Density data

The number of PVCs in the hour immediately prior to the data storage time

Subject Activity data

Sum of 2 second activity counts for the 15 minutes immediately prior to the data storage time

Optivol data

Minimum of 1 day of TPD OptiVol data stored prior to the event (no one hour or six hour data)

CareLink Transmission of Data:

Control data transmissions are triggered by a countdown timer at programmable intervals.

Once an event occurs or control data collection completes, the study data will be frozen and the RAMware will trigger a CareAlert to send the collected data to the CareLink Network. Once the device has transmitted the data to the patient monitor or a CareLink Express monitor, the RAMware will clear the CareAlert and reset the study data collection. The minimum frequency of transmission is every 3 months.

6.2. Intended Population

All subjects in this investigation have received or will receive a Medtronic Evera MRI® ICD for approved indications and have a documented history of ventricular arrhythmias.

6.3. Equipment

The following equipment must be available at each site to support study activities:

- Site has access to high-speed internet to submit data
- The subject must have CareLink equipment, properly working with access to a cellular network
- Site must have 2090 CareLink Programmer

6.4. Product Training Requirements

At a minimum, documented training on the TPD CIP and User Manual for the Principal Investigator (PI) is required prior to the clinical site's first enrollment. Prior to subject enrollment, Medtronic will train site personnel on the Clinical Investigation Plan, relevant standards and regulations, if needed, informed consent, and on data collection and reporting tools. If new members join the study center team afterwards, they will receive training on the applicable clinical study requirements relevant to their role before contributing to the clinical study.

6.5. Product Receipt and Tracking

A device disposition log will be maintained at each investigational site to track all investigational components and will be available within the electronic data management system (see section 17.2). These records will consist of:

- TPD Software Application/Programmer Disposition Log (eCRF)
- RAMware/ICD Device Disposition Log (eCRF)

The TPD Software Application will be distributed to a site only when Medtronic has received all required documentation and has notified the site of site activation. Distribution of the TPD Software Application to study sites during the clinical study will be managed by Medtronic. The TPD Software Application will be distributed via the SDN. Software distributed via the SDN will be installed onto study programmers over a secure internet connection.

The TPD Software Application is considered investigational in all geographies. Once the TPD Software Application is installed on a programmer, the presence of that application on that programmer will need to be tracked until the TPD Software Application is removed. While the TPD software is installed on the 2090 Programmer, the programmer will contain a statement indicating the presence of the investigational software application including any statements required by law. This label will be removed once the TPD Software Application is removed from the programmer.

The disposition logs should also be updated in the event the programmer is returned to MDT for software removal.

The TPD RAMware is considered investigational in all geographies. Once the TPD RAMware is installed on an Evera MRI ICD, that ICD is considered investigational and must be tracked as an investigational device until the RAMware is removed. The disposition logs should also be updated in the event a device is explanted and still contains the TPD RAMware.

In the event that a subject does not come in for the follow-up/exit visit within 400 days of TPD RAMware installation, the TPD RAMware will self-terminate. The disposition log should be updated accordingly.

In summary, a device disposition log will be maintained at each investigational site and will be updated appropriately whenever the status of a component has changed.

6.6. Product Storage

The investigational components are programmer software and device RAMware only. The investigational software application will be distributed through a software distribution network, so there are no media storage requirements. Once the investigational components are loaded, the programmer will carry a label indicating the investigational application is installed as described in section 6.5. The device RAMware is loaded onto the ICD by the programmer equipped with the TPD Software Application. There are no changes to the physical components of the system and therefore no new storage requirements.

It is the responsibility of the investigator to correctly handle, store, and track the investigational components (programmers containing the investigational TPD Software Application and ICDs with TPD RAMware installed). Further details can be found in the TPD User Manual.

For additional product handling and storage requirements, please refer to the original packaging and manuals for each piece of equipment (Programmer, ICD, etc.).

6.7. Product Return

The TPD data collection RAMware will be removed from devices at study exit (or self-terminated at 400 days). The TPD Software Application will subsequently be removed from the 2090 programmers.

7. Selection of Subjects

7.1. Study Population

This study will enroll subjects who have a Medtronic Evera MRI® ICD system per local guidelines and who meet all of the specific study inclusion criteria and none of the exclusion criteria.

7.2. Subject Enrollment

Subjects are considered enrolled in the study upon signing the Medtronic & IRB-approved IC Form. Informed consent must be obtained prior to performing any of the study-related procedures. The complete informed consent process will include giving the subject adequate information about the study and ensuring that there is sufficient time to comprehend the information in the IC Form and have all questions answered before making a decision to participate in the study.

7.3. Inclusion Criteria

Subjects must meet all of the inclusion criteria and none of the exclusion criteria below to be eligible for this study:

- Subject is implanted or will be implanted with an Evera MRI device with properly functioning Medtronic tachycardia lead placed in the right ventricle (with or without atrial lead) with remaining device longevity of 4 years or more for:
  - Secondary Prevention or
  - Primary Prevention and has had a device treated VT/VF or a device recorded episode of sustained VT/VF
- Subject is ≥ 18 years old
- Subject has previously documented history of VT/VF
- Subject must be willing and able to use Medtronic CareLink network monitoring system
- Subject provides signed and dated authorization and/or consent per institution and local requirements
- Subject is willing and able to comply with the protocol

7.4. Exclusion Criteria

The following are the exclusion criteria for the study:

- Subject who received device for Primary Prevention indication and who has not had either a device treated VT/VF episode or a device recorded episode of sustained VT/VF
- Subject is enrolled in a concurrent study that may confound the results of this study, without documented pre-approval from a Medtronic study manager
- Subject has chronic AF
- Subject has inherited disorders of ion transport mechanisms that predispose the subject to sudden death (“Channelopathies”): Long QT and Brugada Syndromes
- Subject with multiple implanted active devices that may cause an interruption of a transmission of device data to CareLink

- Subject has active electronic medical device other than an ICD
- Subject requires more than 25% atrial or ventricular pacing
- Subject has medical conditions that would limit study participation (per investigator judgment)
- Subject has projected life expectancy of less than 1 year
- Subject is pregnant or plans to be pregnant over the next year (females of child-bearing potential must have a negative pregnancy test within one week of enrollment and must practice a reliable form of birth control while enrolled in the study)
- Subject meets exclusion criteria required by local law (e.g. age, breastfeeding, etc.)

7.5. Selection Criteria

The inclusion and exclusion criteria are designed to include subjects that are at elevated risk for additional ventricular arrhythmias, as defined by either a secondary prevention indication or a primary prevention indication with subsequent history of VT/VF, who will be able to successfully complete study participation.

8. Study Procedures

Prior to performing study related procedures, all sites must have Institutional Review Board (IRB)/Ethics Committee (EC) approval and documentation of site readiness from Medtronic.

Medtronic representatives may perform the following activities at the study sites during the study if appropriately trained and under the supervision of the PI and/or appropriate delegate (e.g. appropriately trained and delegated sub-investigator):

- Study training relevant and pertinent to the involvement of personnel conducting study activities and Investigator responsibilities
- Technical support at all visits (e.g. programming of the ICDs according to study requirements, performing device interrogations/save-to-media, etc.), but no electronic case report form (eCRF) data entry shall be performed by Medtronic personnel
- Monitoring activities
- Auditing activities

8.1. Investigator/Investigation Site Selection

The PI will provide oversight for the entire study team at his/her site, implement and manage the day-to-day conduct of the clinical study, ensure data integrity, and the rights, safety, and well-being of the subjects involved in the clinical study.

