Medtronic

Clinical Investigation Plan	
Clinical Investigation Plan/Study Title	Lead Evaluation for Defibrillation and Reliability in Left Bundle Branch Area Pacing (LEADR LBBAP)
Short Title	LEADR LBBAP
Clinical Investigation Plan Identifier	MDT22048
Study Product Name	Model 093000 lead, further referenced as the 'Next Generation ICD Lead'
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1. Glossary

Term	Definition
ACI tool	AccuRead analyzer Cable Interface tool
ADE	Adverse Device Effect
AE	Adverse Event
ACE	Angiotensin-Converting Enzyme
AF	Atrial Fibrillation
AP/PA	Anterior-Posterior/Posterior-Anterior
ARBs	Angiotensin Receptor Blockers
ARNIs	Angiotensin Receptor-Neprilysin Inhibitors
ASADE	Anticipated Serious Adverse Device Effect
ATP	Anti-Tachycardia Pacing
BiV	Biventricular
CA	Competent Authority
CCS	Clinical Composite Score
CEC	Clinical Event Committee
CFR	Code of Federal Regulation
CHF	Congestive Heart Failure
CIP	Clinical Investigation Plan
COI	Current of Injury
CRT(-D)	Cardiac Resynchronization Therapy (Defibrillator)
CS	Coronary Sinus
CTA	Clinical Trial Agreement
CV	Curriculum Vitae
DD	Device Deficiency
DMC	Data Monitoring Committee
DoH	Declaration of Helsinki
DSP	Deep Septal Pacing
DXAC	Dexamethasone acetate
eCRF	Electronic Case Report Form
ECG	Electrocardiogram
EC/IRB/HREB	Ethics Committee/Institutional Review Board/Human Research Ethics Board
EDC	Electronic Data Capture
EMEA	Europe, Middle East and Africa
ERC	Episode Review Committee
EU MDR	European Union Medical Device Regulation
EV ICD	Extravascular Implantable Cardioverter Defibrillator
FDA	Food and Drug Administration
FDAAA	Food and Drug Administration Amendments Act

Term	Definition
GCP	Good Clinical Practice
HBP	His Bundle Pacing
HF	Heart Failure
HIPAA	Health Insurance Portability and Accountability Act
IC	Informed Consent
ICF	Informed Consent Form
ICD	Implantable Cardioverter Defibrillator
IFU	Instructions For Use (inclusive of User Manual and Technical Manual)
ISF	Investigator Site File
KCCQ	Kansas City Cardiomyopathy Questionnaire
LAO	Left Anterior Oblique
LBBP	Left Bundle Branch Pacing
LBBAP	Left Bundle Branch Area Pacing
LBFP	Left Bundle Fascicular Pacing
LOT-CRT	Left Bundle Branch-Optimized Cardiac Resynchronization Therapy
LV	Left Ventricular
LVEDD	Left Ventricular End Diastolic Diameter
LVEF	Left Ventricular Ejection Fraction
LVESV(i)	Left Ventricular End-Systolic Volume (Index)
LVSP	Left Ventricular Septal Pacing
MCTA	Master Clinical Trial Agreement
MSA	Master Service Agreement
MCRD	Monolithic Controlled Release Device
MDCG	Medical Device Coordination Group
MedDRA	Medical Dictionary for Regulatory Activities
MR	Magnetic Resonance
MRAs	Mineralocorticoid Receptor Antagonists
MRI	Magnetic Resonance Imaging
NID	Number of Intervals to Detect
NYHA	New York Heart Association
NMPA	National Medical Products Administration
PHD	Pre-Hospital Discharge
PHI	Protected Health Information
PCI	Percutaneous Coronary Intervention
Pt/Ir	Platinum – Iridium
RA	Right Atrium/Right atrial
RAO	Right Anterior Oblique
RV	Right Ventricle/Right Ventricular
RVCM	Right Ventricular Capture Management
RVNA	RV non-apical

Term	Definition
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SCD	Sudden Cardiac Death
SGLT2	Sodium-glucose cotransporter-2
S-ICD	Subcutaneous Implantable Cardioverter Defibrillator
SID	Subject Identification
SSI	Significant Safety Issue
SSVA	Sustained Shockable Ventricular Arrhythmia
TTE	Transthoracic echocardiogram
UADE	Unanticipated Adverse Device Effect
US	United States
USADE	Unanticipated Serious Adverse Device Effect
USM	Urgent Safety Measure
VF	Ventricular Fibrillation
WO	Work Order

2. Synopsis

Title	Lead Evaluation for Defibrillation and Reliability in Left Bundle Branch Area Pacing (LEADR LBBAP) Study
Clinical Study Type	Prospective, pre-market, pivotal, non-randomized, multi-site, interventional, global study
Product Name	Model 093000 Lead, further referenced as the "Next Generation ICD Lead"
Sponsor	Medtronic, Inc. 8200 Coral Sea Street NE Mounds View, MN 55112 United States of America +1 800 328 2518
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European Union Legal Representative of the Sponsor	Medtronic Bakken Research Center B.V. Endepolsdomein 5 6229 GW Maastricht

<table>
<tr><td></td><td>The Netherlands
+31 43 35 66 566</td></tr>
<tr><td>External Organizations</td><td>Echocardiography Core Laboratory, Steering Committee, Episode Review Committee, Data Monitoring Committee, and Clinical Events Committee. Contact information will be provided under separate cover upon request.</td></tr>
<tr><td>Indication under investigation</td><td>The Next Generation ICD Lead is indicated for use in the right ventricle (RV) or for placement in the left bundle branch area as an alternative to right ventricular stimulation for sensing, pacing, cardioversion, and defibrillation when a cardiac implantable electronic device is indicated to treat patients who have experienced, or are at significant risk of developing, life threatening ventricular tachyarrhythmias. This includes adolescent pediatric patients who are at least 30 kg and are also at least 12 years of age, and whose cardiac anatomy is conducive to RV coil placement.</td></tr>
<tr><td>Investigation Purpose</td><td>The purpose of this study is to confirm the safety and defibrillation efficacy of the Next Generation ICD Lead when placed in the Left Bundle Branch Area Pacing (LBBAP) location in an Implantable Cardioverter Defibrillator (ICD) or Left Bundle Branch-Optimized Cardiac Resynchronization Therapy (LOT-CRT) patient population.</td></tr>
<tr><td>Product Status</td><td>
<table>
<tr><th>Model Number</th><th>Component (Manufacturer)</th><th>Investigational or Market Released*</th></tr>
<tr><td>093000</td><td>Next Generation ICD Lead (Medtronic)</td><td>Investigational</td></tr>
<tr><td>C315</td><td>Delivery Catheter (Medtronic)**</td><td>Market-released</td></tr>
<tr><td>C304</td><td>SelectSite™ Deflectable Catheter System (Medtronic)**</td><td>Market-released</td></tr>
<tr><td>C304-HIS</td><td>SelectSite™ Deflectable Catheter System (Medtronic)**</td><td>Market-released except in Japan and Mainland China, where use of this catheter will not be allowed in the study.</td></tr>
<tr><td>6250V / 6250VI</td><td>Attain Command™ + SureValve™ Guide Catheter for Left-Heart Delivery (Medtronic)**</td><td>Market-released</td></tr>
<tr><td>6248V / 6248VI</td><td>Attain Select™ II + SureValve™ Delivery Catheter System</td><td>Market-released</td></tr>
</table>
</td></tr>
</table>

	(Medtronic)**
	* Depending on geography catheters used with the Next Generation ICD Lead may be considered investigational at the time of implant. **Including accessories as listed in the respective instructions for use (IFU). Includes valves that are labeled for use with C304 and Attain catheters (depending on geography may include Pressure Products SafeSheath® Sealing Adapters Hemostatic Valve System). The Medtronic slitters, Model 6232ADJ and Model 6230UNI will be utilized with these catheters. The study will include current and future market approved Medtronic ICD and Cardiac Resynchronization Therapy Defibrillator (CRT-D) devices that are equipped with SmartShock™ Technology. When applicable, any commercially released right atrial (RA) and left ventricular (LV) lead may also be used within their intended use. Medtronic may incorporate additional catheters or accessories as they receive regulatory approval.
Primary Objectives	Primary Efficacy Objective: Demonstrate the percentage of patients successfully defibrillated at implant with the Next Generation ICD Lead when placed in LBBAP location exceeds a pre-specified threshold of 88%. Successful implant defibrillation is defined as: • First induced SSVA episode successfully terminated with an 18J or maximum output minus 10 Joule (M-10J) shock, or • First therapy of the second induced SSVA episode successfully terminated with a M-10J shock, or • First therapy after a system reposition of an induced SSVA episode successfully terminated with a M-10J shock, or • Two consecutively induced SSVA episodes successfully terminated with a M-10J shock. Primary Safety Objective: Estimate the Next Generation ICD Lead-related major complication rate at 3-months post implant when the Next Generation ICD Lead implant is attempted in the LBBAP location.
Ancillary Objectives	• [redacted]

	[redacted]
Study Design	The LEADR LBBAP study is a prospective, pre-market, pivotal, non-randomized, multi-site, interventional, global study designed to allow controlled access of the Next Generation ICD Lead for placement in a LBBAP application. Subjects providing informed consent and undergoing an implant attempt with the Next Generation ICD Lead in the LBBAP location will be followed from the time of consent and will undergo assessments at baseline, implant, pre-hospital discharge (PHD), three months, six months and every six months thereafter until study closure. Enrolled subjects will be followed until at least 3 months (ICD-indicated subjects) or 6 months (CRT-indicated subjects) post-implant.
Sample Size	Approximately 300 subjects, including a minimum of 150 LOT-CRT implant attempts (no minimum requirements for ICD implant attempts), will enroll at up to 40 worldwide sites. Medtronic may decide to stop or pause ICD or LOT-CRT enrollments (in all or in specific regions), for example, to manage total sample size. In addition, Medtronic may decide to keep enrollments open in specific regions/sites beyond 300 enrollments to address local needs. The final study sample size will depend on enrollment rate and timing of enrollment closure. A sample size of at least 160 subjects completing the defibrillation protocol at implant with the Next Generation ICD Lead placed in the LBBAP location will provide at minimum 90.4% power to test the study's primary efficacy objective provided the true defibrillation success rate is at least 95.5%.

Inclusion/Exclusion Criteria	**Inclusion Criteria:** 1. Subject meets current local clinical practice guidelines for implantation of ICD (single or dual chamber) or CRT-D system* and will undergo one of the following: a. *De novo* Medtronic ICD system implant (single or dual chamber) or b. *De novo* Medtronic CRT-D system implant and is intended to also undergo LV lead implant (for patients indicated for CRT-D according to locally approved indications/guidelines*) 2. Subject is 12 years of age or older and also is greater than 30 kg in weight at time of enrollment, has cardiac anatomy conducive to RV coil placement, and is allowed to participate in study per local law and requirements. Subjects from 12 years of age until adult also have a separate indication for pacing or CRT or are anticipated to develop one. 3. Subject provides written authorization and/or consent per institution and geographical requirements. 4. Subject is geographically stable and willing and able to complete the study procedures and visits for the duration of the follow-up. 5. Subject is willing to undergo implant defibrillation testing if requested. *CRT-D Indications in the United States (US) are based on Class I and II indications per current AHA/ACC/HFSA Guideline **Exclusion Criteria:** 1. Subject has contraindication for screw-in active fixation transvenous lead placement (e.g., mechanical right heart valve). 2. Subject is contraindicated for ≤1 mg dexamethasone acetate. 3. Subject has a life expectancy of less than 12 months. 4. For subjects undergoing defibrillation testing the following medical conditions exclude them: a. Pre-existing or suspected pneumothorax b. Current intracardiac left atrial or left LV thrombus c. Severe aortic stenosis d. Severe proximal three-vessel or left main coronary artery disease without revascularization e. Unstable angina f. Recent stroke or transient ischemic attack (within the last 6 months)

	g. Known inadequate external defibrillation h. Any other known medical condition not listed that precludes their participation in the opinion of the investigator 5. Subject is enrolled or planning to enroll in a concurrent clinical study that may confound the results of this study, without documented pre-approval from a Medtronic study manager. 6. Subject with any exclusion criteria as required by local law (e.g., age or other). 7. Subject is pregnant or breastfeeding, or subject is of childbearing potential and not on a reliable form of birth regulation method or abstinence**. 8. Subject with an existing pacemaker (including transvenous and transcatheter pacing system), ICD (transvenous) or CRT-D (transvenous) device or leads. 9. Subject with previous subcutaneous ICD (S-ICD), extravascular ICD (EV ICD) or Implantable Cardiac Monitor explanted within 30 days before implant. 10. Subject with any evidence of active bacterial infection or undergoing treatment for a bacterial infection within the last 30 days. 11. Recent (or planned) cardiovascular intervention within 30 days before or after implant, such as cardiac surgery, cardiac ablation, Percutaneous Coronary Intervention (PCI), or temporary cardiac pacing for >12 hours. 12. Subjects with end stage renal disease. 13. Subjects with New York Heart Association (NYHA) IV classification. 14. Subjects with a transplanted heart or on the waiting list for a heart transplant. 15. Subjects with previously extracted leads. 16. Subjects with Left Ventricular Assist Device. 17. Subjects that are vulnerable adults. **If required by local law, individuals who are of child-bearing potential must undergo a pregnancy test within seven days prior to study procedures
Study Procedures and Assessments	Subjects indicated for implantation of a single or dual chamber ICD, or CRT-D according to current ACC/AHA/HRS or ESC guidelines will be recruited and implanted with the Next Generation ICD Lead. Once enrolled, a study subject will be assessed at the following visits: • Baseline

	• Implant • PHD • 3 Months • 6 Months • Long-term: Every 6 months thereafter until study closure • Unscheduled (as they occur) • System Modification (as they occur) • Exit Study procedures are outlined in the table below.

Study Procedure		Enrollment /Baseline	Implant	PHD	3 months (in office[3,5])	6 months (in office [3,5])	Long term (post 6 months, remote or in office)	Un- Scheduled	System Modification	Study Exit[3]
All subjects	Informed Consent	X								
	Inclusion/Exclusion Assessment	X								
	Physical Exam, Demographics, NYHA, Cardiovascular Medical History, Surgical History	X								
	System and procedure information		X						X	
	Sensing, Impedance & Pacing Tests[9]		X (including Analyzer EGM printout with COI, if available)	X	X	X	X	X[2]	X	
	Save-to-media/Save Session files		X	X	X	X	X	X	X	X
	Medications		X			X				
	12-Lead ECG Recordings		X[6]			X				
	Defibrillation Testing		X[1]							
	KCCQ	X				X[2]				
CRT-indicated	Echocardiography	X				X[2]				
	NYHA					X[2]	12M[2]			
	Subject Global Assessment					X[2]	12M[2]			
All subjects	Fluoroscopy of final lead position (motion picture in LAO, RAO, AP and, if performed, sheath ventriculography)		X[8]						X[4]	
	Chest radiographs (PA & Lateral (end expiration and end inspiration))			X	3M or 6M				X[4, 7]	
	Device Disposition		X						X	
	Adverse Events (including AEs with fatal outcome, and heart failure related hospitalization)	Upon Occurrence								
	Device Deficiencies	Upon Occurrence								
	Study Deviations	Upon Occurrence								

1. Required for a minimum of the first 160 consecutive subjects with implant in LBBAP location. Physician's discretion to perform defibrillation testing if the Next Generation ICD Lead is implanted in the non-LBBAP RV location.
2. Required, however optional if the Next Generation ICD Lead is implanted in the non-LBBAP RV location.
3. All successfully implanted subjects will be followed until at least their 3 month (ICD-indicated subjects) or 6-month (CRT-indicated subjects) follow up visit.
4. Only required in case the Next Generation ICD Lead is replaced by another Next Generation ICD Lead.
5. For subjects who do not receive a successful LBBAP placement and are implanted with the Next Generation ICD Lead in the non-LBBAP RV location remote visit is also allowed
6. Recommended at implant, but is required to be done prior to discharge.
7. Pre-hospital discharge data to be collected in case the Next Generation ICD Lead is replaced by another Next Generation ICD Lead.

8. If a lead reposition, adjustment of lead slack, or device repositioning occurs due to troubleshooting step during defibrillation testing collect motion picture (cine fluoroscopy) in LAO, RAO and AP of the lead and device position over a minimum of one complete cardiac cycle before repositioning.
9. For CRT-indicated subjects with LBBAP implant, if pacing therapy is discontinued permanently this will need to be reported
Note: In-person visits could be replaced by other options as required per local regulations in the case of e.g., a pandemic

Safety Assessments	All adverse events (AEs) will be collected throughout the study duration, starting at the time informed consent is signed. All instances of shocks delivered via the Next Generation ICD Lead will be considered associated with a reportable AE. Shocks delivered appropriately to treat a ventricular arrhythmia should be noted as treatment delivered within the AE for the ventricular arrhythmia(s) experienced. If device therapy (shocks and/or ATP) are delivered inappropriately due to a Next Generation ICD Lead issue, the issue should be reported as the underlying system related AE. The delivery of appropriate ATP therapy alone does not imply an untoward medical occurrence for the subject, but should be evaluated for a reportable AE if determined to be associated with a new or worsened condition (e.g. arrhythmia resulting in symptoms).
Statistics	Descriptive statistics will be used to summarize baseline demographics, study deviations, system modifications, study exits, and AEs. For the primary efficacy objective, the percentage of subjects successfully defibrillated will be computed as the number of subjects meeting the primary efficacy endpoint divided by the number of subjects completing the defibrillation protocol with the Next Generation ICD Lead in an LBBAP position. A two-sided 95% confidence interval for the defibrillation success rate will be constructed using the exact binomial method, and the lower limit will be compared to the performance goal of 88%. For the primary safety objective, the Kaplan-Meier method will be used to determine the Next Generation ICD Lead-related major complication rate and its two-sided 95% confidence interval at 3-months (90 days) post-implant. All subjects attempting an LBBAP implant with the Next Generation ICD Lead will be included in the analysis of the safety objective. [redacted]

3. Introduction

3.1. Background

Cardiovascular diseases are responsible for approximately 17.9 million deaths every year in the world representing 32% of all global deaths.[1] Sudden cardiac death (SCD) from cardiac arrest accounts for roughly 25% of all cardiovascular deaths.[2, 3] The risk of SCD is higher in men than in women and increases with age due to the higher prevalence of coronary artery disease in older age.[4] Accordingly, the SCD rate is estimated to range from 1.40 per 100,000 person-years (95% confidence interval 0.95, 1.98) in women to 6.68 per 100 000 person-years (95% CI 6.24, 7.14) in men.[4] SCD in younger individuals vary across global regions but have an estimated incidence of 0.46–11.9 events per 100,000 person-years.[5, 6]

Implantable cardioverter defibrillator (ICD) systems are indicated for patients who are at elevated risk of SCD, have exhibited life threatening tachyarrhythmia, or have compromised heart function associated with heart failure (HF). Despite enhancements in design and technologies, the ICD lead is typically the most vulnerable component of the ICD system. Lower profile leads with the same or greater reliability can provide alternatives for physicians to serve patients with challenging or small anatomies.