The PI shall be qualified by education, training, and experience to assume responsibility for the proper conduct of the clinical study. Additional, the site must demonstrate it has the required number of eligible subjects needed within the recruitment period, has one or more qualified Investigators, a qualified study team, and adequate facilities for the foreseen duration of the clinical study.

8.2. Site Initiation

During the initiation process (prior to subject enrollment), Medtronic will train site personnel on the Clinical Investigation Plan, relevant standards and regulations (if needed), informed consent, and data collection and reporting tools. If new members join the study site team, they will receive training on the applicable clinical study requirements relevant to their role before contributing to the clinical study.

A Clinical Trial Agreement (CTA) or Work Order (WO) shall be entered into effect by Medtronic, the participating investigation site and/or the PI (PI) at each investigation site (per the local legal requirements), and returned, fully executed, to Medtronic prior to the commencement of any study activities. Financial aspects of conducting and reporting a study will be specified in the agreement. By signing and dating the agreement, the Investigator indicates approval of the CIP.

Prior to performing study related activities, all sites must have IRB/EC approval, as applicable for that geography.

All local and regional regulatory requirements must be fulfilled prior to site initiation and enrollment of subjects into the study. Each study site must have written documentation of site and Investigator readiness before beginning any study-related activities. Requirements for initiation vary by geography, and may include, but are not limited to:

- Written documentation of IRB/EC approval of the current versions of the CIP and IC Form (approved versions must be retrievable from the IRB/EC approval letter or submission letter) and the corresponding voting list (as required per local law)
- Regulatory authority approval or notification (as required per local law)
- Executed CTA or WO on file with Sponsor
- Current Curriculum Vitae (CV) of Investigators
- Documentation of delegated tasks
- Documentation of study site personnel training

Additional requirements imposed by the IRB/EC and regulatory authority shall be followed, if appropriate. Medtronic will provide each study site with documentation of study site/Investigator readiness; this letter must be received prior to subject enrollment.

8.3. Schedule of Events

Clinical data will be collected at the Baseline and Exit visits, as well as any unscheduled cardiovascular (CV) visits, as applicable. Device data will be collected from Carelink transmissions received during the period between the enrollment and exit until study closure. Data will be collected using eCRFs using an electronic data management system for clinical studies. In addition to eCRF data, non-eCRF data will be collected including device interrogation files and CareLink transmission files. Data will be stored in a secure, password-protected database, which will be backed up nightly. Data will be reviewed using programmed and manual data checks. Data queries will be made available to study sites for resolution. Study management reports will be generated by Medtronic to monitor data quality and study progress. At the end of the study, the data will be frozen and retained indefinitely by Medtronic. Data Collection requirements are summarized in the table below.

Table 2 Data Collection and study procedure requirements at subject visit

Study Procedure	Baseline	Other CV Visit	Study Exit
Patient Informed Consent	X		
Inclusion/Exclusion Assessment	X		
Enrollment Notification	X		
Subject Demographics	X		
Device Information	X		
Medical History	X		
Initial and Final Device Interrogation / CareLink Transmission	X	X	X
Exit Subject			X
Adverse Events (AEs)	As they occur		
Device Deficiencies	As they occur		
System Modifications	As they occur		
Study Deviations	As they occur		
Device Disposition	As they occur		
Death	As it occurs		

8.4. Subject Consent

Informed consent is defined as a legally effective documented confirmation of a subject's voluntary agreement to participate in a particular clinical study after the information has been given to the subject on all aspects of the clinical study that are relevant to the subject's decision to participate. This process includes obtaining an Informed Consent Form (IC Form) and an Authorization to Use and Disclose Personal Health Information/Research Authorization/other privacy language (data protection

authorization) as required by law that has been approved by the study site's IRB/EC, and Medtronic, and personally signed and dated by the subject and the PI or an authorized designee.
Prior to enrolling subjects, each site must have documented IRB/EC approval of the IC Form (and data protection authorization, where applicable) as required by law. Any changes to a previously approved IC Form throughout the course of the study must be reviewed and approved by Medtronic and the IRB/EC reviewing the application before being used to obtain consent or re-consent a study subject. The document(s) must be controlled (i.e. versioned and dated) to ensure it is evident which version(s) were approved by Medtronic and the IRB/EC. All important new information should be provided in written form to new and existing subjects throughout the study. If relevant, all affected subjects must be asked to confirm their continuing informed consent in writing.
Prior to initiation of any study-specific procedures, informed consent must be obtained from the subject. Likewise, privacy or health information protection regulation may require subjects to sign additional forms to authorize sites to submit subject information to the study sponsor. Obtaining informed consent must be conducted by the PI or an authorized designee, and the IC Form and a data protection authorization, as required by law, must be given to the subject in a language he/she is able to read and understand.
The process of obtaining informed consent shall:

- Ensure that the PI or an authorized designee conducts the informed consent process.
- Include all aspects of the clinical study that are relevant to the subject's decision to participate throughout the clinical study.
- Avoid any coercion or undue improper influence on, or inducement of the subject to participate.
- Not waive or appear to waive the subject's legal rights.
- Ensure the IC Form and a data protection authorization as required by law, are given to the subject in a non-technical language the subject is able to read and understand.
- Provide ample time and opportunity for the subject to read and understand the Informed Consent Form to inquire about details of the study, and to consider participation. All questions about the study should be answered to the satisfaction of the subject.
- Include a personally dated signature of the subject acknowledging that their participation in the study is voluntary.
- Include a personally dated signature by the PI, or authorized designee responsible for obtaining the informed consent, as required by local law.
- Provide the subject with a copy of the IC Form and a data protection authorization as required by law.
- Ensure subjects are notified of any significant new findings about the study that become available during the course of the study which are pertinent to the safety and well-being of the subject, as this could impact a subject's willingness to participate in the study.

If the informed consent is obtained the same day the subject begins participating in study-related procedures, it must be documented that consent was obtained prior to participation in any study-related procedures. It is best practice for the process of obtaining the informed consent to be documented in the subject's case history, regardless of circumstance.
In the event the subject cannot read and/or write, witnessed (impartial third party) informed consent will be allowed, provided detailed documentation of the process of obtaining the informed consent is recorded in the subject's case history and the witness signs and dates the Informed Consent Form.

Informed consent shall be obtained through a supervised oral process. An independent witness must be present throughout the process. The IC Form and any other information must be read aloud and explained to the prospective subject if allowed by local law. The witness signs and personally dates the IC Form attesting that the information was accurately explained and that informed consent was freely given. The subject should "make his mark" (sign or otherwise physically mark the document so as to indicate consent) on the IC Form as well. The IC Form should document the method used for communication with the prospective subject and the specific means by which the prospective subject communicated agreement to participate in the study.
The original of the signed IC Form must be filed in the hospital/clinical chart and/or with the subject's study documents.
The IC Form and a data protection authorization as required by law must be available for monitoring, auditing, and regulatory inspections. Any Medtronic personnel who support the initial programming of the TPD study RAMware download must be able to review the subject's signed and dated IC Form and verify its completeness prior to proceeding with the programming. In the event the designated Medtronic personnel identify the IC Form as being incomplete, the programming will not be allowed to occur until the consent of the subject can be adequately and appropriately obtained.