Current Medtronic market released transvenous defibrillator leads (Sprint Quattro™ lead portfolio) have a lead body diameter of 8.6 Fr (2.87 mm). To address needs for long term reliability, reduced defibrillation lead diameter, and ease of extraction, Medtronic has developed a next generation defibrillation lead: The Model 093000 lead (further referenced as the 'Next Generation ICD Lead'). The Next Generation ICD Lead is built off the reliable and experienced platform of the Medtronic SelectSecure™ Model 3830 bradycardia lead which is catheter delivered, as opposed to other pacing and defibrillation leads that are delivered using a stylet. The absence of a stylet lumen allows the center lumen space to be available for a cable from the connector to the tip, enabling a smaller overall diameter and potential for improved flex performance (see Figure 1). The Model 3830 lead received CE mark on January 31st, 2003, and Food and Drug Administration (FDA) approval on August 3rd, 2005 with a lead failure rate of 3.0% at 11.5 years post implant when placed in the right ventricle.[7]

The Next Generation ICD Lead is a 4.7 Fr (1.57 mm), steroid-eluting, catheter delivered, active fixation, polyurethane insulated, integrated bipolar single coil defibrillation lead. The lead is designed for pacing, sensing, cardioversion, and defibrillation therapies. The right ventricular (RV) coil delivers cardioversion and defibrillation therapies. Pacing and sensing occur between the helix and RV coil electrode. [redacted]. All components and/or materials have been used for more than 10 years with acceptable field performance.[8]

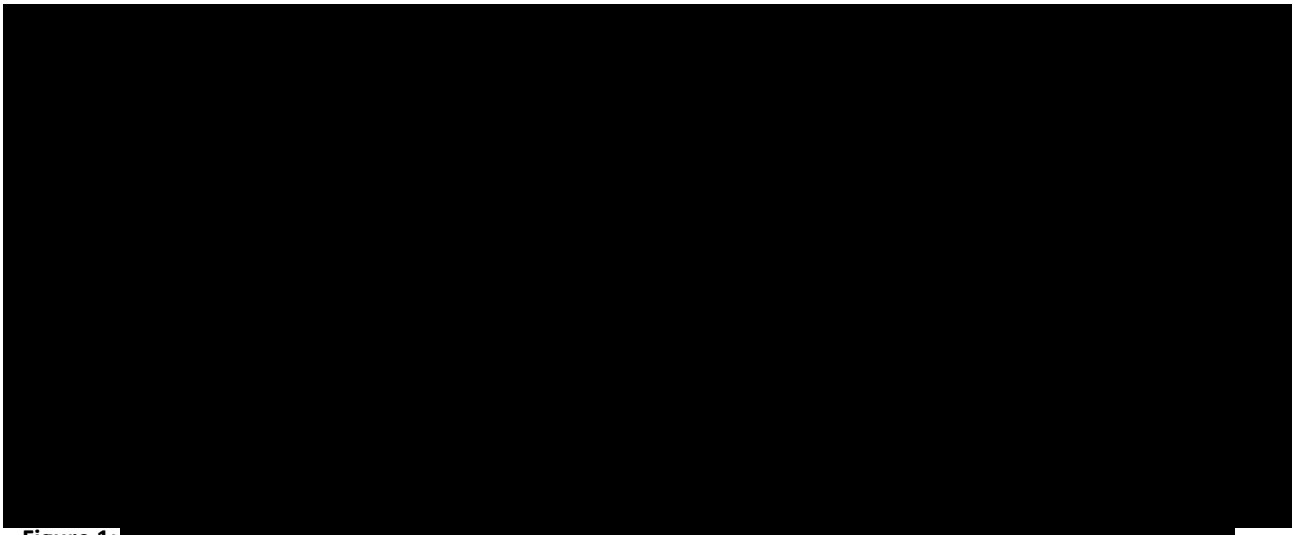


Figure 1:

RV pacing causes a dyssynchronous pattern of activation, contraction, and relaxation within and between the left and right ventricles. Several meta-analyses suggest that hemodynamic impacts of RV pacing may be most pronounced when pacing from the apex.[9-11] A number of large studies reported deleterious clinical effects of chronic RV pacing in the form of increased risk of Atrial Fibrillation (AF), Left Ventricular (LV) dysfunction, and congestive heart failure (CHF).[12-14]

Current pacemaker systems offer various features to reduce ventricular pacing. The SAVE PACe trial confirmed dual-chamber minimized ventricular pacing prevents ventricular desynchronization and moderately reduces risk of persistent AF.[15]

The medical community recognizes the importance of balancing the life-saving benefits of long-term ventricular pacing against the desire to minimize ventricular pacing when recommending the choice of optimal pacing mode (DDD[R] in combination with AV delay management) in patients with sinus node disease, as well as in patients with intermittent AV block as suggested in the ESC guidelines. Pacing from alternative (non-apical) RV (RVNA) sites may be an option to avoid the impacts of RVA pacing. A meta-analysis by Hussain et al.[9] comparing Left Ventricular Ejection Fraction (LVEF) outcomes between RVA and RVNA suggested both RVA and RVNA are acceptable in patients with preserved LV function. However, in patients with mild to moderate LV function impairment (LVEF 30-50%) there is support for RVNA lead placement in combination with regular LVEF monitoring. In patients with LV dysfunction (LVEF of 35-50%), mild to moderate heart failure and standard indications for bradycardia pacing, the use of cardiac resynchronization therapy was shown to reduce the risk of progression of heart failure as measured by a composite endpoint (all-cause mortality, heart failure event requiring intravenous therapy, or increase of >15% in left ventricular end-systolic volume index) when compared to RVA pacing.[16]

Traditionally ventricular pacing has been primarily achieved by placing a lead on the surface of the RV endocardium. HBP was first reported in humans in 2000[17] ,and has steadily gained interest for providing a more physiological alternative to RV pacing.[18] The first case of left bundle branch area pacing (LBBAP) was reported by Huang in 2017.[19] This first case was an attempted His bundle pacing case where the His threshold was high, so more distal positions were attempted. The result was a position with a low pacing threshold, large sensing amplitude, and an electrocardiogram (ECG) ventricular activation signature similar to His bundle pacing. Since that first case, LBBAP has been discussed in numerous publications and meta-analyses have demonstrated advantages of low thresholds, high sensing amplitudes, and high implant success rate.[20-22]

In some patients, it is recommended that LBBAP may be considered as an alternative to CRT with BiV pacing.[23] LBBAP use is increasing in patients with HF or Cardiac Resynchronization Therapy (CRT)-indications as reflected in the growing number of peer-reviewed publications.[18] In these patients, reported benefits of LBBAP relative to RV pacing include less dyssynchrony, shorter paced QRS duration, higher LVEF/maintenance of LVEF over time, lower Left Ventricular End Diastolic Diameter (LVEDD) over time, and fewer HF hospitalizations and/or the composite of HF hospitalization and either upgrade to Biventricular (BiV) pacing or mortality.[24-28] Within the CRT-indicated populations, physicians are using Left Bundle Branch-Optimized Cardiac Synchronization Therapy (LOT-CRT) to provide resynchronization therapy by simply moving the traditionally located RV lead to the LBBAP location. LOT-CRT may provide greater electrical resynchronization as compared with BiV-CRT or LBBAP alone.[29]

Without a viable defibrillation lead for use in the LBBAP location, physicians are implanting complex system configurations or choosing to sacrifice the LV lead in favor of LBBAP alone. The Next Generation ICD Lead provides an opportunity to simplify the system configuration, combining the RV, LBBAP and defibrillation leads into a single Next Generation ICD Lead in the LBBAP location. Fewer implanted leads can reduce risk to the patient for lead-to-lead interaction, and long-term complications (e.g., venous occlusion, lead failure, infection, valve insufficiency, extraction risk) and non-Magnetic Resonance Imaging (MRI) conditionality. Figure 2 depicts what LOT-CRT will look like with the Next Generation ICD Lead.

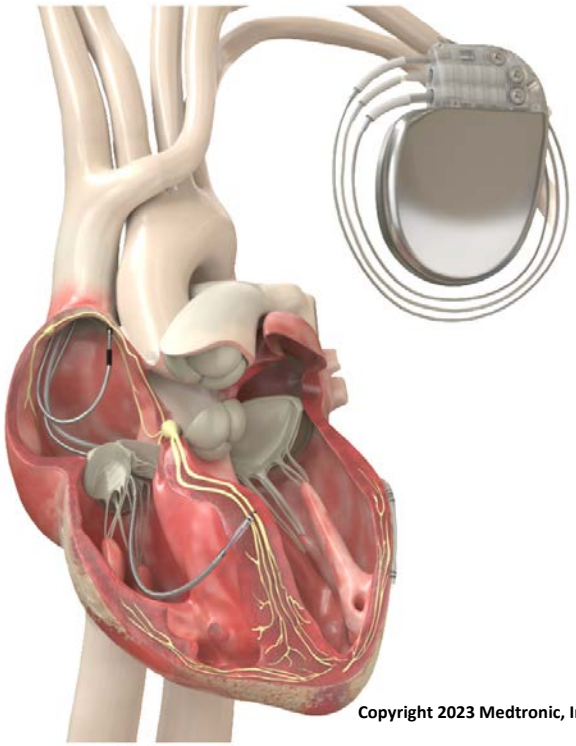


Figure 2: LOT-CRT lead configuration. Note: The LV lead is illustrated in a light, transparent horizontal line traversing the LV, ending in the coronary vasculature.

The Next Generation ICD Lead is an optimal solution for LBBAP placement due to the unique design characteristics, which enable a highly flexible and reliable lead that is anticipated to withstand the use conditions of an LBBAP implant location. The reduced lead diameter enables the lead to be positioned in the septal wall of the right ventricle via catheter delivery, enabling an easier implant on the septum. Note, when LBBAP is referred to in this study, LBBAP includes Left Bundle Branch Pacing (LBBP), Left Bundle Fascicular Pacing (LBFP), Left Ventricular Septal Pacing (LVSP), and Deep Septal Pacing (DSP).

3.2. Purpose

Medtronic, Inc. is sponsoring the Lead Evaluation for Defibrillation and Reliability in Left Bundle Branch Area Pacing (LEADR LBBAP) Study, a prospective, pre-market, pivotal, non-randomized, multi-site, interventional, global study. The purpose of this study is to confirm the safety and defibrillation efficacy of the Next Generation ICD Lead when placed in the LBBAP location in ICD and LOT-CRT patient population.

4. Objectives and/or Endpoints

4.1. Primary Objectives

4.1.1. Primary Efficacy Objective

Demonstrate the percentage of patients successfully defibrillated at implant with the Next Generation ICD Lead when placed in the LBBAP location exceeds a pre-specified threshold of 88%.

Endpoint Definition

Successful implant defibrillation is defined as:

- First induced SSVA episode successfully terminated with an 18J or maximum output minus 10 Joule (M-10J) shock, or
- First therapy of the second induced SSVA episode successfully terminated with a M-10J shock, or
- First therapy after a system reposition of an induced SSVA episode successfully terminated with a M-10J shock, or
- Two consecutively induced SSVA episodes successfully terminated with a M-10J shock.

Rationale

While defibrillation testing may not be common practice in all geographies, termination of induced ventricular arrhythmias provides a measure of anticipated device performance in an ambulatory setting, and in this trial at least the first 160 consecutive subjects will undergo defibrillation testing to demonstrate the performance of the lead in terminating ventricular arrhythmias exceeds a pre-specified threshold. The endpoint definition allows for termination of one episode at 18J or M-10J to be tested first to reduce the number of ventricular arrhythmias and device shocks which the subject may experience during testing. Following the same rationale this definition allows termination of the first episode after a system reposition at M-10J.

4.1.2. Primary Safety Objective

Estimate the Next Generation ICD Lead-related major complication rate at 3-months post implant when the Next Generation ICD Lead implant is attempted in the LBBAP location.

Endpoint definition

For an adverse event (AE) to meet the endpoint, defined as a subject's first occurrence of a major complication related to the Next Generation ICD Lead, as determined by an independent Clinical Events Committee (CEC), the event must have occurred within 90 days (inclusive) of the Next Generation ICD Lead implant attempt and be adjudicated by the CEC as being a major complication related (causal relationship) to the Next Generation ICD Lead. Major complications are those complications resulting in:

- Death
- Hospitalization (in-patient)
- Lead Fracture
- Prolongation of an existing hospitalization by at least 48 hours

- System Revision (reposition, replacement, explant)

Rationale

This composite endpoint was chosen to encompass AEs related to the Next Generation ICD lead which requires invasive intervention (leading to the AEs being classified as a complication, see section 11.4) as well as serious outcome (in-patient hospitalization, prolongation of an existing hospitalization by at least 48 hours, system revision, death). The majority of Next Generation ICD Lead related complications occur within 3-months of implant attempt. Additionally, electrical performance of cardiac implantable electrical devices is stable within 3-months post-implant.

[redacted]

5. Study Design

The LEADR LBBAP study is a prospective, pre-market, pivotal, non-randomized, multi-site, interventional, global study designed to allow controlled access of the Next Generation ICD Lead for placement in a LBBAP application. The study is expected to be conducted at up to 40 study sites. Participating geographies may include but are not limited to: Australia, Mainland China, Japan, Hong Kong, Malaysia, Europe, Middle East, and Africa (EMEA), Canada, and the United States.

Approximately 300 subjects, including a minimum of 150 LOT-CRT implant attempts (no minimum requirement for ICD implant attempts), will be enrolled. Assuming one lead is used per subject, as well as a 6% increase to account for system revisions, sterility compromised products, etc., it is expected that approximately 320 Next Generation ICD Leads will be used in the study. Medtronic may decide to stop

or pause ICD or LOT-CRT enrollments (in all or in specific regions), for example to manage total (or per cohort) sample size. In addition, Medtronic may decide to keep enrollments open in specific regions/sites beyond 300 enrollments to address local needs. The final study sample size will depend on enrollment rate and/or timing of official enrollment closure (see section 15.10.1). A sample size of at least 160 subjects completing the defibrillation protocol at implant with the Next Generation ICD Lead placed in the LBBAP location will provide at minimum 90.4% power to test the study's primary efficacy objective provided the true defibrillation success rate is at least 95.5%.

Subjects will be considered enrolled into the study upon signing the Informed Consent Form (ICF) and will be followed prospectively from consent to implant, 3-months post-implant, 6-months post-implant, and at subsequent 6-month intervals until study closure. Enrolled subjects from all geographies will be followed until at least 3-months post-implant (ICD-indicated subjects) or 6-months post-implant (CRT-indicated subjects).

There is no minimum number of subjects to be enrolled per study site. Enrollment parameters are included in the study to avoid introduction of bias to the study results due to disproportionate enrollment. Enrollment should not exceed 10% (i.e., 30 subjects if 300 subjects are enrolled) of the final sample size at any individual site. Enrollment will be competitive across study sites. The per-study site enrollment cap may be increased upon Sponsor approval.

5.1. Duration

The first enrollment is projected to occur in 2024. Successfully implanted study subjects will be followed until study closure, with an Exit electronic Case Report Form (eCRF) entered for each subject. Official study closure is defined as when all enrolled subjects have been followed until at least 3 months (ICD-indicated subjects) or 6 months post-implant (CRT-indicated subjects) or have been exited, and applicable regulatory authority agency or governing body requirements have been satisfied per the Clinical Investigation Plan (CIP) and/or by a decision by Medtronic or regulatory authority to stop or close the study. The duration of individual subject participation will vary based on timing of study site activation and their enrollment. The approximate duration for each subject participant will be 1.5 to 3 years. The expected study duration is approximately 3 years from first site activation until the study closure criteria are met. Official study closure is anticipated in 2027.

5.2. Rationale

The main purpose of the LEADR LBBAP study is to demonstrate safety and efficacy of the Next Generation ICD Lead when placed in the LBBAP location in ICD and LOT-CRT patient populations.

The performance goal for the primary efficacy objective (defibrillation testing) is chosen based on the known performance of market-approved Medtronic leads or historical study data and the objective is designed to show that the Next Generation ICD Lead will perform comparably with regard to efficacy to existing leads on the market. To characterize safety, the primary safety objective will estimate the lead-related major complication rate at 3-months post implant.

Implantable defibrillators have been available for more than 40 years with numerous reports on the performance of many defibrillation leads from which to construct performance benchmarks. The primary LEADR LBBAP study outcomes are defibrillation efficacy and safety. A single arm study is appropriate given the objective physiologic outcome measures based upon known well-performing lead performance.

Prior to the LEADR LBBAP study, bench test studies of Next Generation ICD Lead prototypes were performed to evaluate mechanical performance and reliability (further pre-clinical data are described in detail within the Investigator's Brochure). Fatigue testing and modeling has predicted robust performance of Next Generation ICD lead implanted in the LBB area, representative of 10 year long-term in-vivo performance in line with defined confidence and reliability requirements. Expected fatigue use conditions have been assessed through multiple imaging studies including subjects implanted with the Next Generation ICD lead (LEADR) as well as subjects implanted with Model 3830 leads in the LBB area (IMAGE-LBBP). Perforation and dislodgement performance is expected to be comparable to Model 3830 leads based on having the same active fix helix design and similar distal lead characteristics. In addition, components and/or materials used in the Next Generation ICD Lead have been utilized in predicate lead models with proven reliability.

Electrical performance of the Next Generation ICD Lead when implanted in the LBBAP location is expected to be similar to both:

- Next Generation ICD Lead electrical performance when implanted in the RV
- Model 3830 lead electrical performance when implanted in the LBBAP

This is based on canine study evidence from Next Generation ICD Lead implanted in the LBBAP location versus the Next Generation ICD Lead implanted in the RV, as well as evaluating real-world evidence on 3830 and comparing to electrical performance data In Vivo on the Next Generation ICD Lead. Therefore, the LEADR LBBAP study is intended to be confirmatory and human use is warranted.

5.3. Study Oversight

The study will utilize a Steering Committee. The Steering Committee advises on the scientific content of the study and provides input for the execution. Members may be study site investigators. The purpose of the Steering Committee is to provide unbiased opinions and expertise. The Steering Committee will support the execution of the LEADR LBBAP study and provide guidance, feedback and direction to the study. The Steering Committee members and contact details will be provided under separate cover.

6. Product Description

6.1. General

The study will include current and future market approved Medtronic ICD and CRT-D devices that are equipped with SmartShock™ Technology. A list of currently compatible ICD and CRT-D devices is

included in Appendix A: List of Compatible ICD and CRT-D Devices. When applicable, any commercially released right atrial (RA) and LV lead may also be used within their intended use.
Materials used for the Next Generation ICD Lead have been used in previous market released leads. Catheters used in the LEADR LBBAP study are commercially available except for model C304-HIS in Mainland China and Japan. Use of the C304-HIS catheter in Mainland China and Japan will not be allowed in the study. Table 1 lists the lead and catheters that will be utilized in the study. Medtronic may incorporate additional catheters or accessories as they receive regulatory approval and become market released. An additional list of other accessories will be provided under separate cover, when requested. Instructions for use (IFU) of the devices in this study are provided in their respective manuals.

Table 1: Product Information

Model Number	Component (Manufacturer)	Investigational or Market-released*
093000	Next Generation ICD Lead (Medtronic)	Investigational in all participating countries
C315	Delivery Catheter (Medtronic)**	Market-released in all participating countries
C304	SelectSite™ Deflectable Catheter System (Medtronic)**	Market-released in all participating countries
C304-HIS	SelectSite™ Deflectable Catheter System (Medtronic)**	Market-released in all participating countries except in Japan and Mainland China, where use of this catheter will not be allowed in the study
6250V / 6250VI	Attain Command™ + SureValve™ Guide Catheter for Left-Heart Delivery (Medtronic)**	Market-released in all participating countries
6248V / 6248VI	Attain Select™ II + SureValve™ Delivery Catheter System (Medtronic)**	Market-released in all participating countries

* Depending on geography catheters used with the Next Generation ICD Lead may be considered investigational at time of implant.

**Including accessories as listed in the respective IFU. Includes valves that are labeled for use with the C304 and Attain catheters (depending on geography and may include Pressure Products SafeSheath® Sealing Adapters Hemostatic Valve System). The Medtronic slitters, Model 6232ADJ and Model 6230UNI will be utilized with these catheters.

In Japan, products listed in Table 1 that are already market-released are considered “The Devices used for clinical study”. “The Devices used for clinical study” refers to all medical devices used to evaluate the efficacy and safety of investigational devices in the clinical study. Among these devices, those used for the clinical study shall refer to only a limited range of products as per the scope definition, and/or limited to a specific model or type, etc. Devices for which a product name, etc. has not been defined in the CIP are not included as “The Devices Used for Clinical Study” even if used in physical combination with the investigational device.

All materials from the investigational Next Generation ICD Lead as well as the market-released catheters, which may become investigational upon use with the Next Generation ICD Lead, that may directly contact tissues and/or body fluids are presented in Table 2. This table includes the accessories that are packaged with the lead and catheters that are in direct contact with tissues and/or body fluids. There are no human and/or animal tissues or their derivatives, or other biologically active substances present in the Next Generation ICD lead or catheters mentioned in Table 2 that will be used during the study. Medtronic may incorporate additional catheters or accessories as they receive regulatory approval.

Table 2: Materials in contact with tissues and/or body fluids

Component	Materials
Next Generation ICD Lead	[redacted]
C315 Delivery Catheter (Medtronic)	[redacted]
C304 SelectSite™ Deflectable Catheter System (Medtronic)	[redacted]
C304-HIS SelectSite™ Deflectable Catheter System (Medtronic)	[redacted]

Component	Materials
	[redacted]
6250V / 6250VI Attain Command™ + SureValve™ Guide Catheter for Left Heart Delivery (Medtronic)	[redacted]
6248V / 6248VI Attain Select™ II + SureValve™ Delivery Catheter System (Medtronic)	[redacted]

6.1.1. Next Generation ICD Lead

The investigational Model 093000 Lead (Next Generation ICD Lead) (Figure 3) is intended for use in the right ventricle or for placement in the left bundle branch area as an alternative to right ventricular stimulation for sensing, pacing, cardioversion, and defibrillation when a cardiac implantable electronic device is indicated to treat patients who have experienced or are at significant risk of developing life-threatening ventricular tachyarrhythmias. This includes adolescent pediatric patients who are at least 30 kg and are also at least 12 years of age and whose cardiac anatomy is conducive to RV coil placement.

The Next Generation ICD Lead [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

Table 3: [redacted]

Component or Attribute	SelectSecure 3830 lead	Next Generation ICD Lead	Rationale for difference
Implant Method	[redacted]	[redacted]	[redacted]
Lead Connector	[redacted]	[redacted]	[redacted]

1 https://wwwp.medtronic.com/productperformance/

Component or Attribute	SelectSecure 3830 lead	Next Generation ICD Lead	Rationale for difference
Inner insulation	[redacted]	[redacted]	[redacted]
Tip Conductor	[redacted]	[redacted]	[redacted]
Outer Conductor coil	[redacted]	[redacted]	[redacted]
Conductor Coil Insulation	[redacted]	[redacted]	[redacted]
Outer Insulation	[redacted]	[redacted]	[redacted]
Defibrillation coil	[redacted]	[redacted]	[redacted]
Distal sleeve	[redacted]	[redacted]	[redacted]
Steroid	[redacted]	[redacted]	[redacted]
Helix fixation	[redacted]	[redacted]	[redacted]

6.1.2. Medtronic Catheters

Any of the market released Medtronic catheters within the families shown in Table 4 may be utilized in the LEADR LBBAP study: C304, C304-HIS, C315, 6250V / 6250VI and 6248V / 6248VI. These catheters are market released and commercially available with the exception of Medtronic C304-HIS which is not commercially available in Mainland China and Japan. In Mainland China and Japan, use of the C304-HIS catheter will not be allowed in the study. Medtronic may incorporate additional catheters or accessories as they receive regulatory approval and become market released. Indications (6250V / 6250VI & 6248V / 6248VI) or compatible lead diameter (C304, C304-HIS, & C315) in current versions of the catheter Manuals/ IFU might not allow using the Next Generation ICD Lead with these catheters (see Table 4).

Hence, these catheters may be considered investigational when used with the Next Generation ICD Lead in the clinical investigation at the time of implant. Once catheters are regulatory approved for use with the Next Generation ICD Lead, depending on geography, catheters may no longer be considered investigational. The Medtronic slitters, Model 6232ADJ and Model 6230UNI will be utilized with these catheters to assist in removal of catheters during the implant.

Table 4: Catheter families

	Catheter Family				
	C315	**C304**	**C304-HIS**	**6250V / 6250VI**	**6248V / 6248VI**
Maximum Compatible lead diameter	1.4 mm (4.2 Fr, 0.055 in)	1.5 mm (4.6 Fr)	1.5 mm (4.6 Fr)	2.1 mm (6.2 Fr, 0.081 in)	1.77 mm (5.3 Fr, 0.070 in)
Indications	RV indications	RV + LV (via Coronary Sinus (CS)) indications	RV + LV (via CS) indications	RV* + LV (via CS) indications	RV* + LV (via CS) indications

*In certain geographies, these catheters may become indicated for use in the RV + LV upon receiving regulatory approval for use in the right chambers of the heart during the course of the study, but may be considered investigational.

6.2. Manufacturer

The investigational Next Generation ICD Lead is manufactured by Medtronic. The manufacturing and validation of the lead complies with applicable national regulations.

Manufacturer Name	Manufacturer Address
Medtronic, Inc.	Medtronic, Inc. 710 Medtronic Parkway Minneapolis, MN 55432 USA www.medtronic.com +1 763 514 4000

6.3. Packaging

Packaging and labeling for all market approved system components can be found with each package insert. Manuals can be found on http://manuals.medtronic.com. For CE Marked devices and marketed devices in other regions where the study is executed, the labeling is in the appropriate local language. A

list of compatible ICD and CRT-D devices is included in Appendix A: List of Compatible ICD and CRT-D Devices.

For investigational products, the language of labeling and clinical manuals will be in English and/or local language where it is required. Investigational leads will be clearly labeled indicating they are exclusively for clinical investigation and with the study identifier "Protocol# MDT22048" per local requirements (e.g., in accordance with US law, FDA federal investigational statement is required on US clinical product). Catheters will be labelled per regional requirements. Updated catheter manuals may be appended or attached to the CIP or provided under separate cover if required by local requirements.

In some geographies, the IFUs may be delivered via an alternate format (e.g., CD-ROM format, USB, or electronic format) if allowed within local requirements.

The labeling for all components may include but is not limited to the following:

- Device Name
- Model number
- Serial or Lot number, as applicable
- Date of manufacture
- Expiration date

6.4. Intended Population

The Next Generation ICD Lead is intended for use in the right ventricle or for placement in the left bundle branch area as an alternative to right ventricular stimulation for sensing, pacing, cardioversion, and defibrillation when a cardiac implantable electronic device is indicated to treat patients who have experienced or are at significant risk of developing life-threatening ventricular tachyarrhythmias. The intended population to receive the Next Generation ICD Lead includes subjects who are indicated for implantation of a single or dual chamber ICD or CRT-D according to current ACC/AHA/HRS or ESC guidelines.[2-5] The intended population also includes adolescent pediatric patients who are at least 30 kg and are also at least 12 years of age, and whose cardiac anatomy is conducive to RV coil placement.

6.5. Equipment

All commercially available equipment will be used according to their approved intended use.

6.5.1. Medtronic CareLink (2090) Programmer, Medtronic CareLink Encore 29901 Programmer and Medtronic CareLink Smart Sync™ 24970A device manager

The programmers will be used to provide user interface with which the user can interrogate and program Medtronic approved ICD or CRT-D devices. There are no updates required to programmer software with the investigational Next Generation ICD Lead as manual entry for the model can occur. If

remote monitoring is needed the Medtronic CareLink system should be utilized. Medtronic may incorporate additional programmers as they receive regulatory approval.

6.5.2. Pacing System Analyzer

Medtronic's commercially available Model 2290 or SmartSync 24970A analyzers must be available at each site during the implant procedure to determine acceptable electrical parameters. Medtronic may incorporate additional analyzers as they receive regulatory approval.

6.5.3. Site Equipment

Sites are responsible for maintaining and calibrating site equipment used in the course of this study (e.g., radiograph machine, ECG machine, fluoroscope, etc.) as applicable in accordance with established site practice and local regulation. Medtronic may provide a 12-lead ECG machine if an investigational site's ECG equipment does not have the capability to meet the requirements for ECG collection specified in sections 9.9.3.3 and 9.11.2. Records shall be maintained per site and local requirements and provided during monitoring visits and upon request by the Sponsor or regulatory agency.

6.6. Product Use

Instructions for use of the Next Generation ICD Lead are located in the 093000 Technical Manual and the LEADR LBBAP Study User Manual. Instructions for use for the catheters are located in the IFU for each component (see Appendix B: User Manual and Instructions for Use). Additionally, trained and experienced Medtronic personnel may provide support at implant on-site or remote.

6.7. Product Training Requirements

Prior to investigation site activation or subsequent involvement in study activities, Medtronic will provide study training relevant and pertinent to the involvement of personnel conducting study activity, investigator responsibilities, as well as device training (usage and handling of device under investigation). Study-specific training will be conducted and documented prior to site activation or study related activities.

The Next Generation ICD Lead implant procedure is to be performed by an investigator who has received training on the implant procedure which may include hands on training and/or didactic training as determined by previous LBBAP implant experience. The didactic training will include but is not limited to specifics on lead design, implant procedure steps, system programming and defibrillation protocol. All implant training will be documented in the Investigator Site File (ISF).

6.8. Product Receipt and Tracking

The study site is responsible for maintaining tracking of the investigational devices used during the study. Tracking will be maintained electronically on a Device Accountability eCRF at each study site and

updated when the investigational product is received, opened, implanted, explanted, disposed of, and/or returned to Medtronic. In addition to tracking the date of events, the accountability log tracks product information including, but not limited to, date, model/serial number and expiration date for the received product, subject identification (SID) of the implanted subject, reason(s) for and method of destruction/disposal for explanted components not returned to Medtronic (if applicable) and name of the person responsible for return or destruction/disposal (if applicable). Medtronic will perform periodic reconciliation of the investigational product to ensure traceability.

6.9. Product Storage

All investigational products, once received at the study site, must be stored in a secure location at the study site. It is the responsibility of the investigator to correctly handle, store and track the investigational products maintained at the study site. Investigational products will be used only in the clinical study according to the CIP.

It is the responsibility of the investigator to correctly handle and store market released product.

6.10. Product Return

All explanted devices (e.g., devices or leads) should be returned to Medtronic for analysis when permissible by local laws and regulations. If the products are explanted but not returned, justification will be reported on the appropriate eCRF. To receive a Return Mailer Kit or arrange a return, contact local Medtronic field personnel. All unused investigational products must be returned to Medtronic or confirmed to be destroyed at site upon study closure at the site.

6.11. Product Accountability

The Next Generation ICD Lead is considered investigational in all regions, and catheters may be considered investigational as was mentioned previously (see section 6.1). An investigational product will be distributed to a study site only when Medtronic has received all required documentation and has notified the study site of study site activation. Distribution of an investigational product to study sites during the study will be managed by Medtronic and can only be ordered by Medtronic personnel.

Commercially available product supply will be managed in a manner consistent with other market-released products.

Product accountability will be documented on the Device Accountability eCRF which will be maintained in the Electronic Data Capture (EDC) system.

This eCRF will collect, at a minimum, the following information, as applicable:

- Date of receipt
- Identification of the investigational components (lot or serial number or unique code)
- Expiration date
- Date used

- Subject Identification (SID) number
- Date and reason for return or disposal
- Name of person responsible for receipt, return and/or destruction/disposal
- Explant date of the investigational components

7. Study Site Requirements

7.1. Investigator / Investigation Site Selection

All investigators must be qualified practitioners and experienced in the diagnosis and treatment of subjects indicated to receive an ICD or CRT-D per local guidelines. Furthermore, all implanting physicians must be trained in the handling and implantation of the Next Generation ICD Lead.
The role of the principal investigator is to implement and manage the day-to-day conduct of the clinical investigation as well as ensure data integrity and the rights, safety and well-being of the subjects involved in the clinical investigation.
The principal investigator shall:

- Be qualified by education, training and experience to assume responsibility for the proper conduct of the clinical investigation
- Be experienced in the field of application and training in the use of the product and associated procedures
- Disclose potential conflicts of interest, including financial, that interfere with the conduct of the clinical investigation or interpretation of results
- Be able to demonstrate that the proposed investigational study site:
    - Has access to an adequate number of eligible subjects needed within the recruitment period
    - Has one or more qualified investigators, a qualified investigational study site team and adequate facilities for the foreseen duration of the clinical investigation

Study site personnel training will be completed and documented prior to their participation in this study.
The following additional criteria were considered when selecting sites for the LEADR LBBAP study:

- Investigator/site expects to have adequate time and resources to conduct the study throughout the duration of the study
- Ability to comply with Ethics Committee (Institutional Review Board (IRB) or Human Research Ethics Board (HREB), as applicable) and regulatory requirements
- Investigator is not debarred, disqualified or working under sanctions in applicable regions
- Site has demonstrated experience working with Medtronic clinical research in the last 3 years
- Site can support timely data entry (e.g., coordinator)
- Investigator is experienced with left bundle branch area lead implantation and LBBAP treatment

Medtronic contracts with participating institutions/investigators through a Clinical Trial Agreement (CTA), Master Service Agreement (MSA), or a Master Clinical Trial Agreement (MCTA) with associated Work Oder (WO) that defines the scope and responsibilities and associated compensation related to carrying out the obligations under a clinical study sponsored by Medtronic.