8.5. Enrollment/Baseline

When a patient and the PI or authorized designee (if applicable) signs and dates the IC Form, the patient is considered a subject enrolled in the study. The date the subject signed the IC Form and data protection authorization must be documented in the subject's medical records. Enrollment can be a stand-alone visit or can occur on the same day as the baseline visit. Medtronic should be notified (via Enrollment eCRF) as soon as possible to aid in enrollment tracking. Once consent is obtained, report adverse events, device deficiencies, study deviations, system modifications, and subject exits or deaths as they occur.

The following information is required to be collected at the baseline visit:

- Patient Informed Consent Date (Enrollment Date)
- Eligibility Verification (Inclusion/Exclusion Assessment)
- Patient Demographics
- Medications
- Relevant Medical History
- Device Characteristic (including presence of atrial lead, if applicable)
- Device Interrogation (Initial and Final) and Save-to-media/USB
- Device Disposition Log
- Adverse Event Assessment

8.5.1. Subject History

Demographic, medical history, and cardiac arrhythmia/intervention information will be collected at the Baseline Visit.

8.5.2. Prior and Concomitant Medications

There are no medications or treatments that are required for this study. In addition, there are no medications or treatments that are excluded from this study.

8.5.3. Initial Interrogation and Save-to-media/USB

An initial device interrogation is recommended. If completed, save the data via save-to-media/USB and submit the data to Medtronic.

8.5.4. Device Programming Prior to Installation of the TPD

The following device conditions must be satisfied before the TPD feature set can be installed on a device:

- Device cannot have a projected longevity of less than 4 years
- Must be one of the Evera MRI models found in Table 1 System Component Information
- Must not have an active electrical reset

8.5.5. TPD Download

The investigational TPD Software Application is used to install the TPD RAMware into an Evera MRI device. The TPD Research System requires an access code to be entered before the investigational RAMware can be installed on the device.

The TPD Research System uses the source and range of one of the EGM channels (EGM1) and will lock the desired configuration for the TPD study. The TPD Software Application will add the RVcoil-Can programmable option to EGM1 such that the TPD Software Application will properly display the EGM1 source and EGM1 signal data. If the EGM1 source is programmed to something other than RVcoil-Can during the programmer session, the RAMware will program the EGM1 source to RVcoil-Can upon session end.

The EGM source TPD Research System is using (RVcoil-Can) is not an available option for EGM1 in the market-released software. Therefore, if the device with RAMware is interrogated by the standard market released Evera MRI 2090 programmer software, “???” will display for the EGM1 source.

The TPD Research System will not control the EGM2 source and range. This EGM configuration is reserved for the Wavelet feature, and TPD will not impact this feature. It is recommended that, during the study, the EGM2 configuration remains at nominal: Can to RVcoil.

Refer to the TPD User Manual for instructions on how to download the TPD RAMware onto the Medtronic ICD.

8.5.6. Post-Download TPD Parameters

The functions of the installed TPD parameters are described in the TPD User Manual.

8.5.7. Final Interrogation and Save-to-media/USB

Perform an "Interrogate all" with the device using the TPD RAMware download. Save the data via save-to-media and submit the data to Medtronic.

8.6. Study Follow-up/Exit

Whenever possible, subjects should remain in the study for 365 days or until all data required to meet study objectives has been collected (whichever comes first). An in-office visit is required for study exit and must be completed within 400 days of TPD RAMware download to the device to ensure all required study data is collected and that the subject's device is optimally programmed at the time of study exit.

The list below outlines the required data to be collected at study exit:

- Device Interrogation (Initial and Final) and Save-to-media/USB
- Device Disposition
- RAMware Removal (In-Office)
- Adverse Event Assessment
- Exit CRF

Table 3 Follow-Up/Exit Window

Window Start	Target	Window End
365 Days	383 Days	400 Days

If a subject fails to return for study exit before 400 days post-RAMware installation on their device, the TPD RAMware will self-terminate 400 days after installation. If the RAMware self-terminates, it is imperative that the subject's device programming is reviewed and optimized as soon as possible to ensure optimal device performance.

8.6.1. Initial Interrogation and Save-to-media/USB

It is recommended to complete an initial interrogation using the programmer. If completed, save the data via save-to-media/USB and submit the data to Medtronic.

8.6.2. RAMware Removal

The investigational RAMware is intended to be uninstalled at study exit. Refer to the User Manual for instructions on how to remove the RAMware from the Medtronic ICD.

8.6.3. Uninstall Software from Programmer

The investigational TPD Software Application hosted on the Medtronic 2090 programmer will be uninstalled using the Desktop software maintenance functions after all TPD RAMware has been removed from the implantable devices and prior to study closure.

8.6.4. Final Interrogation and Save-to-media/USB

Perform a device interrogation by selecting “Interrogate All.” Save the data via save-to-media and submit the data to Medtronic.

8.6.5. Device Programming Post TPD Removal

At the time of exiting the subject optimize device programming via market released software.

Patient Home Monitor parameter was programmed to “Yes” at the time of TPD installation, but will not revert to pre-study programming after Removal of TPD Feature Set. Ensure this parameter is programmed appropriately at the study exit.

All Therapies in a Zone Exhausted for an Episode parameter was programmed to “On” at the time of TPD installation, but will not revert to pre-study programming after Removal of TPD Feature Set. Ensure this parameter is programmed appropriately at the study exit.

Using the Non-TPD, Market Released Evera MRI programmer software application, choose and program an available option for the EGM1 source and range.

Confirm the Monitored configuration is programmed as appropriate, since this may have been modified in response to the TPD Study configuration.

Confirm device programming on the Data Collection Setup screen.

8.7. Other Cardiovascular Visit

“Other Cardiovascular Visit” is defined as a cardiovascular visit not required by the protocol that occurs between enrollment and exit.
If such a visit occurs, the following information, if applicable is recommended to be collected.

Data collected may include, but is not limited to:

- Device Interrogation and Save-to-media
- Confirm TPD Parameters
- System Modification, if applicable
- Document any reportable AEs

8.8. System Modifications

A system modification will be reported in the event the device and/or leads require invasive modification (e.g., generator or lead explant, generator or lead replacement, lead repositioning). In the event of a system modification, the follow-up schedule for the subject will remain unchanged and will continue to be followed until the subject is exited. For a system modification, the following activities are required:

- Complete a system modification eCRF
- Initial Device Interrogation and Save-to-media
- Download of TPD RAMware, as applicable (e.g., ICD changeout for new Evera MRI device)
- Final Device Interrogation "Interrogate All" and Save-to-media

If the device is taken out of service (e.g., explanted) and there is a possible replacement Evera MRI at a later date, the subject should remain in the study if possible. If a replacement Evera MRI device is received, the TPD RAMware should be loaded on it, as applicable. If the device is taken out of service and a replacement will not be implanted or the replacement is not a study approved device, the subject will be exited from the study.

All explanted product (device, leads, etc.) should be returned to the respective manufacturer for analysis when permissible by local laws and regulations.

In the event that a subject has a re-attempt after a previous unsuccessful system modification, the subsequent attempt(s) must be reported via eCRF as separate system modifications.

8.9. Subject Consent

Prior to initiation of any study-specific procedures, informed consent must be obtained from the subject. Likewise, privacy or health information protection regulation may require subjects to sign additional forms to authorize sites to submit subject information to the study sponsor. Additional information is found in Section 8.4.

8.10. Assessment of Safety

Medtronic has established procedures to ensure appropriate reporting of safety information, further detailed in Section 10.

8.11. Recording Data

Data will be collected using Oracle Clinical, an electronic data management system for clinical studies. eCRF data will be stored in a secure, password-protected database which will be backed up nightly. More details are provided in Section 13.2.