7.2. Study Site Activation

During the activation process (prior to subject enrollment), Medtronic will train applicable study site personnel on the current version of the CIP, on relevant standards and regulations, Informed Consent and on data collection and reporting tools. If new members join the study site team, they will receive training on the applicable clinical investigation requirements relevant to their role before contributing to the study.

Prior to performing study-related procedures all regulatory requirements shall be fulfilled, including, but not limited to the following:

- Regulatory authority approval or notification (as required per local law)
- Ethics Committee approval (and voting list, as required by local law) of the current version of the CIP and ICF
- Fully executed CTA, MSA, or MCTA with associated WO
- Current Curriculum Vitae (CV) of investigators and key members of the investigation study site team (as required)
- Financial disclosure for investigators
- Documentation of delegated tasks
- Documentation of study training
- Additional requirements imposed by local regulations, the EC and Regulatory Authority shall be followed, if appropriate

In addition, all participating study site staff must be trained on the current version of the CIP as well as on the applicable study requirements depending on their role and must be delegated by the principal investigator to perform study related activities.

Medtronic will provide each study site with written documentation of study site/investigator readiness. This letter must be received prior to performing study-related activities.

For China, the medical institution shall be filed at the National Medical Products Administration (NMPA) Filing System.

7.3. Role of the Sponsor Representatives

In addition to performing monitoring and auditing activities, sponsor representatives may provide support at the study site, as required for the study, under supervision of the Principal Investigator, including:

- Providing study training relevant and pertinent to the involvement of personnel conducting study activities and investigator responsibilities.

- If needed, providing technical support at study visits (on site or remote) under the supervision of a study investigator, including device programming, but no data entry on eCRFs shall be performed by Medtronic personnel or their representatives at sites.

In addition, for this study, sponsor representatives may be authorized by the Principal Investigator to perform the following significant trial related duties:

- Support a study investigator at the Implant Visit (on site or remote) by proactively providing support and feedback during the implant procedure and may include support in data collection during the implant procedure and device testing.
- Support data collection (on site or remote) during the follow-up visits.

Any data collection completed by Medtronic personnel will be clearly identified as such.

8. Selection of Subjects

8.1. Study Population

A diverse population of subjects that give Informed Consent per local and national law who have an indication for implantation of a single or dual chamber ICD or CRT-D according to current ACC/AHA/HRS or ESC guidelines[2-5] and who meet all inclusion criteria and no exclusion criteria are eligible for enrollment in the study.

8.2. Subject Enrollment

Subjects will be screened to ensure they meet all inclusion and none of the exclusion criteria prior to study enrollment in order to be eligible for this study. When a subject and the principal investigator or authorized designee, as required, have personally signed and dated the ICF, the subject is considered a subject enrolled in the study. The date the subject signed the ICF, and data protection authorization if applicable, must be documented in the subject's medical records.

8.3. Inclusion Criteria

Table 5: Subject Inclusion Criteria

	Inclusion Criteria	Rationale
1.	Subject meets current local clinical practice guidelines for implantation of ICD (single or dual chamber) or CRT-D system* and will undergo one of the following: a) *De novo* Medtronic ICD system implant (single or dual chamber) or b) *De novo* Medtronic CRT-D system implant and is intended to also	Study will be evaluated in the standard subject population that is indicated for the device under evaluation

	undergo LV lead implant (for patients indicated for CRT-D according to locally approved indications/guidelines*)	
2.	Subject is 12 years of age or older and also is greater than 30 kg in weight at time of enrollment, has cardiac anatomy conducive to RV coil placement, and is allowed to participate in study per local law and requirements. Subjects from 12 years of age until adult also have a separate indication for pacing or CRT or are anticipated to develop one.	Study will be evaluated in adolescent pediatric and adolescent population
3.	Subject provides written authorization and/or consent per institution and geographical requirements.	Ensure appropriate Informed Consent is provided
4.	Subject is geographically stable and willing and able to complete the study procedures and visits for the duration of the follow-up	Ensure ascertainment of data required for clinical evaluation
5.	Subject is willing to undergo implant defibrillation testing if requested	Ensure ascertainment of data required for study objectives

*CRT-D indications in the U.S. are based on Class I and II indications per current AHA/ACC/HFSA Guideline

8.4. Exclusion Criteria

Table 6: Subject Exclusion Criteria

	Exclusion Criteria	Rationale
1.	Subject has contraindication for screw-in active fixation transvenous lead placement (e.g., mechanical right heart valve)	Standard exclusion criterion to minimize lead displacement and untoward complications associated with mechanical right heart valve
2.	Subject is contraindicated for ≤1 mg dexamethasone acetate	Ensure subjects contraindicated for ≤1 mg dexamethasone acetate (e.g., due to allergy) are not included in the study as the Next Generation ICD lead tip elutes dexamethasone acetate
3.	Subject has a life expectancy of less than 12 months	Standard exclusion criterion to ensure study cohort is expected to survive to the time of primary endpoint evaluation.
4.	For subject undergoing defibrillation testing the following medical conditions exclude them: o Pre-existing or suspected pneumothorax	Exclude subjects who may be more vulnerable to potential increased risk during

	Exclusion Criteria	Rationale
	o Current intracardiac left atrial or LV thrombus o Severe aortic stenosis o Severe proximal three-vessel or left main coronary artery disease without revascularization o Unstable angina o Recent stroke or transient ischemic attack (within the last 6 months) o Known inadequate external defibrillation o Any other known medical condition not listed that precludes their participation in the opinion of the investigator	the evaluation of the clinical study defibrillation protocol
5.	Subject is enrolled or planning to enroll in a concurrent clinical study that may confound the results of this study, without documented pre-approval from a Medtronic study manager	Standard exclusion criterion to avoid confounding procedural requirements due to multiple experimental studies
6.	Subject with any exclusion criteria as required by local law (e.g., age or other)	Standard exclusion criterion to comply with any additional local requirements which may apply
7.	Subject is pregnant or breastfeeding, or subject is of childbearing potential and not on a reliable form of birth regulation method or abstinence**	Pregnant subjects are excluded to avoid harm to the fetus caused by fluoroscopy/x-ray requirements Breastfeeding subjects are excluded to avoid potential harm to infant during breastfeeding caused by device shocks
8.	Subject with an existing pacemaker (including transvenous and transcatheter pacing system), ICD (transvenous) or CRT-D (transvenous) device or leads	Avoid possible confounding factors (e.g., complications due to changeout procedure)
9.	Subject with previous subcutaneous ICD (S-ICD), extravascular ICD (EV ICD) or Implantable Cardiac Monitor explanted within 30 days before implant	Avoid increased risk of infection
10.	Subject with any evidence of active bacterial infection or undergoing treatment for a bacterial infection within the last 30 days	Standard exclusion criterion for device implant, to reduce the risk of possible explant, system modification and ongoing complications related to infection which

	Exclusion Criteria	Rationale
		could impact attrition and confound study results
11.	Recent (or planned) cardiovascular intervention within 30 days before or after implant, such as cardiac surgery, cardiac ablation, Percutaneous Coronary Intervention (PCI), or temporary cardiac pacing for >12 hours	Avoid increased risk of procedural complications, lead damage and infection
12.	Subjects with end stage renal disease	Avoid impact on subject life expectancy
13.	Subjects with NYHA IV classification	Contraindication for a primary prevention ICD. Avoid impact on subject life expectancy
14.	Subjects with a transplanted heart or on the waiting list for a heart transplant	Avoid increased complication risk
15.	Subjects with previously extracted leads	Avoid associated events which could confound complication rates
16.	Subjects with Left Ventricular Assist Device	Avoid impact on subject life expectancy, increased complication risk and unexpected interactions with the implanted device
17.	Subjects that are vulnerable adults	Subjects must be mentally capable of giving consent, consistent with the Declaration of Helsinki

**If required by local law, individuals who are of child-bearing potential must undergo a pregnancy test within seven days prior to study procedures

9. Study Procedures

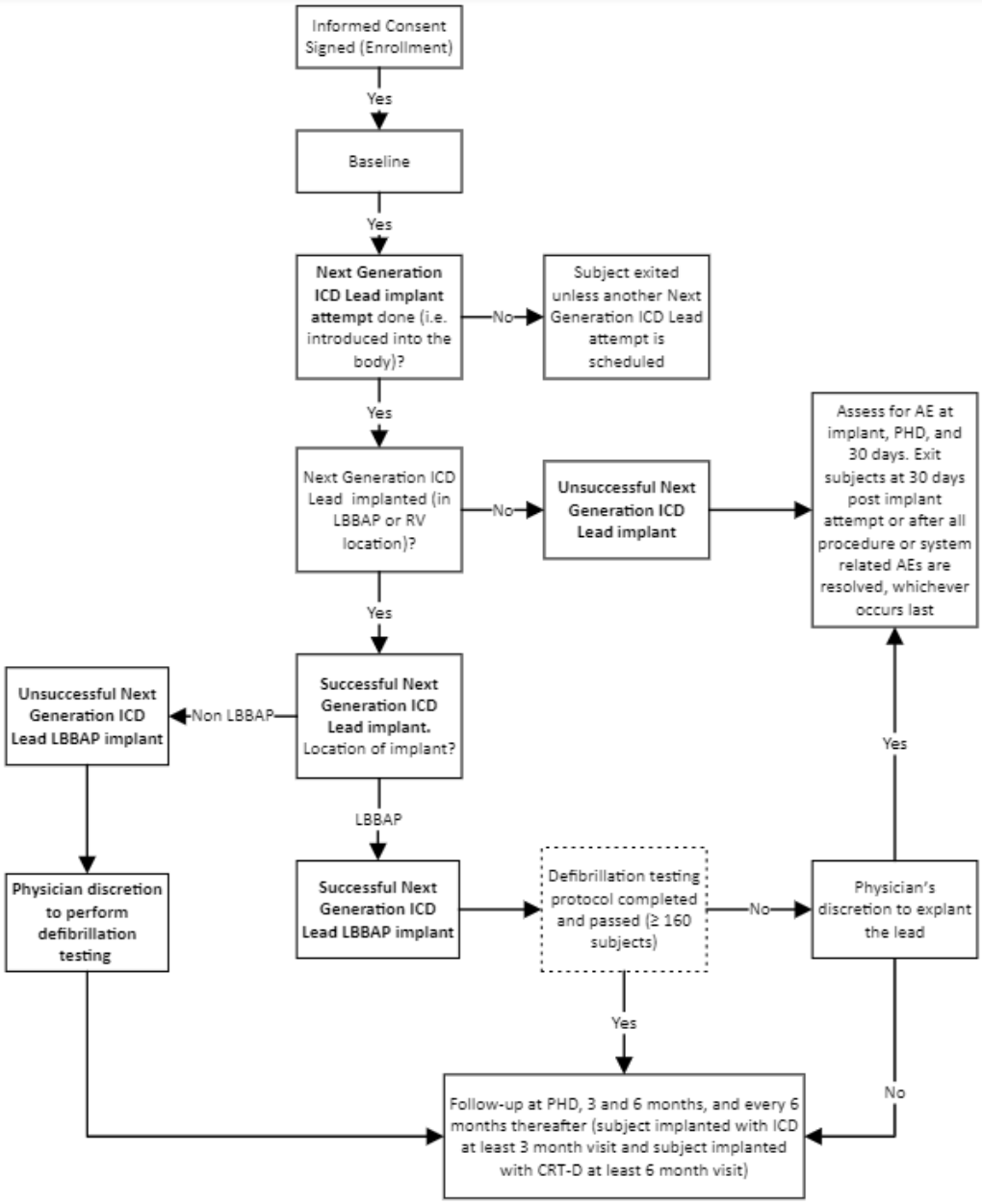


Figure 4: Overview of the LEADR LBBAP Study

9.1. Schedule of Events

Clinical data will be collected at the study visits detailed in Table 7 below. Data will be collected via eCRFs, echocardiography, chest X-ray, fluoroscopic images, analyzer/programmer printouts, interrogation files and printed or digital ECG recordings. Post-implant follow-up visits apply only to those subjects in whom a Next Generation ICD Lead was successfully implanted. Subjects where the investigational lead is not placed in the body following implant will be followed for 30 days or until all procedure or system related AEs are resolved, whichever occurs later, after which they will exit the study. Subject visits will occur at enrollment, baseline, implant, prehospital discharge (PHD), 3- and 6-months post-implant and every 6 months thereafter until study closure. All enrolled ICD-indicated subjects will be followed until at least 3 months post-implant and all enrolled CRT-indicated subjects will be followed until at least 6 months post-implant. Trained Medtronic personnel may assist study personnel during implant and study visits on site or remotely (see section 7.3).

9.2. Data Collection and Study Procedure Requirements

Data collection requirements are summarized in Table 7.

Table 7: Data Collection and Study Procedure Requirements at Subject Visits

Study Procedure		Enrollment/ Baseline	Implant	PHD	3 months (in office[3,5])	6 months (in office)[3,5]	Long term (post 6 months, remote or in office)	Un- Scheduled	System Modification	Study Exit[3]
All subjects	Informed Consent	X								
	Inclusion/Exclusion Assessment	X								
	Physical Exam, Demographics, NYHA, Cardiovascular Medical History, Surgical History	X								
	System and procedure information		X						X	
	Sensing, Impedance & Pacing Tests[9]		X (including Analyzer EGM printout with COI, if available)	X	X	X	X	X[2]	X	
	Save-to-media/Save Session files		X	X	X	X	X	X	X	X
	Medications		X			X				
	12-Lead ECG Recordings		X[6]			X				
	Defibrillation Testing		X[1]							
	KCCQ	X				X[2]				
CRT-indicated	Echocardiography	X				X[2]				
	NYHA					X[2]	12M[2]			
	Subject Global Assessment					X[2]	12M[2]			
All subjects	Fluoroscopy of final lead position (Motion picture in LAO, RAO, AP and, if performed, sheath ventriculography)		X[8]						X[4]	
	Chest radiographs (PA & Lateral (end expiration and end inspiration))			X	3M or 6M				X[4, 7]	
	Device Disposition		X						X	
	Adverse Events (including AEs with fatal outcome, and heart failure related hospitalization)	Upon Occurrence								
	Device Deficiency	Upon Occurrence								
	Study Deviations	Upon Occurrence								

1. Required for a minimum of the first 160 consecutive subjects with implant in LBBAP location. Physician's discretion to perform defibrillation testing if the Next Generation ICD lead is implanted in the non-LBBAP RV location.
2. Required, however optional if the Next Generation ICD Lead is implanted in the non-LBBAP RV location.
3. All successfully implanted subjects will be followed until at least their 3-month (ICD-indicated subjects) or 6-month visit (CRT-indicated subjects) follow up visit.

4. Only required in case the Next Generation ICD Lead is replaced by another Next Generation ICD Lead.
5. For subjects who do not receive a successful LBBAP placement and are implanted with the Next Generation ICD Lead in the non-LBBAP RV location, remote visit is also allowed.
6. Recommended at implant, but is required to be done prior to discharge.
7. Pre-hospital discharge data to be collected in case the Next Generation ICD Lead is replaced by another Next Generation ICD Lead
8. If a lead reposition, adjustment of lead slack, or device repositioning occurs due to troubleshooting step during defibrillation testing collect motion picture (cine fluoroscopy) in LAO, RAO and AP of the lead and device position over a minimum of one complete cardiac cycle before repositioning.
9. For CRT-indicated subjects with LBBAP implant, if pacing therapy is discontinued permanently this will need to be reported

Note: In-person visits could be replaced by other options as required per local regulations in the case of e.g., a pandemic.

9.3. Scheduled Follow-up Visit Windows

After receiving notice of successful implantation, Medtronic will provide the target dates and windows for each visit to the study site if applicable. Should a subject miss a visit or the visit fall outside the pre-specified window, a study deviation must be reported, and the original follow-up schedule maintained for subsequent visits.

Data analyses include follow-up visits, regardless of whether the visit occurs within the window. Therefore, an out of window visit (and/or CareLink transmission) is preferred over a missed visit but must be accompanied by a deviation eCRF (see section 9.15). Follow-up visit windows are listed in Table 8 and are based on days post-implant.

Table 8: Scheduled follow-up visit windows

Study Follow-up Visit	Window (Calculated days post-implant)		
	Window Start (days post-implant)	Target (days post-implant)	Window End (days post-implant)
3 Month	90	90	120
6 Month	152	182	212
12 Month	335	365	395
18 Month	518	548	578
24 Month	700	730	760
30 Month	883	913	943
36 Month	1066	1096	1126

All subjects with a Next Generation ICD Lead will remain in the study and be followed at pre-defined study visits per Table 8 until official study closure. After their study participation ends, the Next Generation ICD Lead will remain implanted and the subject will be provided with standard medical care by their physician.

9.4. Subject Screening

A screening log is not required for the study. A screening log will be utilized in those geographies where required and implemented per local requirements.

9.5. Prior and Concomitant Medications/Therapies

There are no medication/therapy restrictions in the study unless they are investigational and may confound the study results, in which case, prior approval is required from a Medtronic study manager. Specific medications will be collected at implant and 6 month follow-up, see sections 9.8, 9.9.1 and 9.11.1 for details.

9.6. Subject Consent/Assent

Informed Consent (IC) is defined as a legally effective documented confirmation of a subject's voluntary agreement to participate in a particular study after information has been given and explained to the subject on all aspects of the study that are relevant to the subject's decision to participate. This process includes obtaining an ICF/Assent Form (if applicable) and an Authorization to Use and Disclose Personal Health Information/Research Authorization/Health Insurance Portability and Accountability Act (HIPAA)/other privacy language as required by law that has been approved by the study site's Ethics Committee and signed and dated by the subject prior to enrollment. A subject may only consent after information has been given and explained to the subject on all aspects of the clinical investigation that are relevant to the subject's decision to participate.