8.12. Deviation Handling

The investigator may not deviate from the CIP, unless the deviation is necessary in an emergency situation to protect the rights, safety and wellbeing of the subject. Procedures for documenting, reporting, and analyzing of deviations should be included. Notification requirements and timeframes for reporting by region are included in Section 13.7.

8.13. Subject Withdrawal or Discontinuation

A study exit eCRF is required for all subjects except in the case of death. Prior to exiting a subject from the study, it is recommended to follow the subject until all AEs are resolved. Following exit, subjects will continue to receive standard medical care. Upon exiting from the study, no further study data will be collected or study visits will occur for the subject. Exited subjects will not be replaced with newly enrolled subjects.

Subjects are urged to remain in the study as long as possible, but may be exited from the study for any of the following situations:

- Study closure
- Subject lost to follow-up (refer to Section 8.13.1)
- Subject did not meet inclusion/exclusion criteria
- Subject did not provide consent or data use protection authorization
- Subject chooses to withdraw (refer to section 8.13.2 for more information)
- Investigator deems withdrawal necessary (e.g., medically justified, inclusion/exclusion criteria not met)
- Subject completed study
- Medtronic may recommend subject exit at any time if the assessment of accumulated episodes per subject is high.

For study exit visits the following information is required:

- Document any reportable AEs (refer to section 10**Error! Reference source not found.**).
- Perform a device interrogation and save on a USB flash drive. Device interrogation data must be sent to Medtronic, with a copy being maintained at the site in the subject's file. A deviation is required if a device interrogation is missed. RAMware should be removed from the device and programming reviewed and optimized for the patient.
- Document the reason for subject exit or withdrawal.

8.13.1. Lost to Follow-Up

In the case that the subject is determined to be lost to follow-up, a minimum of two attempts to contact the subject must be documented. The recommended method of contact is one letter and one phone record or two letters. In addition, follow the regulations set forth by the governing IRB/EC.

8.13.2. Subject Withdrawal

A subject will be exited from the study in the event that he or she is unable to participate, expresses a desire to withdraw, or is unwilling to continue participation in the study. In addition, a subject may be exited from the study if an investigator feels it is necessary to withdraw the subject from the study due to a medical condition, if the inclusion/exclusion criteria are not met, or other reason. In such cases, the subject will be notified and provided an explanation regarding the reason for the study exit. If the TPD RAMware has been installed on the subject's ICD, the subject should have the TPD RAMware removed, and their device programming reviewed and optimized.

The subject should be informed that their future care or treatment will not be affected in any way as a result of choosing to not participate in this study. Furthermore, alternative treatments and medical consequences of exiting the study should be discussed with the subject. Any significant new findings related to the study that may develop, which may relate to the subject's willingness to continue participation, should be communicated to the subject.

9. Risks and Benefits

9.1. Potential Risks

Medtronic follows rigorous Quality Assurance and Control procedures throughout the life of the product, from the research and development phase through the study phase.

Although the rate of occurrence is expected to be low, a detailed review of potential hazards associated with the TPD Research System identified possible scenarios that could occur.

First and foremost, the study personnel and a Medtronic representative will be properly trained on the investigational TPD system and study protocol. In addition, the TPD User Manual will provide the proper instructions. Risks normally associated with device follow-ups will be minimized by selecting investigators that have demonstrated previous experience with the programming, interrogation, and monitoring of these devices.

The TPD Research System will cause an increase in current drain on the device battery resulting in a device longevity reduction of six months or fewer during 400 days of TPD operation, with 95% of patients having less than 5.33 months of reduction.

Because the TPD feature changes the source and range of one of the EGM channels, the EGM source value will appear as invalid ("???") to a clinician using the market released software. This could present a risk to the subject by delaying appropriate action when receiving emergency care.

To transmit data in a timely manner, the TPD feature uses an existing CareAlert to trigger data transmission. This may cause additional burden when triaging CareLink data. This could present a risk to the subject by being called in for in-office follow-up when it is not necessary. This could also present the risk of becoming desensitized to the CareAlert with a potential to miss a non-study cause for the alert. In addition, the CareAlert will be reset by the TPD feature once it is transmitted to the monitor. As such, the alert may not be presented as being active when interrogated by a programmer, either by study personnel or other clinicians.

There may be additional risks related to study participation that are unknown at this time.

9.2. Risk Minimization

Medtronic has minimized the risks to the subject by the following:

- Implementing quality control measures into development and production processes.
- Providing guidelines for subject selection and evaluation, and subject inclusion and exclusion criteria.
- Providing adequate instructions and training.
- Selecting Investigators that have demonstrated previous experience with the programming, interrogation, and monitoring of pacemaker devices.
- After enrollment in the clinical study, at each protocol required follow-up, the Investigator must evaluate the subject's health, assess for any adverse events, and interrogate the study device to verify appropriate study device function.
- Providing notification on the market released software indicating the subject's participation in a study.
- Providing the subject with a card indicating participation in the study and impact to the displayed data
- If the subject is lost to follow-up, the investigational software system has an internal timer that automatically deactivates the software 400 days after the date of installation.

- Additionally, subjects cannot be in concurrent studies as the device will allow the download and operation of only one investigational feature at a time.

9.3. Potential Benefits

The TPD data collection RAMware download in the Evera MRI device offers no direct/immediate benefit. The potential benefits of having the TPD data collection RAMware download in the Evera MRI device include:

- Closely monitoring the patient which may lead to more prompt follow-up following clinical events.
- Additionally, information collected from this study may assist in the design and improvements of new product(s)/therapy(ies) and/or instructions for use.

9.4. Risk-Benefit Rationale

All identified risks as described in the previous sections have been mitigated to as low as possible. While there may be minimal or no benefit of participation in the study, there is the potential to aid in collecting information that may lead to more prompt follow-up following clinical events.

10. Adverse Events and Device Deficiencies

Timely, accurate, and complete reporting and analysis of safety information for clinical studies are crucial for the protection of subjects. Medtronic has established procedures to ensure appropriate reporting of safety information.

10.1. Definitions/Classifications

10.1.1. Adverse Event Definitions

Adverse Event definitions are provided in Table 4 Adverse Event and Device Deficiency Definitions. To ensure that all AEs that are potentially relevant are collected, the following will be collected throughout the study duration, starting at the time of signing the Informed Consent Form:

- All potential TPD RAMware Related AEs
- All potential TPD Software Application Related AEs
- All subject deaths (regardless of relatedness)

Reporting of these events to Medtronic will occur on an AE Form, including date of AE, treatment, resolution, assessment of both the seriousness of the AE and the relatedness. Each AE must be recorded on a separate AE eCRF.

For AEs that require immediate reporting (see Table 6 Reporting Requirements) initial reporting may be done by phone, fax, or on the eCRF completing as much information as possible. The original completed AE eCRF must be submitted to Medtronic as soon as possible.

Each AE must be reported separately. Any medication, whether cardiovascular or not, associated with the treatment of an adverse event must be reported on the medication log.

Subject deaths are also required to be reported. Refer to Section 10.4 for Subject Death collection and reporting requirements.

10.1.2. Device Deficiencies

Device deficiency (DD) information will be collected throughout the study and reported to Medtronic. Note that DDs that result in an Adverse Device Effect (ADE) to the subject should be captured as an AE eCRF only. Device Deficiencies that did not lead to an AE but could have led to a Serious Adverse Device Effect (SADE) (i.e., if suitable action had not been taken, if intervention had not been made, or if the circumstances had been less fortunate) require immediate reporting (see Table 4 Adverse Event and Device Deficiency Definitions. For DDs that require immediate reporting, initial reporting may be done by contacting the study sponsor per the sponsor contact information.

10.1.3. Event Updates and Resolution

For any changes in the status of a previously reported AE (i.e. change in actions taken, change in outcome, change in relatedness), an update to the original AE must be provided. Each AE must be followed until the AE has been resolved, the subject exits the study, or until study closure, whichever occurs first.

At the time of study exit, all collected AEs with an outcome of ”not recovered / not resolved”, “recovering / resolving”, or “unknown” must be reviewed and updated provided as applicable.

10.2. Definitions/Classifications

Where the definition indicates “device,” it refers to any device used in the study. This might be the device under investigation, or any market released component of the system and includes, but is not restricted to, the Evera MRI™ ICD, the programmer, and Carelink Monitor.

Table 4 Adverse Event and Device Deficiency Definitions

General	
Adverse Event (AE) (ISO 14155:2011, 3.2)	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 investigational medical device 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.
Adverse Device Effect (ADE) (ISO 14155:2011, 3.1)	Adverse event related to the use of an investigational medical device. NOTE 1: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device.
Device Deficiency (DD) (ISO 14155:2011, 3.15)	Inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance.

Relatedness	
Software Related	An adverse event that results from the presence or performance (intended or otherwise) of the software downloaded on the programmer.
RAMware Related	An adverse event that results from the presence or performance (intended or otherwise) of the RAMware downloaded on the device.
Not Related	Relationship to the device or procedures can be excluded when: • The event is not a known side effect of the product category the device belongs to or of similar devices and procedures; • The event has no temporal relationship with the use of the device or the procedures; • The serious event does not follow a known response pattern to the medical device (if the response pattern is previously known) and is biologically implausible; • The discontinuation of medical device application or the reduction of the level of activation/exposure – when clinically feasible – and reintroduction of its use (or increase of the level of activation/exposure) do not impact the serious event; • The event involves a body-site or an organ not expected to be affected by the device or procedure; • The serious event can be attributed to another cause (e.g., an underlying or concurrent illness/clinical condition, an effect of another device, drug, treatment, or other risk factors); • The event does not depend on a false result given by the device used for diagnosis (when applicable); • Harms to the subject are not clearly due to use error; • In order to establish the non-relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the event.
Unlikely	The relationship with the use of the device seems not relevant and/or the event can be reasonably explained by another cause, but additional information may be obtained.
Possible	The relationship with the use of the investigational device is weak but cannot be ruled out completely. Alternative causes are also possible (e.g. an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment). Cases were relatedness cannot be assessed or no information has been obtained should also be classified as possible.
Probable	The relationship with the use of the investigational device seems relevant and/or the event cannot reasonably be explained by another cause, but additional information may be obtained.
Causal Relationship	•The event is associated with the device or study procedures beyond reasonable doubt when: ○ The event is a known side effect of the product category the device belongs to or of similar devices and procedures; ○ The event has a temporal relationship with device use/application or procedures; ○ The event involves a body-site or organ that the device or procedures are applied to or the device or procedures have an effect on; ○ The serious event follows a known response pattern to the medical device (if the response pattern is previously known); ○ The discontinuation of medical device application (or reduction of the level of activation/exposure) and reintroduction of its use (or increase of the level of activation/exposure) impact on the serious event (when clinically feasible); ○ Other possible causes (e.g., an underlying or concurrent illness/clinical condition or/and an effect of another device, drug, or treatment) have been adequately ruled out; ○ Harm to the subject is due to error in use; ○ The event depends on a false result given by the device used for diagnosis (when applicable); ○ In order to establish the relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the serious event.

Seriousness	
Serious Adverse Event (SAE) (ISO 14155:2011, 3.37)	Adverse event that a) led to death, b) led to serious deterioration in the 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 or prolonged 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, c) led to fetal distress, fetal death or a congenital abnormality or birth defect NOTE 1: Planned hospitalization for a pre-existing condition, or a procedure required by the CIP, without serious deterioration in health, is not considered a serious adverse event.
Unanticipated Adverse Device Effect (UADE) (21 CFR 812.3(s))	Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death, was not previously identified in a nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

10.3. Reporting of Adverse Events

All reported Adverse Events and Device Deficiencies will be reviewed by a Medtronic representative. AEs will be classified according to the definitions provided.

Upon receipt of an Adverse Event/Device Deficiency at Medtronic, a Medtronic representative will review the Adverse Event/Device Deficiency for completeness and accuracy and when necessary will request clarification and/or additional information from the Investigator. Medtronic will utilize MedDRA, the Medical Dictionary for Regulatory Activities, to assign a MedDRA term for each adverse event based on the information provided by the Investigator.

Regulatory reporting of AEs and Device Deficiencies will be completed according to local regulatory requirements. Refer to Table 6 Reporting Requirements for a list of required Investigator and Medtronic reporting requirements and timeframes. It is the responsibility of the Investigator to abide by any additional AE reporting requirements stipulated by the IRB/EC responsible for oversight of the study.

For emergency contact regarding an Unanticipated Adverse Device Effect (UADE), contact a clinical study representative immediately (refer to the study contact list provided in the site's study documents binder/Investigator site file or refer to the Sponsor Contact Information section provided in the CIP).

Adverse Events and deaths will be classified according to the standard definitions as outlined below:

Table 5 Adverse Event Classification Definitions

What is classified?	Who classifies?	Classification Parameters
Relatedness	Investigator	Software, RAMware
	Sponsor	Software, RAMware
Seriousness	Investigator	SAE
	Sponsor	SAE, UADE
Diagnosis	Investigator	Based on presenting signs and symptoms and other supporting data
	Sponsor	MedDRA term assigned based on the data provided by Investigator
Death Classification	Investigator	Sudden Cardiac, Non-sudden Cardiac, Non-Cardiac, Unknown

10.3.1. Adverse Events and Device Deficiency Reporting Requirements

Regulatory reporting of AEs and device deficiencies will be recorded and reported according to local regulatory requirements. It is the responsibility of the Investigator to abide by the adverse event reporting requirements stipulated by local law and the site's IRB/EC.

Table 6 Reporting Requirements

Unanticipated Adverse Device Effects (UADEs)	
Investigator submits to:	
Medtronic	US: Submit as soon as possible, but no later than within 10 working days after the investigator first learns of the event. (21 CFR 812.150(a)(1)) Hong Kong: Submit per local reporting requirement
Regulatory authorities	All geographies: Submit to regulatory authority per local reporting requirement
Ethics Committee	US: Submit as soon as possible, but no later than within 10 working days after the investigator first learns of the event. (21 CFR 812.150(a)(1)) Hong Kong: Submit per local reporting requirement
Sponsor submits to:	
Regulatory authorities	Submit within 10 working days after first receives notice of the effect. (21 CFR 812.150(b)(1))

Ethics Committee	Submit within 10 working days after first receives notice of the effect. (21 CFR 812.150(b)(1))
Investigators	Submit within 10 working days after first receives notice of the effect. (21 CFR 812.150(b)(1))
All other Reportable Adverse Events	
Investigator submits to:	
Medtronic	Submit in a timely manner after the investigator first learns of the event.
Regulatory authorities	Submit to regulatory authority per local reporting requirement.
Ethics Committee	Submit to Ethics Committee per local reporting requirement.
Device Deficiencies	
Investigator submits to:	
Medtronic	Submit in a timely manner after the investigator first learns of the deficiency.
Regulatory authorities	Submit to regulatory authority per local reporting requirement.
Ethics Committee	Submit to Ethics Committee per local reporting requirement.