If the subject is below legal age to consent, they should be informed about the study to the extent compatible with the subject's understanding. Per EC, if the subject could give consent to decisions about participation in research, the investigator must obtain that IC/Assent in addition to the consent of their parent(s)/guardian. Consent by a legal parent(s)/guardian is only possible for subjects who are younger than legal age according to their state/country requirements. Legal IC will be obtained by the time the subject becomes adult according to local regulations.

Prior to enrolling subjects, the ICF/Assent Form and the Authorization to Use and Disclose Personal Health Information/Research Authorization/other privacy language as required by law must be approved by the EC and the sponsor. The document(s) must be controlled (i.e., versioned and dated) to ensure it is clear which version(s) was approved by the EC. Any adaptation of the sample ICF or Assent form (if applicable) must be reviewed and approved by Medtronic and the EC reviewing the application prior to enrolling subjects.

The investigator must notify the subject (and parent/guardian if applicable) of any significant new findings about the study that become available during 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 relevant, IC may be requested from subjects (and their parent/guardian if applicable) to confirm their continued participation.

The template ICF and Assent form will be provided under separate cover.

Prior to initiation of any study-specific procedures, IC must be obtained from the subject (and parent/guardian if applicable). Likewise, privacy or health information protection regulation may require subjects to sign additional forms to authorize study sites to submit subject information to the study sponsor. The IC process must be conducted by the principal investigator or an authorized designee, and the ICF/Assent form (if applicable) and Authorization to Use and Disclose Personal Health Information/Research Authorization/other privacy language as required by law must be given to the subject (and parent/guardian if applicable) in a language they are able to read and understand. The process of IC must be conducted without using coercion or undue improper influence on or inducement of the subject to participate by the investigator or other study site personnel. The IC process shall not waive or appear to waive the subject's legal rights. The language used shall be as non-technical as possible and must be understandable to the subject (and parent/guardian if applicable) and the impartial witness, where applicable.

The subject (and parent/guardian if applicable) must have ample time and opportunity to read and understand the ICF/Assent form (if applicable), to inquire about details of the study and to decide whether to participate in the study. All questions about the study should be answered to the satisfaction of the subject (and parent/guardian if applicable).

When the subject decides to participate in the study, the ICF/Assent form (if applicable) must be signed and personally dated by the subject (and parent/guardian if applicable) and investigator or authorized designee, as required by the ICF/Assent form (if applicable) and ensured by the principal investigator or their authorized designee.

A copy of the ICF/Assent form (if applicable) and the Authorization to Use and Disclose Personal Health Information/Research Authorization/other privacy language, signed and dated as required by law, must be provided to the subject (and parent/guardian if applicable). This must be a signed copy for regions following ISO 14155.

If the IC is obtained the same day the subject begins participating in study-related procedures, it must be documented in the subject's case history that consent was obtained prior to participation in any study-related procedures. The IC process is to be documented in the subject's medical chart, regardless of circumstance.

In the event the subject cannot read and/or write, the IC process shall be obtained through a supervised oral process. An independent and impartial witness must be present during this process. The ICF/Assent form (if applicable) and any other information must be read aloud to the prospective subject. Whenever possible, the subject (and parent/guardian if applicable) shall sign and personally date the ICF/Assent form (if applicable). The witness signs and personally dates the ICF/Assent form (if applicable) attesting that the information was accurately explained, and that informed consent was freely given.

The original signed ICF/Assent form (if applicable) must be filed in the hospital/clinical chart and/or with the subject's study documents.

The ICF/Assent form (if applicable) and Authorization to Use and Disclose Personal Health Information/Research Authorization/HIPAA/other privacy language as required by law must be available

for monitoring and auditing. Any Medtronic Field personnel who support the study procedure must be able to review the subject's signed and dated ICF/Assent form (if applicable) and verify its completeness prior to proceeding with the study procedure. In the event the Medtronic Field personnel identify the ICF/Assent form (if applicable) as being incomplete, the study procedure will not be allowed to occur until the consent of the subject can be adequately and appropriately obtained.

Consistent with the Declaration of Helsinki, vulnerable adults (i.e., those subjects incapable of giving consent) are excluded from this protocol. Any subjects with mental incompetence (e.g., Alzheimer's, dementia, psychiatric disorders, developmental disorders) should be assessed for vulnerable status. This protocol defines vulnerable adults as those subjects incapable of giving consent, in the investigator's opinion. The investigator should consider the definition of vulnerable adult per ISO 14155, which defines vulnerable adults as: "individuals who are unable to fully understand all aspects of the investigation that are relevant to the decision to participate, or who could be manipulated or unduly influenced as a result of a compromised position, expectation of benefits or fear of a retaliatory response." For example, this could include individuals with loss of autonomy due to immaturity or through mental disability, persons in nursing homes, impoverished persons, subjects in emergency situations, ethnic minority groups, homeless persons, nomads, refugees, and those incapable of giving IC. Other vulnerable subjects could include, for example, members of a group with a hierarchical structure such as university students, subordinate hospital and laboratory personnel, employees of the sponsor, members of the armed forces, and persons kept in detention.

In some countries, patients must specifically opt-in for data use for other purposes than the study objectives. In those countries, patients (and/or parent/guardian if applicable) will have the option to indicate that in the consent form (e.g., via a checkbox or via a separate signature).

In Japan, only the monitor assigned to this study may be able to review the signed ICF/Assent form (if applicable) as direct access or source data verification.

9.7. Enrollment

A subject is considered enrolled when the consent process has been finalized. The date the subject signed the ICF and Data Protection Authorization, as required by law, must be documented in the subject's medical records. A log of all subjects enrolled in the study should be maintained (for those study sites following ISO 14155, or per local requirements). Enrollment can be a stand-alone visit or can occur on the same day as the baseline visit. Medtronic shall be notified (via Enrollment eCRF) as soon as possible to aid in enrollment tracking. Once consent is obtained, AEs/deaths, device deficiencies, study deviations, system modifications and subject exits will be reported as they occur.

9.8. Baseline

The baseline visit can be a stand-alone visit or can be performed on the same day, but prior to the implant procedure. The following information is required to be collected at the baseline visit:

- Inclusion/Exclusion Assessment

- Physical Exam: a basic physical exam will be performed, including height and weight
- Demographics including age, sex at birth, race and ethnicity (if allowed per local regulations)
- Relevant cardiovascular medical history, including NYHA classification
- Relevant Surgical History
- Primary indication for ICD or CRT-D implant
- AEs and study deviations (as they occur)
- KCCQ Quality of Life Survey (see section 9.12)
- For CRT-indicated subjects:
    - Transthoracic Echocardiography (TTE) including LVEF, LVESV (within 60 days prior to baseline visit). Note, use of whether used or not, utilization of contrast should be consistent between baseline and 6-month follow-up TTE and preferably be performed by same technician. Copies of echocardiographic images in DICOM format will be submitted to Medtronic (see section 9.16) and kept on file at the site.

Subjects that are enrolled and exited prior to Implant, need to have a baseline visit completed (KCCQ and TTE data collection are optional).

9.9. Implant

It is recommended that the implant visit occurs within 30 days after subject enrollment. If the implant does not occur within 30 days of enrollment, verification of all inclusion and all exclusion criteria should be reassessed before an implant attempt and reassessment should be documented. If not all inclusion or any exclusion criteria are met during reassessment, the subject must be exited. The implant, catheter usage, and electrical measurements eCRFs will be used to collect data at implant. The implanted system must include a Medtronic commercially released ICD or CRT-D device equipped with SmartShock™ Technology (see section 6.1). Any commercially released RA and LV lead may also be implanted. The implant of the market released Medtronic ICD or CRT-D device and market released leads must be performed according to the IFU provided with the applicable device. Off-label use of market released leads is not allowed.

Information required to be collected at the implant visit is described in the following sub-sections. The configuration of the successfully implanted system components will be collected. This will include the serial number of each implanted component and the location of Next Generation ICD Lead placement.

9.9.1. Medications at Implant

The daily dosage of cardiovascular medications will be collected at implant (including medication that was stopped for the implant procedure):

- Angiotensin-converting enzyme (ACE) inhibitors
- Angiotensin receptor blockers (ARBs)
- Mineralocorticoid receptor antagonists (MRAs)

- Angiotensin receptor-neprilysin inhibitors (ARNIs)
- Antiarrhythmics
- Anticoagulants
- Antiplatelets
- Antihypertensives
- Antilipidemics (including statins)
- ß-blockers
- Calcium channel blockers
- Diuretics
- Digitalis
- Inotropes
- Nitrates
- Digoxin
- Sodium-glucose cotransporter-2 (SGLT2) inhibitors
- Vasodilators.

For sotalol, amiodarone, propafenone, flecainide, mexiletine, dofetilide, and dronedarone the start date needs to be collected.

9.9.2. Next Generation ICD Lead Implant Procedure Steps

The Next Generation ICD Lead must be implanted in the left bundle branch area according to the implant instruction in the LEADR LBBAP Study User Manual. For complete information regarding the Next Generation ICD Lead, reference the 093000 Technical Manual. Both provided under separate cover (see Appendix B: User Manual and Instructions for Use). Prior to performing the implant procedure, it is required that implanting investigators have documented training by Medtronic.
A Next Generation ICD Lead attempt is defined as any time a Next Generation ICD Lead is introduced into the body. Three leads are allowed per subject. Proceed with a new lead if any of the following occurs:

- Lead damage
    - During fixation, when more than 20 clockwise turns are applied to the lead (while engaged with tissue) while the lead is not advancing
    - During repositioning, when more than 10 counter clockwise turns are applied without allowing it to unwind
    - Any other lead damage observed per physician discretion
- Lead sterility compromised
- Lead has been inserted into the catheter 5 times
- Lead length is not compatible with catheter

- Lead fixation into septum has been attempted 5 times. Fixation is defined as application of additional lead body rotations after the helix has engaged the tissue
- Physician discretion

If a third lead is unsuccessful in the LBBAP location or non-LBBAP RV location, such as RV endocardial placement, no additional Next Generation ICD Lead implant attempts are allowed. If the subject does not have a successful Next Generation ICD Lead implant at the conclusion of the initial implant procedure, the subject will be followed for 30 days or until all procedure or system related AEs are resolved, whichever occurs later, after which they will exit the study. If an attempt to implant the Next Generation ICD Lead does not occur or if the Next Generation ICD Lead cannot be implanted, the reasons why the lead implant was not attempted or attempted but not implanted must be documented on the Study Exit or on the lead implant eCRF, respectively. Total enrollment will not be increased with additional subjects to replace subjects who have an unsuccessful implant. See additional definitions below.

Implantation of the Next Generation ICD Lead is considered successful when the ICD or CRT-D device is connected to the lead(s), including the Next Generation ICD Lead, and the subject has been transported out of the procedure room from their initial implant. LBBAP implantation of the Next Generation ICD Lead is considered successful when one of the following criteria is met. Note, when LBBAP is referred to in this study, LBBAP includes Left Bundle Branch Pacing (LBBP), Left Bundle Fascicular Pacing (LBFP), Left Ventricular Septal Pacing (LVSP), and Deep Septal Pacing (DSP).

1. LBBAP is determined acceptable via implanting physician by any of these methods (recorded (printed or digital form) and stored at site and a copy sent to Medtronic):
    a. Diagnostic QRS morphology transition during threshold test or programmed stimulation
    b. Presence of left bundle branch potential
    c. Paced QRS complex includes a terminal R/r wave in ECG lead V1 along with either of the following criteria:
        i. Pacing stimulus to V6/V5 RWPT (R-wave peak time in lead V6 or V5) (LVAT) (recommended <100 ms)
        ii. V6-V1 or V5-V1 interpeak interval (recommended >33 ms)

    OR
2. Deep inter-ventricular septal lead position is obtained and confirmed by sheath ventriculography via contrast injection to confirm lead helix tip is located in the deep inter-ventricular septum.
    - Note, If the subject is unable to receive contrast (e.g., contrast allergy), an alternative method is to advance catheter tip to RV endocardial wall, using it to measure the depth of the implanted lead tip.

No Next Generation ICD Lead Attempted (lead not inserted into the body)
A Next Generation ICD Lead attempt is defined as any time a Next Generation ICD Lead is introduced into the body. Subjects that do not have a Next Generation ICD Lead implant attempted will be exited from the study following their implant procedure unless another Next Generation ICD Lead attempt is scheduled. AEs, device deficiencies (DDs) and deviations must be documented before the subject is exited.

Next Generation ICD Lead Attempted but Not Implanted
A Next Generation ICD Lead that is inserted into the body that is not successfully placed in the LBBAP location or non-LBBAP RV location will be considered an unsuccessful Next Generation ICD Lead attempt. The subject may receive an alternative lead that is not a Next Generation ICD Lead. Note: An unsuccessful implant itself is not considered an AE. AEs occurring during an unsuccessful implant (e.g., dissection, perforation) will be recorded and classified. Subjects meeting this definition will be followed for 30 days or until all procedure or system related AEs have been resolved, whichever occurs later, after which they will be exited.

Next Generation ICD Lead in LBBAP Attempted but Implanted in Non-LBBAP RV Location
A Next Generation ICD Lead that is inserted into the body that is not successfully placed in a LBBAP location, but is successfully implanted in a non-LBBAP RV location, will be considered an unsuccessful Next Generation ICD Lead LBBAP attempt. Note: An unsuccessful implant itself is not considered an AE. AEs occurring during an unsuccessful implant (e.g., dissection, perforation) will be recorded and classified. Subjects meeting this definition will continue to be followed per the data collection requirements specified in section 9.2.

LV Lead Implant Attempted but Not Implanted
For LOT-CRT implants, an LV Lead that is inserted into the body that is not successfully placed in the LV will be considered an unsuccessful LV Lead attempt. Note: An unsuccessful implant itself is not considered an AE. AEs occurring during an unsuccessful implant (e.g., dissection, perforation) will be recorded and classified. Subjects meeting this definition will be followed based on definition of success of implant of Next Generation ICD Lead as described above.

9.9.3. Next Generation ICD Lead Implant Electrical Testing

9.9.3.1. Pacing System Analyzer Testing

Perform the following tests of the implanted Next Generation ICD Lead by connecting the leads to the preferred Pacing System Analyzer via cables (see section 6.5.2). The sensing, impedance, and pacing tests should be performed in the integrated bipolar (tip to coil) configuration. Ensure that the catheter is pulled back and the defibrillation coil is fully exposed prior to taking integrated bipolar measurements. Record final electrical testing after catheter is slit and final position is obtained.

Current of Injury Observation

It is recommended to connect the Pacing System Analyzer to the lead to observe Current of Injury (COI) and confirm fixation. It is suggested to print a strip and send to Medtronic. For LBBAP lead placement, the current of injury observation is recommended to utilize the unipolar configuration (tip to skin/pocket).

Sensing Testing

Assess the measured R-Wave amplitude as described in the 093000 Technical Manual for the Next Generation ICD Lead. The sensing test should be in the integrated bipolar configuration. Ensure that the catheter is pulled back and the coil is fully exposed. Observe for extra cardiac over sensing on the Right Ventricular EGM such as: T-wave oversensing, P-wave oversensing, R-wave double sensing, or other types of oversensing and reposition lead or adjust sensing parameters per physician discretion. It is recommended that the R-wave amplitude for sensing be greater than or equal to 5mV. If the R-wave amplitude is less than 5mV, inspect lead position on fluoroscopy and adjust or reposition as needed per physician discretion.

Save and print the Sensing Test Report on the Analyzer to PDF or paper and store at site. Record the final measured R-Wave amplitude on the eCRF. Print final Sensing Test Report to PDF or paper and send a copy to Medtronic.

Impedance Testing

Assess the measured pacing lead impedance as described in the 093000 Technical Manual and record the measured impedance on the eCRF. The impedance should be in the integrated bipolar configuration. Ensure that the catheter is pulled back and the coil is fully exposed. The pacing lead impedance is to measure between 200 – 1500 ohms. If the impedance is outside this range inspect on fluoroscopy for lead position and drape and adjust or reposition as needed.

Save and print the impedance Test Report on the Analyzer to PDF or paper and store at site. Record the final measured pacing lead impedance on the eCRF. Print final impedance Test Report to pdf or paper and send a copy to Medtronic.

Pacing Testing

Pacing capture threshold testing will be performed using the Lead Analysis Threshold Test. The pacing tests should be in the integrated bipolar configuration. Ensure that the catheter is pulled back and the coil is fully exposed. Adjust the lower rate to an appropriate rate to assess pacing capture. Using a pulse width of 0.4 ms, decrement pacing voltage amplitude starting at 5.0 volts until ventricular capture is lost and record the pacing capture threshold on the eCRF. Sensitivity settings during pacing capture threshold testing are at the discretion of the physician.

Save and print the Lead Analysis Threshold Test Report on the Analyzer to PDF or paper and store at site. Record the final measured pacing capture threshold on the eCRF. Print final capture threshold report to PDF or paper and send a copy to Medtronic.

9.9.3.2. Device Testing

Perform the following tests of the implanted ICD System after the Next Generation ICD Lead is in the final lead position and connected to the ICD/CRT-D device and the device is placed into the pocket. For subjects undergoing Defibrillation Testing, the following must be collected after full cardiac electrical recovery, evidenced by restoration of the subject's pre-implant intrinsic 12-lead ECG. Use a device programmer as mentioned in section 6.5.1. A final (interrogate all) save-to-media/save session file must be collected at the end of the implant visit and a copy provided to Medtronic. Note: Pacing sensation or discomfort observed during device testing will not be considered a reportable AE.

Sensing Testing

Perform an R-Wave sensing test. Adjust sensing parameters to avoid T-wave oversensing or P-wave oversensing, or other oversensing. Once configured, perform the Sensing Test. Print the Sensing Test Report on the programmer to PDF or paper and store at site and provide a copy to Medtronic. It is recommended that the R-wave amplitude for sensing be greater than or equal to 5mV. If the R-wave amplitude is less than 5mV, it is recommended to run the EGM on paper and assess R-wave amplitude for greater than or equal to 5mV. Save report on the programmer to PDF or paper and store at site and provide a copy to Medtronic. If still less than 5mV, inspect on fluoroscopy and adjust or reposition per physician's discretion.

Impedance Testing

Ensure the device is programmed "SVC OFF" and the "Pace Polarity" and "Sense Polarity" are set to "Tip to Coil". Measure subthreshold lead impedance by performing a lead impedance test and the RV impedances will be measured for the following electrode pairs:

- Pacing impedance (RVtip to RVcoil)
- RV Defib impedance

Print the Lead Impedance Test Report to PDF or paper and send a copy to Medtronic.

Pacing Testing

Pacing capture threshold testing will be performed using the Pacing Threshold Test. Adjust the lower rate to an appropriate rate to assess pacing capture (and/or adjust AV interval as needed). Using a pulse width of 0.4 ms, decrement pacing voltage amplitude until ventricular capture is lost and record pacing capture threshold on eCRF. Sensitivity settings during pacing capture threshold testing are at the discretion of the physician.

Print final capture threshold report to PDF or paper and send a copy to Medtronic.

9.9.3.3. 12-Lead ECG Recordings

Either with the Analyzer or with the implanted system, collect 12-lead ECGs during threshold testing of the Model 093000 lead at the final implant location. For Analyzer use, either unipolar (e.g., tip to

skin/pocket) or integrated bipolar (tip to coil, making sure the coil is not shielded by the catheter) pacing are acceptable. For subjects undergoing Defibrillation Testing, the 12-Lead ECG recordings must be collected after full cardiac electrical recovery, evidenced by restoration of the subject's pre-implant intrinsic 12-lead ECG. To avoid fusion, use either DDD pacing with lower rate at least 10 BPM above the intrinsic sinus rate and short AV delays (e.g., 30-50ms) or VVI pacing with lower rate set at least 10 BPM above the intrinsic rate. Using a pulse width of 0.4 ms, decrement pacing voltage amplitude starting at 5.0 volts until ventricular capture is lost. For each 1.0 or 0.5 V decrease in amplitude, either print the 12-lead ECG at highest available sweep speed (preferably 100-200mm/s, although 50mm/s is also acceptable) and mark with the pacing amplitude or store the 12-lead ECG digitally with timed comments to indicate the pacing amplitude and provide a copy to Medtronic. Ensure at least 4 beats are recorded for each voltage output. For subjects not in complete heart block, collect 12-Lead ECG during intrinsic rhythm for at least 4 beats.

For dual chamber or CRT-D devices

After the pocket is closed, record the following 12-lead ECGs and provide a copy (printed or digital form, annotated if applicable) to Medtronic. Ensure that at least 4 beats are recorded for each setting, at the highest available sweep speed (preferably 100-200 mm/sec, although 50 mm/sec is also acceptable):

- For subjects not in complete heart block AND not in AF AND with dual-chamber or CRT-D device:
    1. Measure the interval from A sense to LBB sense (RV sense on the device) during intrinsic rhythm. If the subject requires atrial pacing support, measure the interval from A pace to LBB sense (RV sense on the device).
    2. Determine a default AV delay as 60% of the measured A sense / A paced to LBB sense interval (rounded to 10ms). Maintain the atrial pacing or sensing while pacing LBBAP in DR devices or pacing either LBBAP or LOT-CRT (with VV = 0) in CRT devices, and collect a 12-lead ECG during:
        - Default AV - 60ms
        - Default AV - 30ms
        - Default AV
        - Default AV + 30ms
        - Default AV + 60ms

       Annotate or store the 12-lead ECGs digitally with timed comments to indicate the AV delay.

Collection of all 12-lead ECG recordings is recommended at implant, but is required to be done prior to discharge.

9.9.4. Induction and Defibrillation Testing

Routine defibrillation testing is not common practice in many geographies. To estimate the Next Generation ICD Lead defibrillation testing success rate in LBBAP location, SSVA induction and defibrillation testing is required at implant for at least the first 160 consecutive subjects with a successful implant in the LBBAP location (see section 13.4.1). Adjust device programming to the minimum sensitivity to assess Ventricular Fibrillation (VF) sensing and set defibrillation energies as specified by the defibrillation protocol during SSVA induction and defibrillation testing (see section 9.9.4.2).

The testing protocol may require up to 6 successful SSVA episodes induced and up to 12 device shocks and up to 5 external rescue shocks delivered (see section 9.9.4.2).

9.9.4.1. General Requirements

Induction of SSVA will be achieved using one of the following methods:

- 50 Hz Burst Induction
- T-shock (up to 18J)

If a subject cannot be induced using these methods, other methods may be employed at the discretion of the investigator (e.g., EP catheter). The investigator may choose to attempt induction on another day prior to discharge.

Ensure a Wavelet template is collected and the detection is enabled prior to induction. Ensure an external transthoracic defibrillation system is present and ready to deliver rescue shocks during defibrillation testing, and at least one set of rescue patches are in place in locations that will not compromise the implanted system defibrillation vector or sterile operating field. If the subject's health is at risk, defibrillation testing should be terminated.

It is recommended to wait five minutes between the end of an SSVA episode and subsequent induction to ensure that the subject is hemodynamically stable. Waiting periods after failed induction attempts are at the investigator's discretion.

Defibrillation testing may be continued on a future day, but prior to hospital discharge, if episodes remain within the testing protocol.

Reminder: After each induced SSVA episode, save-to-media/save session files shall be collected (see section 9.15). Print the live strip for the duration of each SSVA episode. Retain a copy of the live strip for each episode not recorded by the ICD/CRT-D. If requested, send a pseudonymized copy of the live strip to Medtronic using a secure and compliant electronic transfer. Print the SSVA episode report to PDF or paper and store at the site.

Record shock outcome and shock impedance for each device and rescue shock. If manual shock is delivered through the device an interrogation of the device is required to obtain shock impedance. Print the results to PDF or paper and send to Medtronic. A shock will be considered successful if it results in termination of the induced SSVA episode, with termination defined as a return to normal intrinsic

rhythm or to a supraventricular tachycardia before the next shock is given. Additional processing of the VF sensing data may be performed after implant data collection.

9.9.4.2. Testing and Programming Defibrillation Therapy

Defibrillation testing success is defined as meeting one of the following criteria in a final LBBAP system configuration:

- First induced SSVA episode successfully terminated with an 18J or maximum output minus 10 Joule (M-10J) shock, or
- First therapy of the second induced SSVA episode successfully terminated with a M-10J shock, or
- First therapy after a system reposition of an induced SSVA episode successfully terminated with a M-10J shock, or
- Two consecutive induced SSVA episodes successfully terminated with a M-10J shock.

Follow the defibrillation testing as outlined in Figure 5, beginning at Episode 1 (18J). The following requirements shall be observed while conducting defibrillation testing:

- Defibrillation at a given energy will be deemed successful if SSVA is terminated, regardless of whether the shock is delivered manually or automatically by device.
- To achieve final system configuration, changing the position of the device generator and/or the lead is permitted.
    - If the device generator position is modified during defibrillation testing: all previous device electrical measurements (Section 9.9.3.2) must be reassessed.
    - If the lead position is modified during defibrillation testing: all previous device electrical measurements (Section 9.9.3.2), confirmation of LBBAP implant success criteria (Section 9.9.2), and 12 lead ECG recording (Section 9.9.3.3) must be completed with the final lead position.
    - If the lead slack is adjusted during defibrillation testing: all previous device electrical measurements (Section 9.9.3.2) must be completed with final lead position. If lead tip movement is suspected, confirmation of LBBAP implant success criteria (Section 9.9.2) must be completed with the final lead position. 12 lead ECG recording (Section 9.9.3.3) must be completed with the final lead position.
- If the device or lead position are altered prior to completing the defibrillation protocol (e.g., position changed as part of troubleshooting), defibrillation success must be demonstrated with the new system configuration. Defibrillation testing will resume at the point in the protocol where the system reposition occurred. Additional episodes will not be allowed within the protocol.
- If defibrillation protocol episodes are not exhausted, remaining episodes may be used on a subsequent day (recommended for episodes 5 and 6), though prior to hospital discharge, (e.g., next day or during the admission) to complete the defibrillation testing protocol.
- The polarity for all therapies (Rx1 – Rx6) shall be set to B>A.

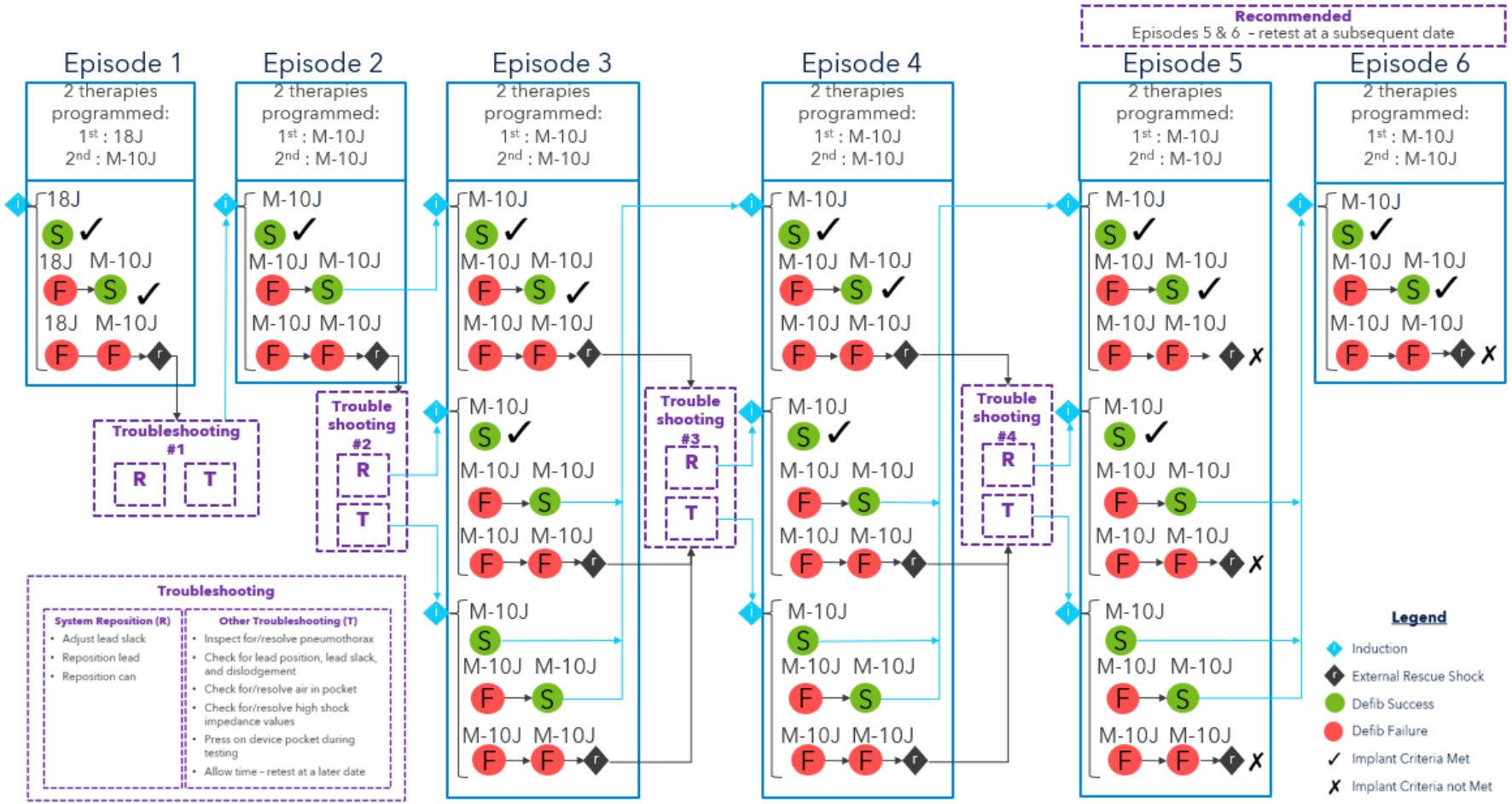


Figure 5: Diagram outlining the process of SSVA induction and defibrillation testing

9.9.4.3. Testing and Programming VF Detection

VF detection success at implant is defined as successful VF detection in a single SSVA episode in the RV–tip - RVcoil configuration at the minimum sensitivity value of 1.2 mV. VF detection and defibrillation success do not need to be demonstrated on the same episode(s), but each must be demonstrated in the final system configuration.

Follow the VF detection testing as outlined below, beginning at Episode 1. The following requirements shall be observed while conducting VF detection testing:

- The VF detection shall be demonstrated in the RV–tip - RVcoil vector with Number of Intervals to Detect (NID) setting of 30/40.
- Begin Testing with VF sensitivity programed to RV tip-RV Coil, 1.2 mV. If VF detection is demonstrated in the RV–tip - RVcoil vector on a SSVA with current lead position, the remaining induction attempts may be programmed with a NID setting of 18/24.
- Redetect NID should be programmed to 9/12 for Rx2.
- If undersensing of VF occurs at the 1.2 mV, the sensitivity can be adjusted at the investigator's discretion for additional episodes. Ensure a save to media/save to disk/save session is collected after each episode.
- Additional inductions beyond those specified in Figure 5 are allowed if needed per medical judgment (e.g., to program sensitivity or to obtain supplementary information on an alternate energy setting) and will be reported on the eCRF.
- If undersensing occurs leading to a manual shock, VF detection must be demonstrated using 30/40 NID using a sensitivity setting at the physician's discretion.
- If the lead position is altered (e.g., as part of troubleshooting), previously demonstrated VF detection success is invalidated and success must be demonstrated with the new system configuration with an NID setting of 30/40.

9.9.4.4. Implant Defibrillation Troubleshooting Recommendations

Prior to inducing and throughout the defibrillation protocol, it is recommended to consider the following to improve defibrillation outcome or troubleshooting in the event of episode failure:

- Check for/resolve pneumothorax (e.g., fluoroscopy).
- Check for Next Generation ICD Lead position, slack and dislodgement (e.g., fluoroscopy).
- Check for/resolve high shock impedance values.
- Check for/resolve air in pocket (e.g., flush with saline or antibiotic wash, massage air out of pocket).
- Press on device pocket during testing.
- Allow time (e.g., next day or during the admission) to minimize transient factors affecting defibrillation success.

- If all of the above measures are exhausted, consider repositioning of ICD/CRT-D generator or Next Generation ICD Lead.
    - Adjust lead slack
    - Reposition lead
    - Reposition can

When the device is unable to detect an SSVA following troubleshooting the lead shall be explanted. When the device does detect the SSVA but defibrillation protocol cannot be successfully completed it is at the physician's discretion to explant the lead.

9.9.4.5. Programming Requirements at End of Implant Procedure

At the end of the procedure, VF Detection, VF Therapies and Pacing therapies shall be programmed at the discretion of the investigator, however, 'SVC' is required to be programmed OFF. It is recommended to program pace and sense polarities to 'Tip to Coil'. Refer to section 9.17 for the required alert programming and recommended EGM vectors programming.
Final device interrogation data via a save-to-media/save session file must be collected (see section 9.15) and sent to Medtronic, with a copy being maintained at the site in the subject's file. Device data shall be sent to Medtronic using secure and compliant electronic file transfer services.

9.9.4.6. Final Lead Placement Imaging Data Collection

Following fixation and once the final position of the lead is determined, the following fluoroscopic images will be collected:

- Sheath ventriculography of lead depth made visible via contrast injection before slitting catheter
    - Required if performed or utilized to confirm LBBAP acceptance criteria
    - Motion picture (cine fluoroscopy) recording in Left Anterior Oblique (LAO)
- Final placement of lead system, including the device
    - Motion picture (cine fluoroscopy) recording in Anterior-Posterior (AP), LAO, and Right Anterior Oblique (RAO) view over a minimum of one (1) complete cardiac cycle of the final placement of the lead system, including the device.
    - No panning. However, if patient size or fluoroscopy field of view does not allow for cine fluoroscopy of lead and device, panning is allowed.

If a lead reposition, adjustment of lead slack, or device repositioning occurs due to troubleshooting step during defibrillation testing, the following imaging will be collected of the lead and device position before repositioning.

- Placement of lead system before lead reposition, including the device

- Motion picture (cine fluoroscopy) recording in AP, LAO, and RAO view over a minimum of one (1) complete cardiac cycle of the final placement of the lead system, including the device.
- No panning. However, if patient size or fluoroscopy field of view does not allow for cine fluoroscopy of lead and device, panning is allowed.

Copies of the images in DICOM format will be submitted to Medtronic (see section 9.16) and kept on file at the site.