10.4. Subject Death

10.4.1. Death Data Collection

All subject deaths must be reported by the investigator to Medtronic on an AE form (AE with the outcome of fatal) as soon as possible after the investigator first learns of the death.

In the event of a subject's death, it is recommended that the implanted system be explanted and returned to Medtronic for analysis whenever possible per local process. Local laws and procedures must be followed where applicable.

For the ICD system, the VT and VF detection capabilities must be disabled to avoid inadvertent shocks. If any system component is returned to Medtronic, internal return product reporting systems may be used to gather additional information about the returned device/component.

A copy of the death certificate, if available and allowed by state/local law, should be sent to the Medtronic study team. When a death occurs in a hospital, a copy of the death summary report and all relevant hospital records should be sent to the Medtronic study team, if available. If an autopsy is conducted, the autopsy report should also be sent to the Medtronic study team if available and allowed by state/local law. When the death occurs at a remote site, it is the investigative site's responsibility to attempt retrieval of information about the death. Additionally, device disposition information should be updated. In summary, the following data will be collected:

- Date of death
- Detailed description of death
- Cause of death
- Relatedness to system and/or procedure
- Device interrogation and Save-to-Media (if available)
- Device disposition information
- Death summary/hospital records (if available and allowed by state/local law)
- Autopsy report (if available and allowed by state/local law)
- Death certificate (if available and allowed by state/local law)

10.4.2. Death Classification and Reporting

Sufficient information will be required in order to properly classify the subject's death. The Investigator shall classify each subject death per the following definitions:

Cardiac Death: A death directly related to the electrical or mechanical dysfunction of the heart.

Sudden Cardiac Death (SCD): Natural death due to cardiac causes, indicated by abrupt loss of consciousness within one hour of the onset of acute symptoms; preexisting heart disease may have been known to be present, but the time and mode of death are unexpected. If the time of onset cannot be determined, SCD will alternatively be defined as any unexpected cardiac death occurring out of the hospital or in the emergency room as dead on arrival.

Non-sudden Cardiac Death: All cardiac deaths that are not classified as sudden deaths, including all cardiac deaths of hospitalized subjects on inotropic support.

Non-cardiac Death: A death not classified as a cardiac death.

Unknown Classification: Unknown death classification is intended for use only when there is insufficient or inadequate information to classify the death.

Table 7 Subject Death Classification Responsibilities

What is classified?	Who classifies?	Classification Parameters
Death Classification	Investigator	Sudden Cardiac, Non-sudden Cardiac, Non-cardiac, Unknown

Regulatory reporting of Subject Deaths will be completed according to local regulatory requirements.

10.5. Product Complaint Handling

In geographies where devices are market-released, product complaint reporting is applicable. This includes when an AE is related to a market-released device during the study. The reporting of product complaints is not part of the clinical study and should be done in addition to the Clinical Adverse Event reporting requirements. Refer to local regulations for reporting requirements.

Product Complaint: Any written, electronic or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness or performance of a medical device that has been placed on the market. It is the responsibility of the investigator to report all product complaint(s) associated with a medical device distributed by Medtronic, regardless whether they are related to intended use, misuse or abuse of the product. Reporting must be done immediately and via the regular channels for market-released products. Medtronic will notify the regulatory authorities, as applicable for the following incidents immediately upon learning of them:

- Any malfunction or deterioration in the characteristics and/or performance of a device, as well as any inadequacy in the labeling or instructions for use which led or might have led to the death or serious deterioration in the state of health of a patient, user, or other person.
- Any technical or medical reason resulting in the withdrawal of a device from the market by the manufacturer.
- A serious deterioration in the state of heath includes:
- Life-threatening illness or injury, or
- Permanent impairment of a body structure function or a body function, or
- In-patient or prolonged hospitalization, or
- Medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function.

11. Statistical Design and Methods

The purpose of the study is data collection for future research and development. Therefore, the TPD study is not powered to formally test a hypothesis.

12. Ethics

12.1. Statement(s) of Compliance

This study will be conducted in compliance with international ethical and scientific quality standards, known as good clinical practice (GCP). GCP includes review and approval by an independent IRB/EC before initiating and obtaining and documenting the freely given patient informed consent of a subject before initiating the study.

- The study will be conducted according to federal, national and local laws, regulations, standards, and requirements where the study is being conducted. The principles of the Declaration of Helsinki have been implemented through the patient informed consent process, IRB/EC approval, study training, clinical trial registration, preclinical testing, risk-benefit assessment, and publication policy. In the US, the study will be conducted in compliance with 21 CFR Parts 11, 50, 54, 56 and 812.2(b)(abbreviated requirements).
- In Hong Kong, the study will be conducted in compliance with the Declaration of Helsinki version 2013
    - The study will be publicly registered prior to first enrollment in accordance with the 2007 Food and Drug Administration Amendments Act (FDAAA PL 110-85, section 810(a)) and Declaration of Helsinki on http://www.clinicaltrials.gov.
    - Approval of the CIP and CIP amendments is required from the following groups prior to any study procedures at a study center:
- Medtronic
- PIs (where required by local law/regulations)
- Geography-specific regulatory authorities (if regulatory approval is required)
- An Independent Ethics Committee

13. Study Administration

13.1. Monitoring

It is the responsibility of Medtronic to ensure proper monitoring of this clinical study. Trained Medtronic personnel or delegates appointed by Medtronic may perform study monitoring at the study site in order to ensure that the study is conducted in accordance with the CIP, the Clinical Trial Agreement or Work Order, and applicable regulatory and local requirements. Medtronic, or delegates, must therefore be allowed access to the subjects' case histories (clinic and hospital records, and other source data/documentation) upon request as per the Informed Consent Form and Authorization to Use and Disclose Personal Health Information/Research Authorization/other privacy language (data protection authorization) as required by law and Clinical Trial Agreement or Work Order. The PI should also be available during monitoring visits.

Monitoring for the study will be done in accordance with the study-specific monitoring plan. Monitoring visits may be conducted periodically to assess site study progress, the investigator's adherence to the CIP, regulatory compliance including but not limited to IRB/EC approval and review of the study, maintenance of records and reports, and review of source documents against subject eCRFs. Monitors review site regulatory and study compliance by identifying findings of non-compliance and communicating those findings along with recommendations for preventative/corrective actions to site personnel. Monitors may work with study personnel to determine appropriate corrective action recommendations and to identify trends within the study or at a particular site. Regulatory documents may be reviewed at each study site.

The frequency of monitoring visits may be based upon subject enrollment, duration of the study, study compliance, number of adverse events, number of deviations, findings from previous monitoring visits and any suspected inconsistency in data that requires investigation.

13.2. Data Management

Data will be collected using Oracle Clinical, an electronic data management system for clinical studies. eCRF data will be stored in a secure, password-protected database which will be backed up nightly. Data will be reviewed using programmed and manual data checks. Data queries will be made available to sites for resolution. Study management reports may be generated to monitor data quality and study progress. At the end of the study, the data will be frozen and will be retained indefinitely by Medtronic. All records and other information about subjects participating in this study will be treated as confidential. Data will be transferred and processed by Medtronic or a third party designated by Medtronic in a key coded form, unless it's impossible to make it anonymous, for instance, where the subject's name cannot be removed from the data carrier.