9.9.5. Subject Exit for Incomplete Implant Visit

The subject shall be exited if any of the following occur during the implant visit:

- No Next Generation ICD Lead attempted (lead not inserted into the body) (see section 9.9.2).
- Next Generation ICD Lead attempted but not implanted (see section 9.9.2) whether in the LBBAP location or non-LBBAP RV location (i.e. lead is explanted) due to one of the following reasons, as determined per physician's discretion:
  - The subject fails or begins but does not complete the defibrillation protocol
  - Adequate ventricular sensing or SSVA sensing cannot be achieved
  - Adequate pacing thresholds cannot be achieved

If a Next Generation ICD Lead was attempted but not implanted at the completion of the implant procedure, for instance due to any of the reasons specified above, the subject will be followed for 30 days or until all procedure or system related AEs have been resolved, whichever occurs later, after which they will be exited (see section 9.24). If the subject receives an alternative lead, any AEs related to the alternate lead will be recorded during the course of subject participation but will not be considered related to the Next Generation ICD Lead.
Incomplete placement of the lead, and incomplete or failed electrical or defibrillation testing (including prolongation of hospital stay by allowing time to minimize transient factors affecting defibrillation) are not considered AEs; however, any AEs occurring during an unsuccessful implant attempt (e.g., subject allergy to electrodes used during implant) must be recorded and classified on an AE eCRF. Unsuccessful Next Generation ICD Lead implants and/or failed defibrillation testing shall be evaluated for reporting as a device deficiency.
If the Next Generation ICD Lead is explanted after the subject has been transported out of the procedure room from their initial implant, this shall be captured on a System Modification eCRF.

9.10. Pre-Hospital Discharge

The following procedures will be completed and data will be collected during the pre-hospital discharge visit. This should be completed at any time after implant, but prior to discharge.

- Electrical testing of the Next Generation ICD Lead (Sensing, Impedance, Pacing test (see section 9.11.4)). Initial (interrogation) and final (interrogate all) save-to-media/save session files (see section 9.15)
- AE assessment
- DD assessment
- Study Deviations
- Four Chest X-rays: Posterior-Anterior (PA) end expiration, Posterior-Anterior (PA) end inspiration, Lateral end expiration and Lateral end inspiration.

Note: if 12-lead ECG Recordings have not been collected at implant, complete prior to discharge (see section 9.9.3.3)

9.11.Scheduled Follow-up Visits

9.11.1. 3- and 6-Month Follow Up Visit

The following procedures will be completed and data will be collected during an in office follow-up visit:

- Electrical testing of the Next Generation ICD Lead (Sensing, Impedance, Pacing test, see section 9.11.4).
- Initial (interrogation) and final (interrogate all) save-to-media/save session files (see section 9.15)
- AE assessment
- DD assessment
- Study deviations

At the 3-Month visit or 6-Month visit the following additional data will be collected during an in-office follow-up visit:

- Four Chest X-rays: Posterior-Anterior (PA) end expiration, Posterior-Anterior (PA) end inspiration, Lateral end expiration and Lateral end inspiration.

At the 6-Month visit the following additional data will be collected during an in-office follow-up visit:

- 12-lead ECG Recordings (see section 9.11.2)*
- Any changes to cardiovascular medications referenced in section 9.9.1
- KCCQ Quality of Life Survey* (see section 9.12)

For CRT-indicated subjects, the following data will be collected during an in office 6-Month follow-up visit*:

- TTE including LVEF, LVESV (within 30 days of visit date). Note: whether used or not, utilization of contrast should be consistent between baseline and 6-month follow-up TTE and preferably be performed by same technician. Copies of echocardiographic images in DICOM format will be submitted to Medtronic (see section 9.16) and kept on file at the site.

- NYHA classification
- Subject Global Assessment

Note: In-person visits could be replaced by other options as required per local regulations in the case of e.g., a pandemic. In such cases, ensure a CareLink transmission is performed (see section 9.15).
* Required however optional if the Next Generation ICD Lead is implanted in the non-LBBAP RV location.

9.11.2. 6-Month 12-Lead ECG Recordings

At the 6-month follow up visit, complete the following 12-lead ECG recordings. The ECG should be printed at highest available sweep speed (preferably 100-200mm/s, although 50mm/s is also acceptable) or stored digitally and sent to Medtronic. Ensure that at least 4 beats are recorded for each setting.

- Collect 12-lead ECG from the current pacing settings (the ambulatory settings of the subject as they arrived for the 6 month follow-up visit).
- Conduct a threshold test for LBBAP while avoiding fusion, using either DDD pacing with lower rate at least 10 BPM above the intrinsic sinus rate and short AV delays (e.g., 30-50ms) or VVI pacing with lower rate set at least 10 BPM above the intrinsic rate. Using a pulse width of 0.4 ms, decrement ventricular pacing voltage amplitude starting at 5.0 V until ventricular capture is lost. For each 1.0 or 0.5 V decrease in amplitude, either print the 12-lead ECG and mark with the pacing amplitude or store the 12-lead ECG digitally with timed comments to indicate the pacing amplitude.

9.11.3. Long-Term Follow-Up Visits

After the 6 month visit post-implant, subjects will be followed every 6 months until the study is closed. These scheduled follow-ups after the 6 month visit are considered “Long-term follow-up visits”. It is preferred that scheduled follow-up visits occur in the clinic where device interrogations can occur and device programming can be adjusted. However, remote visits via telephone or internet service (e.g. WebEx®, Zoom®) are an acceptable alternative in cases where the subject is enrolled in CareLink and an in-clinic visit is not possible or is not standard of care (see section 9.15.1).
The following data will be collected at these visits:

- Electrical testing of the Next Generation ICD Lead (Sensing, Impedance, Pacing test, see section 9.11.4, in office visit only)
- Initial (interrogation) and final (interrogate all) save-to-media/save session files (see section 9.15, in office visit only)
- AE assessment
- DD assessment
- Study deviations

In addition, for CRT-indicated subjects, the following data will be collected at the 12-Month follow-up visit*:

- NYHA classification
- Subject Global Assessment

* Required, however optional if the Next Generation ICD Lead is implanted in the non-LBBAP RV location

9.11.4. Next Generation ICD Lead Electrical Testing

An initial interrogation save-to-media/save session file shall be collected at the beginning of the visit, and a final (interrogate all) save-to-media/save session file shall be collected at the end of the visit (see section 9.15). Note: Pacing sensation or discomfort observed during device testing will not be considered a reportable AE.

9.11.4.1. Sensing Testing

At the PHD, 3-Month, 6-Month and Long-Term follow up visits, perform the Sensing Test. Print the Sensing Test Report to PDF or paper and send a copy of the report to Medtronic. A Sensing Test is not required at Long-Term follow-up visits if the long-term visit is conducted remotely. However, in this case a CareLink transmission is required (see section 9.15).

9.11.4.2. Impedance Testing

At the PHD, 3-Month, 6-Month and Long-Term follow up visits, perform the Impedance Test. Print the Impedance Test Report to PDF or paper and send a copy of the report to Medtronic. An Impedance Test is not required at long-term follow-up visits if the long-term visit is conducted remotely. However, in this case a CareLink transmission is required (see section 9.15).

9.11.4.3. Pacing Capture Threshold Test

At the PHD, 3-Month, 6-Month and Long-Term follow up visits, perform pacing capture threshold testing. The RVtip - RVcoil configuration will be evaluated. Pacing capture will be defined as loss of right ventricular capture at 0.4 ms pulse width. If post pace oversensing is observed, sensing parameters should be adjusted to eliminate or minimize oversensing. Print the final capture threshold report to PDF or paper and send a copy to Medtronic. A Pacing Capture Threshold Test is not required at Long-Term follow-up visits if the long-term visit is conducted remotely. However, in this case a CareLink transmission is required (see section 9.15).

9.12. Quality of Life Questionnaire

The KCCQ is a 23-item, self-administered instrument that quantifies physical function, symptoms (frequency, severity and recent change), social function, self-efficacy and knowledge, and quality of life.

The KCCQ will be collected by site personnel at the baseline visit and at 6 months post-implant for all implanted subjects, however it is optional if the Next Generation ICD Lead is implanted in the non-LBBAP RV location.

9.13.Subject Global Assessment

The Subject Global Assessment will be collected for the CRT-D indicated subjects at the 6 and 12-month follow-up visit. The subject will be asked “Specifically in reference to your heart failure symptoms, how do you feel today as compared to how you felt before your device was implanted?”. The subject will respond to this question by selecting one of the following response options.

- Markedly improved
- Moderately improved
- Mildly improved
- No change
- Slightly worse
- Moderately worse
- Markedly worse

9.14.Unscheduled Follow-up Visits

An Unscheduled follow-up visit is defined as any non-standard of care visit by the subject to the investigative study site due to the Next Generation ICD Lead between CIP-required visits.
If an Unscheduled Visit occurs:

- Document any AEs and/or DDs on the associated eCRFs, as applicable
- Where possible, initial (beginning of the visit) and final (end of the visit) device interrogation data (interrogate all) should be collected via a save-to-media/save session file (see section 9.15)
- If electrical testing is conducted (see section 9.9.3), print the Testing Reports to PDF or paper and send a copy of the reports to Medtronic. Electrical testing is required in case of a Next Generation ICD Lead related AE.

9.15.Device Interrogation and Save-to-Media/Save Session Files

A full “Interrogate ALL” device interrogation file must be obtained at implant, PHD and all scheduled follow-up visits. It is recommended that device data is not cleared during any interrogation.
As described below, a CareLink transmission may replace an in-office device interrogation for specific cases.
When an in-office interrogation occurs, the original device data file must be stored at the study site and a copy sent to Medtronic using a secure and compliant electronic transfer, with a copy being maintained at the site in the subject’s file.

Missed device interrogations (without a corresponding CareLink transmission) are considered a protocol deviation and must be documented in the protocol deviation eCRF.

9.15.1. CareLink Transmissions

An in-office device interrogation file is required for the 3- and 6-months follow up visits. However, for those visits and in those scenarios (e.g., a pandemic) where the hospital/clinic does not allow in-clinic visits, it is acceptable to collect and utilize data via CareLink transmissions. Also, for subjects who do not receive a successful LBBAP placement and are implanted with the Next Generation ICD Lead in the non-LBBAP RV location, and for long-term follow up visits, a remote visit is allowed (see section 9.11.3). A CareLink file transmission may replace an in-office interrogation but should occur within the applicable visit window. CareLink transmitted data may be used to help study management and assist event review, however they will not serve as a substitution of 3 and 6 month follow-up visits, as all procedures outlined in section 9.2 are required to be completed at each respective visit. CareLink transmissions should be reviewed for reportable AEs. If review of a CareLink transmission results in a subject visit to the study site between scheduled visit windows, an Unscheduled Visit eCRF shall be completed.

9.16. Images and recordings

All images and recordings shall be retained in the subject's file. Pseudonymized copies of images sent to Medtronic shall be transferred in DICOM format. Pseudonymized copies of 12-lead ECG recordings sent to Medtronic can be in printed or digital format.

9.17. Alert and Diagnostic Monitoring Programming

Table 9 and Table 10 and display the required and recommended programming. All programming parameters that are different from their nominally set values are in bold. Note that RV lead impedance monitoring alerts and Number of Shocks Delivered in an Episode are required to be enabled, however the thresholds triggering those alerts are left to the discretion of the clinician. Home monitor or wireless alerts should be programmed to active when CareLink CareAlert monitoring is available. For regions where CareLink is not available, the audible alerts/Device Tone must be programmed to active.

Table 9: Required programming

Parameter Type	Parameter	Device Model	Required Value	Nominal Value
Alerts	RV Lead Integrity Enable	Evera, Cobalt/Crome	ON for Device Tone ON for Patient Home Monitor/Wireless Alert	ON for Device Tone ON for Patient Home Monitor/Wireless Alert
	RV Lead Noise Enable	Evera, Cobalt/Crome	ON for Device Tone or ON for Patient Home	ON for Device Tone

Parameter Type	Parameter	Device Model	Required Value	Nominal Value
			Monitor/Wireless Alert	ON for Patient Home Monitor/Wireless Alert
	RV Pacing Impedance Enable	Evera, Cobalt/Crome	ON for Device Tone or ON for Patient Home Monitor/Wireless Alert	ON for Device Tone ON for Patient Home Monitor/Wireless Alert
	RV Defibrillation Impedance Enable	Evera, Cobalt/Crome	ON for Device Tone or ON for Patient Home Monitor/Wireless Alert	ON for Device Tone ON for Patient Home Monitor/Wireless Alert
	SVC Defibrillation Impedance Enable	Evera, Cobalt/Crome	**OFF for Device Tone and OFF for Patient Home Monitor/Wireless Alert**	ON for Device Tone ON for Patient Home Monitor/Wireless Alert
	All Therapies in a Zone Exhausted for an Episode	Evera	**ON for Device Tone or ON for Patient Home Monitor**	OFF for Device Tone OFF for Patient Home Monitor
	Number of Shocks Delivered in an Episode	Evera, Cobalt/Crome	**On for Device Tone or On for Patient Home Monitor/Wireless Alert**	Off for Device Tone Off for Patient Home Monitor/Wireless Alert
Therapy Delivery	Active Can/SVC Coil	Evera, Cobalt/Crome	**SVC OFF**	Can + SVC ON

Note: Evera devices include: Evera MRI, Visia AF MRI, Primo MRI, Claria MRI, Amplia MRI, Compia MRI.

Table 10: Recommended programming

Parameter Type	Parameter Description	Device Model	Recommended Value	Nominal Value
Diagnostic	EGM Vectors for CRT-D	Evera, Cobalt/Crome	EGM1: Atip-Aring EGM2: Can-RVcoil EGM3: **RVtip-RVcoil** **Monitored: include RVtip-RVcoil or RVtip-RVring**	EGM1: Atip-Aring EGM2: Can-RVcoil EGM3: RVtip-RVring
	EGM vectors for DR	Evera, Cobalt/Crome	EGM1: Atip-Aring EGM2: Can-RVcoil	EGM1: Atip-Aring EGM2: Can-RVcoil

			EGM3: RVtip-RVcoil Monitored: include RVtip-RVcoil or RVtip-RVring	EGM3: RVtip-RVring
	EGM vectors for VR	Evera, Cobalt/Crome	EGM1: RVtip-RVring EGM2: Can-RVcoil EGM3: RVtip-RVcoil **Monitored/Stored(Ventricular): include RVtip-RVcoil or RVtip-RVring**	EGM1: RVtip-RVring EGM2: Can-RVcoil EGM3: RVtip-RVcoil

Note: Evera devices include: Evera MRI, Visia AF MRI, Primo MRI, Claria MRI, Amplia MRI, Compia MRI.

9.18. Device Troubleshooting

Troubleshooting is generally required per standard of care for ICD and CRT-D systems and may require additional testing. Additional imaging or data collection may be necessary, and a Holter Recorder (Medtronic mHolter Model MH01 Digital Recorder or DR220 Digital Holter, North East Monitoring, Inc) may be provided, if market-released in the country where it's being used, for up to 24 hours of Holter monitoring. Contact a Medtronic study representative to obtain a Medtronic mHolter or DR220 Holter. If additional data is collected, data shall be submitted to Medtronic.

9.19. System Modification

A system modification eCRF form shall be completed in the event the device and/or leads require invasive modification (e.g., generator or lead explant, generator or lead replacement, lead repositioning, etc.) after the subject has been transported out of the procedure room from their initial implant. In the event of a system modification, subjects should remain in the study when possible if a Next Generation ICD Lead remains in the body and the follow-up schedule for the subject will remain unchanged.
For a system modification, the following information/activities are required to be collected:

- Modification or replacement/explant date
- Reason for modification
- Information on device and/or lead modified
- Information on any replacement device(s)
- A save-to-media/save session file prior to the system modification (interrogate all, if possible, upon initial interrogation, see section 9.15)
- Final device interrogation/save-to-media/save session after system modification
- Study deviations (as applicable)
- AEs (as applicable)
- In the event of a system modification not related to the Next Generation ICD Lead, evaluate the electrical performance of the Next Generation ICD Lead after system modification.

- In the event of a Next Generation ICD Lead dislodgement, perform chest X-rays (PA and Lateral) prior to system modification. If X-rays are collected for any other system modifications per standard of care, please provide to Medtronic

Next Generation ICD Lead Explanted and Not Replaced with a Next Generation ICD Lead
In cases where a Next Generation ICD Lead is explanted the subject will be exited according to section 9.24. In the event the Next Generation ICD Lead is replaced by a non-Next Generation ICD lead, evaluate electrical performance of the Next Generation ICD Lead before system modification and evaluate electrical performance of the other RV ICD lead replacement (Non-Next Generation ICD lead), if available

Next Generation ICD Lead Explanted and Replaced with a Next Generation ICD Lead
If deemed clinically necessary, lead replacement with a new Next Generation ICD Lead is allowed within 30 days post initial implant. The same data must be collected as during the initial Implant visit, section 9.9 (except Section 9.9.1 Medications at Implant, section 9.9.4 Induction and Defibrillation testing and section 9.9.3.312-Lead ECG Recordings). In addition, repeat PHD visit data collection, as specified in section 9.10, including chest radiographs (PA & Lateral (end expiration/end inspiration)) at PHD. The procedure shall be completed by a physician who has undergone Next Generation ICD Lead implant procedure training as specified by Medtronic.
All explanted products should be returned to Medtronic for analysis when permissible by local laws and regulations. See section 6.11 for final product disposition details.

Next Generation ICD Lead capped
If the Next Generation ICD Lead is capped while the subject is in the study, it is not allowed to be replaced with a new Next Generation ICD Lead. Subjects will continue to be followed per their original follow-up schedule for safety monitoring until study closure. ICD lead electrical testing and interrogation files will not be required at follow-ups for subjects without the full protocol required system implanted.