Procedures in the CIP require source documentation. Source documentation will be maintained at the site. Source documents, which may include worksheets, patient medical records, echo data, programmer printouts and device interrogation files, must be created and maintained by the investigational site team.

The data reported on the eCRFs shall be derived from source documents and be consistent with these source documents, and any discrepancies shall be explained in writing. The eCRF may be considered the source for the following data collection elements:

- Enrollment Notification
  - Site assigned patient reference
- Baseline
  - Administrative information
- Adverse Event eCRF
  - Date study site became aware of event
  - Relatedness of adverse event
- Device Deficiency eCRF
- System Modification
  - Reason for system modification
- Deviations
  - Reason for Deviation

Save-to-media data collected via CareLink visits will be sent to Medtronic. Upon receipt, device data will be maintained within a Medtronic device database and retrieved for analysis and reporting.

13.3. Direct Access to Source Data/Documents

The sponsor or a regulatory authority may audit/inspect and/or monitor the study site to evaluate the conduct of the study. The Clinical Investigator(s)/institution(s) shall allow study related monitoring, audits, IRB/EC review, and regulatory inspection by providing direct access to source data/documents.

13.4. Confidentiality

All records and other information about subjects participating in this study will be treated as confidential.

13.5. Liability

Medtronic maintains appropriate Clinical Trial liability insurance coverage as required under applicable laws and regulations and will comply with applicable local law and custom concerning specific insurance coverage. If required, a Clinical Trial insurance statement/certificate will be provided to the Ethics Board.

13.6. CIP Amendments

Approval of subsequent revisions to the CIP is required at each study site from the following groups prior to implementation of the revised CIP at the site:

- Medtronic
- PIs (where required by local law)
- An independent IRB/EC.

If a CIP amendment occurs, site personnel will need to be re-trained as necessary and will need to submit any changes to their IRB/EC.

13.7. Record Retention

13.7.1. Investigator Records

The Investigator is responsible for the preparation and retention of the records including, but not limited to, those cited below. All of the below records, with the exception of case history records and case report forms, should be kept in the Investigator Site File (i.e., the study binder provided to the Investigator) or Subject Study Binder. eCRFs must be maintained and signed electronically by an Investigator within the electronic data capture system during the study. Medtronic will provide electronic copies of CRFs (i.e. Patient Data Report) from the database upon request following study closure.

The following records are subject to inspection and must be retained for a period of two years (or longer as local law/regulation or hospital administration requires) after study conclusion. Measures shall be taken to avoid loss or premature destruction.

- All correspondence between the IRB/EC, sponsor, monitor, and/or the Investigator that pertains to the investigation, including required reports.
- Subject's case history records, including:
  - Signed and dated Informed Consent Form, in accordance with local requirements
  - Observations of adverse events/Unanticipated adverse device effects/device deficiencies
  - Medical history
  - Baseline and follow-up data (if applicable)
  - Documentation of the dates and rationale for any deviation from the protocol
- Electronically signed and dated eCRFs and a blank set of eCRFs where required by local law
- All approved versions of the CIP and IC Form
- Signed and dated CTA or WO
- IRB/EC approval documentation. Written information that the Investigator or other study staff, when a member of the IRB/EC, did not participate in the approval process. Approval documentation must include the IRB/EC composition, where required per local law.

- Current curriculum vitae of PIs
- Documentation of delegated tasks
- Study training records for site staff
- Final Study Report, if applicable

13.7.2. Investigator Reports

The Investigator is responsible for preparing and submitting the following complete, accurate, and timely reports as listed in the following tables (as applicable per geography).

Table 8: Investigator Reports for Hong Kong

Report	Submit to	Description/ Constraints
Withdrawal of Ethics Committee approval	Sponsor	The investigator must report a withdrawal of approval by the reviewing Ethics Committee of the investigator's part of the investigation within 5 working days.
Study Deviations	Sponsor and Ethics Committee	Any deviation from the Clinical Investigation Plan shall be reported together with the explanation of the deviation as soon as possible upon the center becoming aware of the deviation. Notice of deviations from the CIP involving a failure to obtain a subject's consent, or is made to protect the life or physical well-being of a subject in an emergency shall be given within 5 working days, or sooner if required by local requirements. Except in such emergency, prior approval is required for changes in the plan or deviations.
Progress Report	Ethics Committee	As required by local Ethics Committee
Final Report	Ethics Committee	This report must be submitted within 3 months of study completion or termination.

Table 9 Investigator Reports for the United States

Report	Submit to	Description/Constraints
Withdrawal of IRB/EC approval (either suspension or termination)	Sponsor	The Investigator must report a withdrawal of approval by the reviewing IRB/EC of the Investigator's part of the investigation within 5 working days. *(21 CFR 812.150(a)(2))*
Progress report	Sponsor and IRB/EC	The Investigator must submit this report to the sponsor and IRB/EC at regular intervals but in no event less than yearly. *(21 CFR 812.150 (a)(3))*.

Study deviations	Sponsor and IRB/EC	Notice of deviations from the CIP to protect the life or physical wellbeing of a subject in an emergency shall be given as soon as possible, but no later than 5 working days after the emergency occurred. Except in such emergency, prior approval is required for changes in the plan or deviations. If the deviation may affect the scientific soundness of the plan or the rights, safety, and welfare of the subjects, the deviation must be approved by Medtronic and the IRB/EC. If the deviation does not affect these issues then only Medtronic must approve it. *(21 CFR 812.150(a)(4))*
Final report	Sponsor and IRBs/ECs	This report must be submitted within 3 months of study completion or termination of the investigation or the Investigator's part of the investigation. *(21 CFR 812.150(a)(6))*
Failure to obtain informed consent prior to investigational device use	Sponsor and IRB/EC	If an investigator uses a device without obtaining informed consent, the investigator shall report such use within 5 working days after device use. *(21 CFR 812.150(a)(5))*
Other	IRB/EC	An Investigator shall, upon request by a reviewing IRB/EC or any other regulatory agency, provide accurate, complete, and current information about any aspect of the investigation. *(21 CFR 812.150(a)(7))*

Reports are subject to inspection and to the retention requirements as described above for Investigator records. Investigator reporting requirements for safety data are listed in Table 6 Reporting Requirements.

13.7.3. Sponsor Records

Medtronic shall maintain the following accurate, complete, and current records including, but not limited to:

- All correspondence which pertains to the clinical study
- Executed Clinical Trial Agreement
- Current curriculum vitae of PIs
- Electronically signed and dated eCRFs
- All approved informed consent templates, and other information provided to the subjects and advertisements, including translations
- Copies of all IRB/EC approval letters and relevant IRB/EC correspondence and IRB/EC voting list/roster/letter of assurance
- Names of the institutions in which the clinical study will be conducted
- Names/contact addresses of monitors
- Monitoring reports (interim monitoring visit reports, follow-up letters, and close-out visit reports)
- Site qualification visit reports
- Statistical analyses and underlying supporting data
- Final report of the clinical study
- The approved Clinical Investigation Plan, study related reports, and revisions
- Documentation of delegated tasks

- Study training records for site personnel and Medtronic personnel involved in the study
- Sample of CRFs
- Any other records that local regulatory agencies require to be maintained

13.7.4. Sponsor Reports

Medtronic shall prepare and submit the following complete, accurate, and timely reports listed in the tables below. In addition to the reports listed below, Medtronic shall, upon request of reviewing IRB/EC or FDA, provide accurate, complete and current information about any aspect of the clinical study. Medtronic reporting requirements for safety are listed in Table 4 Adverse Event and Device Deficiency Definitions.

Table 10 Sponsor Reports for Hong Kong

Report	Submit to	Description/Constraints
Premature termination or suspension of the clinical study	Investigators, Ethics Committee	Provide prompt notification of termination or suspension and reason(s) per Ethics Committee requirement.
Withdrawal of Ethics Committee approval	Investigators, Ethics Committee	Investigators and other Ethics Committees will be notified only if required by the Ethics Committee.
Progress Reports	Ethics Committee	This will be submitted to the Ethics Committee as required by Ethics Committee
Final report	Investigators, Ethics Committee	▪ The Investigator shall have the opportunity to review and comment on the final report. ▪ If a clinical Investigator does not agree with the final report, his/her comments shall be communicated to the other Investigator(s). The coordinating Investigator shall sign the report. If no coordinating Investigator is appointed, then the signature of the PI in each site should be obtained.
Study deviation	Investigators	▪ Ensure that all deviations from the Clinical Investigation Plan are reviewed with the appropriate clinical Investigator(s), are reported on the case report forms and the final report of the clinical study. Site-specific study deviations will be submitted to Investigators periodically.

Table 11 Sponsor Reports for the United States

Report	Submit to	Description/Constraints
Withdrawal of Ethics Committee approval	Investigators, Ethics Committee, and relevant authorities	Notification within five working days (21 CFR 812.150(b)(2))
Progress Reports	Ethics Committee, and relevant authorities	Progress reports will be submitted at least annually. (21 CFR 812.150(b)(5), 812.36(f)
Recall and device disposition	Investigators, Head of Institution, Ethics Committee, and relevant authorities	Notification within 30 working days and will include the reasons for any request that an Investigator return, repair, or otherwise dispose of any devices (21 CFR 812.150(b)(6))
Final report	Investigators, Ethics Committee, Regulatory authorities upon request	A final report will be submitted to the Investigators, and Ethics Committees within six months after completion or termination of this study. (21 CFR 812.150(b)(7))
Study deviation	Investigators	Ensure that all deviations from the Clinical Investigation Plan are reviewed with the appropriate clinical Investigator(s), are reported on the case report forms and the final report of the clinical study. Site-specific study deviations will be submitted to Investigators periodically.
Failure to obtain informed consent	FDA	Investigator's report will be submitted to FDA within five working days of notification. *(21 CFR 812.150(b)(8))*
Other	IRB	Accurate, complete, and current information about any aspect of the clinical study

Medtronic electronic records and reports will be maintained in a password-protected document management system, and paper documents (where applicable) will be stored in stored in secured file cabinets at Medtronic during the course of this study. After the closure of the study, Medtronic will archive records and reports in accordance with local laws and current standard operating procedures.

13.8. Suspension or Early Termination

13.8.1 Planned Study Closure

Study Closure is a process initiated by the distribution of a study closure letter. Study closure is defined as closure of a clinical study that occurs when Medtronic and/or regulatory requirements have been satisfied per the Clinical Investigation Plan and/or by a decision by Medtronic or regulatory authority, whichever occurs first. The study closure process is complete upon the distribution of the Final Report or after final payments, whichever occurs last. Ongoing IRB/EC oversight is required until the overall study

closure process is complete. Upon study closure, subjects should be managed and followed per physician discretion.

13.8.2 Early Termination or Suspension

Early Termination of the Study is the closure of a clinical study that occurs prior to meeting defined endpoints. This is possible for the whole study or a single site. In the event the whole study or a single site is terminated, subjects will be exited. Study Suspension is a temporary postponement of study activities related to enrollment and distribution of the product. This is possible for the whole study or a single site.

Study-Wide Termination or Suspension

Possible reasons for considering study suspension or termination of the study include but are not limited to:

- Adverse events associated with the system or product under investigation which might endanger the safety or welfare of the subject
- Observed/suspected performance different from the product's design intent
- Decision by Medtronic

Investigator/Site Termination or Suspension

Possible reasons for Clinical Investigator or site termination or suspension include but are not limited to:

- Failure to obtain initial IRB/EC approval or annual renewal of the study
- Persistent non-compliance to the clinical investigation (e.g. failure to adhere to inclusion/exclusion criteria, failure to follow subjects per scheduled follow-ups)
- Lack of enrollment
- Noncompliance with regulations and the terms of the CTA or WO (e.g. failure to submit data in a timely manner, failure to follow-up on data queries and monitoring findings in a timely manner, etc.)
- IRB/EC suspension of the site
- Fraud or fraudulent misconduct is discovered (as defined by local law and regulations)
- Investigator request (e.g. no longer able to support the study)

13.8.3 Procedures for Termination or Suspension

Medtronic-Initiated and Regulatory Authority-Initiated

- Medtronic will promptly inform the Clinical Investigators of the (early) termination or suspension and the reasons and inform the regulatory authority(ies) where required
- In the case of study termination or suspension for reasons other than a temporary IRB/EC approval lapse, the Investigator will promptly inform the IRB/EC
- In the case of study termination, the Investigator must inform the subjects and may inform the personal physician of the subjects to ensure appropriate care and follow-up is provided
- In the case of a study suspension, subject enrollment must stop until the suspension is lifted by Medtronic

- In the case of a study suspension, enrolled subjects should continue to be followed out of consideration of their safety, rights, and welfare

Investigator-Initiated

- The Investigator will inform Medtronic and provide a detailed written explanation of the termination or suspension
- The Investigator will promptly inform the institution (where required per regulatory requirements)
- The Investigator will promptly inform the IRB/EC
- The Investigator will promptly inform the subjects and/or the personal physician of the subjects to ensure appropriate care and follow-up is provided
- In the case of a study suspension, subjects enrolled should continue to be followed out of consideration of their safety, rights, and welfare

IRB/EC-Initiated

- The Investigator will inform Medtronic and provide a detailed written explanation of the termination or suspension within 5 business days
- Subject enrollment must stop until the suspension is lifted
- Subjects already enrolled should continue to be followed in accordance with IRB/EC policy or its determination that an overriding safety concern or ethical issue is involved
- The Investigator will inform his/her institution (where required per local requirements)
- The Investigator will promptly inform the subjects, and/or the personal physician of the subjects, with the rationale for the study termination or suspension

14. Publication and Use of Information

In the event a publication committee is formed during the course of the study, a publication plan will be developed which may include, but is not limited to, description of committee member criteria and management of publications. MDT will be furnished with a copy of any proposed publication for review and comment prior to submission for publication. Manuscripts will be forwarded to MDT at least thirty (30) days prior to submission and abstracts at least seven (7) days prior to submission. At the expiration of the thirty (30) or seven (7) day period, the investigator may proceed with submission for publication. In addition, each investigator must agree that no publications will be submitted that will jeopardize a multi-center publication and all clinical data gathered during the study will be pooled into a common database that is the property of MDT.

The first author will be selected on the basis of the following:

- A significant contribution to the design of the clinical study and/or development of the product
- A significant contribution to subject enrollment in the clinical study
- High procedure volume and quality of data as determined by the clinical study requirements.

15. References

Auricchio et al. 2011 and 2015; Wollmann et al. 2014; Köbe et al. 2013; Ruwald et al. 2014). The PainFree SST trial showed 97.5% of single chamber ICD patients were free of inappropriate shocks at 1 year (Auricchio et al. 2011). The MADIT-RIT trial showed that stepwise ICD programming resulted in a low incidence of ICD therapy (8% appropriate and 5% inappropriate therapy) during 1.4 years follow-up (Ruwald et al. 2014)

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