Medtronic ICD/CRT-D device explanted and replacement with a non-Medtronic device and the Next Generation ICD Lead remains implanted
If the Medtronic ICD or CRT-D device is explanted, all attempts should be made to replace it with another market approved Medtronic ICD or CRT-D device. In the event an explanted Medtronic ICD or CRT-D device cannot be replaced with a new Medtronic ICD or CRT-D device, subjects who still have the Next Generation ICD Lead implanted will continue to be followed for safety monitoring in person per their original follow-up schedule until study closure. Events related to the Next Generation ICD Lead should be reported. Electrical testing and interrogation files will not be required at follow ups for subjects without the full protocol required system implanted.

9.20.Assessment of Efficacy

Efficacy of the Next Generation ICD Lead with regards to defibrillation testing will be assessed per the primary efficacy objective at implant (see section 13.4). In addition, efficacy with regard to successful LBBAP lead placement, pacing capture threshold, sensing, and impedance will be assessed using the ancillary objectives (see section 13.6).

9.21.Assessment of Safety

Safety of the Next Generation ICD Lead with regard to major complications will be assessed by way of the primary safety objective (see section 13.5). all AEs will be collected throughout the study duration, starting at the time of signing the ICF.

The prevalence of AEs will further be summarized by Medical Dictionary for Regulatory Activities (MedDRA) key terms. Additionally, any device deficiencies related to the Next Generation ICD Lead, system components, or accessories will be collected. Further information on the collection of AEs is discussed in section 11.

9.22.Recording Data

This study will be conducted using an electronic data capture (EDC) system. The EDC system, which allows the study sites to enter study data into the sponsor's database over a secure internet connection, will be used to capture study required eCRF information. The Principal Investigator or an individual delegated by the Principal Investigator is responsible for entering data for the study on the eCRFs. The Principal Investigator or Sub-Investigator designee (if allowed by local regulation) is required to approve all data on eCRFs via electronic signature.

Data entered must be traceable to source documents. Source documentation is defined as all information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical investigation necessary for the reconstruction and evaluation of the clinical investigation (e.g., hospital records, clinical and office charts, procedure reports, laboratory notes, memoranda, pharmacy dispensing checklists, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate copies, X-rays, subject files, device data and records kept at the pharmacy, at the laboratories and at medico-technical departments involved in the study).

In general, eCRFs (or paper copies) may not serve as source documents. Exceptions to this are referenced below. Source documentation for data elements not routinely captured in medical records may vary from study site to study site; the study site may use source document worksheets if identified as source documents.

The investigator must ensure the availability of source documents from which the information on the eCRFs was derived. The type and location of source documents should be documented. Where printouts of electronic medical records are provided as source documents, or where copies of source documents

are retained as source documents, those should be certified as indicated by a dated signature by a member of the investigation site team unless generated through a validated process.
The source documents must be made available for monitoring or auditing by Medtronic's representative or representatives of the competent authorities and other applicable regulatory agencies.
The eCRF may be considered source for the following data collection elements:

- Device Deficiency
  - Date site became aware of event
- Device Accountability Log
  - Next Generation ICD Lead (except for date used/explanted)
  - Catheters (except for date used)
  - Holters
  - Justification for explanted product not being returned to Medtronic
- 6 And 12 Month Follow Up CRF
  - Subject Global Assessment
- AE eCRF
  - Date study site became aware of event
  - Relatedness of AE
  - Seriousness
- Non-Subject AE
  - Date study site became aware of event
  - Relatedness of AE
  - Seriousness
- Exit
  - Reason for exit
- Deviations
  - Reason for deviation

9.23. Deviation Handling

A study deviation is defined as an event within a study that did not occur according to the CIP or the CTA, MSA, or MCTA with associated WO. Prior approval by Medtronic is expected in situations where the investigator anticipates, contemplates, or makes a conscious decision to deviate. Prior approval is not required when a deviation is necessary to protect the safety, rights, or well-being of a subject in an emergency or in unforeseen situations beyond the investigator's control (e.g., subject failure to attend scheduled follow-up visits, inadvertent loss of data due to computer malfunction, inability to perform required procedures due to subject illness).
For medically justifiable conditions which preempt a subject's ability to complete a study-required procedure, it may be permitted to report only one deviation which will apply to all visits going forward. This may also apply for other unforeseen situations (e.g., the subject permanently refuses to complete a

study required procedure and the data will not contribute to the primary endpoint analysis). However, prior approval from Medtronic is required for such situations.
All study deviations must be reported on the eCRF regardless of whether medically justifiable, preapproved by Medtronic, an inadvertent occurrence, or taken to protect the subject in an emergency. Multiple deviations of the same type at the same visit may be reported on one case report form.
In the event the deviation involves 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, the deviation must be reported to the EC as well as Medtronic within five (5) working days. Reporting of all other study deviations should comply with EC policies and/or local laws and must be reported to Medtronic as soon as possible upon the study site becoming aware of the deviation. Reporting of deviations must comply with EC policies, local laws, and/or regulatory authority requirements. Refer to Investigator Reports, section 15.8 for geography-specific deviation reporting requirements and timeframes for reporting to Medtronic and/or regulatory authorities.
Medtronic is responsible for analyzing deviations, assessing their significance, and identifying any additional corrective and/or preventive actions (e.g., amend the CIP, conduct additional training, analyzing variables, terminate the investigation). Repetitive or serious investigator compliance issues may result in initiation of a corrective action plan with the investigator and study site, and in some cases, may necessitate suspending enrollment until the problem is resolved or ultimately terminating the investigator's participation in the study. Medtronic will provide study site-specific reports to investigators summarizing information on deviations that occurred at the investigational study site on a periodic basis.
Examples of study deviations include but are not limited to:

- Failure to obtain proper informed consent
- Failure to collect required study data
- Inclusion criteria not met/exclusion criteria met
- Missing required device interrogation files
- Missed Visits

9.24.Subject Exit, Withdrawal or Discontinuation

9.24.1. Study Exit

A study exit eCRF is required for all subjects. Prior to exiting a subject from the study, it is recommended to follow the subject until all ongoing system and/or procedure related AEs are resolved. Following exit, subjects will continue to receive standard medical care. All data available through the time of the subject's exit will be used for analysis.

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 completed
- Subject lost to follow-up
- Subject death
- Subject did not meet inclusion or met exclusion criteria
- Subject does not meet inclusion or meets exclusion criteria due to change since initial evaluation, prior to implant
- Subject was not implanted with a Next Generation ICD Lead, or the Next Generation ICD Lead was explanted without replacement
- Subject did not provide consent or data use protection authorization (if applicable)
- Subject chooses to withdraw (e.g., consent withdrawal, relocation to another geographic location)
- Investigator deems withdrawal necessary (e.g., medically justified, inclusion/exclusion criteria not met, failure of subject to maintain adequate study compliance)

If possible, the following procedures should be performed / data collected at the study exit:

- Reason for exit (this shall be documented on the Study Exit eCRF and in the subject's medical record)
- Final interrogation file (or CareLink transmission) for exits occurring prior to the 6-month visit
- AEs and DDs (as applicable)
- Study deviations

Subjects who had undergone an implant attempt and did not have a Next Generation ICD Lead implanted at any location or had their Next Generation ICD Lead removed without replacement with a Next Generation ICD Lead may be exited by phone at the end of 30 days following implant attempt or system removal, or once all system and procedure-related AEs are resolved, whichever occurs later.

9.24.2. Lost to Follow-up

A subject is considered to be lost to follow-up if at least two attempts to contact the subject are unsuccessful. The method of attempt (e.g., one letter and one phone record, or two letters) must be documented in the subject's medical record. In addition, regulation set forth by the governing EC must be followed.

When subjects are lost to follow-up the investigator will make efforts to confirm the vital status of the subject, as described in the informed consent. If allowed per local regulations, a person identified by the subject is informed of the possibility to be contacted by the principal investigator regarding how to reach the subject and the subject's health status and a civil register may be reviewed by the principal investigator to inquire about the subject's whereabouts. Upon withdrawal from the study, no further study data will be collected, and no additional study visits will occur for the subject.

Subjects that are lost to follow-up will not be replaced.

For sites in Switzerland, when subjects are lost to follow-up, every effort allowed per local law should be explored to obtain information about mortality and other severe Serious Adverse Events (SAEs). Procedures per local law should be implemented to obtain and promptly review the data. If trial subjects can no longer be found, the study site should determine the subject's current address and state of health with an appropriate contact person (e.g., the subject's general practitioner). In case subjects can no longer be found, the monitor shall check the appropriateness of the site's attempts to contact both the subject and contact person.

9.24.3. Subject Chooses to Exit (i.e. Revokes Consent)

A subject can withdraw from the study at any time. If the subject wishes to exit from the study (i.e., the subject revokes consent), the study site is required to document the reason for exit on the Exit eCRF. In addition, study sites shall follow the regulations set forth by the governing EC. For countries following ISO 14155, permission may be requested to follow up with the subject outside of the study due to withdrawal based on problems related to the investigational feature's safety or performance. If possible, the following data should be collected prior to subject withdrawal:

- Reason for exit
- Save-to-media/save session
- AEs and DDs (as applicable)
- Study deviations

A withdrawn subject will be treated according to standard of medical care. Subjects will be included in the analyses up to the time that consent was withdrawn, or up to the time that the subject is exited.

9.24.4. Investigator Withdraws Subject

No subjects should be withdrawn by investigators unless compelling medical justification is present. It is recommended investigators discuss any withdrawals with Medtronic study team prior to withdrawing subjects. If an Investigator Withdrawal is necessary, the following data should be collected prior to subject withdrawal if possible:

- Reason for subject withdrawal
- Save-to-media/save session (if possible)
- AEs and DDs (as applicable)
- Study deviations

10. Risks and Benefits

10.1. Potential Risks

Medtronic follows rigorous Quality Assurance and Control procedures throughout the life of a product, from the business analysis phase through development, market release, and post-market surveillance. The Next Generation ICD Lead is assessed via a structured risk analysis process to ensure all potential risks are evaluated and minimized via risk controls. The risk assessment evaluates potential risks associated with lead implant/explant procedure, biological compatibility, therapy delivery, and potential failure modes associated with the finished devices. Risk control strategies for the LEADR LBBAP study risks were developed by a cross functional team and in accordance with the Risk Management process. Risk controls are implemented via safety by design, preventive measures, and information for safe use. The effectiveness of the risk control measure has been demonstrated via verification and validation activities.

During the course of the study, risks will be continuously monitored, assessed and documented by the investigators. It is the Principal Investigator's decision to assess whether to continue the study at their respective site, should safety-related concerns arise. The risks will be reduced as much as possible, with residual risk being documented within the Risk Management Report and disclosed in the ICFs provided to subjects. A summary of the risk analysis and risk assessment will also be listed in the Investigator's Brochure. Standard risks associated with the market released ICD, CRT-D, and pacing leads used in this study and an analysis of Adverse Device Effects are listed in the Instruction for Use or Clinical Manual of those devices.

Possible additional risks for participating in this study include the following (although others are possible):

- The Next Generation ICD Lead is investigational and may be no more effective or less effective than a commercially available ICD lead.
- Defibrillation shocks when using a lead implanted in the septal region could cause tissue, muscle, and/or vascular damage at greater rates than commercially available systems.
- Defibrillation testing at implant could potentially lead to death if there is a failure or delay in defibrillation therapy.
- Study sponsor may decide to stop the study before getting approval of the investigational product but will continue to monitor subjects for safety.
- There may be other discomforts and risks related to the Next Generation ICD Lead and/or this study that are not foreseen at this time.

Possible additional AEs related to the use of the Next Generation ICD Lead include, but are not limited to, the conditions listed in Table 11. Note: Implant and usage of the Next Generation ICD Lead may

result in AEs, which may lead to injury, death, or other serious adverse reactions.

Table 11: Potential AEs related to the use of the Next Generation ICD Lead

Potential Adverse Events	
Allergic reaction	Lead fracture
AV fistula	Lethargy
Bradyarrhythmia	Loss of capture
Cardiac arrest	Loss of pacing
Cardiac inflammation	Mental anguish
Cardiac perforation	Nerve damage
Cardiac tamponade	Oversensing
Cardiac valve damage	Palpitations
Discomfort	Pericardial effusion
Dislodgement	Pneumothorax
Dizziness	Return of cardiac symptoms
Dyspnea	Septal Wall Perforation
Embolism	Seroma
Erosion	Skeletal muscle sensation or twitching
Excessive fibrotic tissue growth	Skin disorders
Extracardiac stimulation	Stroke
Fever	Superior Vena Cava tear
Heart block	Syncope
Heart failure decompensation (hospitalization)	Tachyarrhythmia
Hematoma	Threshold elevation
Hemodynamic compromise	Thrombosis
Hemorrhage	Tissue trauma
Hemothorax	Toxic reaction
Hiccups	Tricuspid valve regurgitation
Hospitalization	Undersensing
Inappropriate shock	Vascular tear
Infection	Venous occlusion
Insulation failure	Vessel perforation

Subjects who are pregnant may be at increased risk (e.g., radiation exposure, and other unforeseen risk to the fetus), and are excluded from participation in the study. If a subject becomes pregnant during the study, they must notify the physician immediately. The subject will remain in the study for analysis, but the investigator will avoid any procedures that may be determined harmful.

For adolescent pediatric subjects additional risk is limited to the effects of the steroid which is delivered through the lead distal end. With the adolescent pediatric subjects limited to those who are at least 30 kg and are also at least 12 years of age, this risk is minimal.
No additional interactions (AEs) with concomitant medical treatments are expected other than the ones identified in the risk analysis process (see Table 12).

The AE collection requirements in this study will ensure that risks associated with the Next Generation ICD Lead are adequately monitored.

10.2.Risk Minimization

The potential risks associated with the Next Generation ICD Lead were identified and have been successfully mitigated (Table 12). Any potential risks associated with this study are further minimized by selecting qualified investigators and training study personnel on the CIP and providing implant training to implanting investigators. Medtronic has also attempted to minimize risk to subjects by implementing a Data Monitoring Committee (DMC) to review safety issues as part of the study.
In addition, investigators will be actively involved in the implantation and follow-up of the subjects implanted with the Next Generation ICD Lead. Risks will be minimized by careful assessment of each subject prior to, during, and after implant of the Next Generation ICD Lead. Prior to implant, it is recommended subjects undergo a complete physical evaluation.
Medtronic has further minimized the possibility of risks by performing required laboratory and preclinical testing prior to the LEADR LBBAP study, implementing quality control measures into production processes, providing guidelines for subject selection and evaluation, and providing adequate instructions and labeling.

After implantation, subjects in the LEADR LBBAP study will be followed at regular intervals to monitor the condition of the implanted system. At each in-person follow-up, the investigator must interrogate the device to verify appropriate function of the Next Generation ICD Lead and to evaluate pacing and sensing characteristics and to assess any AEs. Following remote visits, a CareLink file transmission should be completed, as described in section 9.15.1.

Table 12: Potential risks and risk minimization

Potential risk	Risk Minimization
Procedural risk such as infection, acute/chronic tissue trauma	• Model 093000 design verification ensuring sterility/cleanliness of the device is maintained including adequate instructions in instructions for use. • Model 093000 design verification and reliability analysis ensuring freedom from failures as specified. • Model 093000 design utilizes materials that have proven biological compatibility and performance as demonstrated by a biocompatibility assessment. • LBBAP placement can potentially take longer. IFU states implant technique.
Toxicity	• Model 093000 design utilizes materials that have proven biological compatibility and performance as demonstrated by a biocompatibility assessment.
Bio-incompatibility	• Model 093000 design utilizes materials that have proven biological compatibility and performance as demonstrated by a biocompatibility assessment.
Bio-instability	• Model 093000 design utilizes materials that have proven biological compatibility and performance as demonstrated by a biocompatibility assessment.
Insufficient pacing support	• Model 093000 design verification and reliability analysis ensuring freedom from failure as specified.
Insufficient pacing support (due to LBBAP location lead dislodgement)	• Instruction provided in IFU for implant procedure.
Insufficient pacing support (due to lead placement in the LBBAP location. Lead location closer to the atria could increase the potential of P-wave oversensing.)	• IFU indicates to perform sensing evaluation at implant and to ensure defibrillation coil is placed fully in the right ventricle below the tricuspid valve annulus.

Potential risk	Risk Minimization
Arrhythmia induction (pacing during vulnerable period, proarrhythmic pauses, electrical/mechanical stimulus)	• The IFU indicates the lead as Magnetic Resonance (MR) conditional. In addition, the IFU indicates warning / precautions related to use of lead under MRI. • Model 093000 design verification and reliability analysis ensuring freedom from failure under MRI condition as prescribed per IFU. • Model 093000 design verification and reliability analysis ensuring freedom from failure as specified. • Limitation on SSVA induction attempts during defibrillation testing at implant. • Induction protocols being used in this protocol are considered methods standard in cardiac medicine. • Physician discretion to halt procedure at any time, should a subject's safety be of concern.
Inadequate tachyarrhythmia therapy	• Model 093000 design verification and reliability analysis ensuring freedom from failure as specified. • Instruction provided in IFU for implant procedure. • The CIP requires that the Model 093000 implant procedure is to be performed by an investigator who has received timely hands-on training on all aspects of the implant procedure. • An external defibrillation system(s) is required to be present and ready at all times during the implant defibrillation testing procedure. The external defibrillator(s) is to be prepared to be used in case of emergency. • Exclusion of subjects who may be more vulnerable to potential increased risk during the evaluation of the clinical study defibrillation protocol at implant.
Inappropriate high-voltage therapy	• Model 093000 design verification and reliability analysis ensuring freedom from failure as specified. • Instruction provided in IFU for implant procedure; specifically, with the specific use in Right ventricle and avoiding exposure to Right atrium, appropriate lead fixation using fluoroscopy. • The CIP requires that the Model 093000 implant procedure is to be performed by an investigator who has received timely hands-on training on all aspects of the implant procedure.

Potential risk	Risk Minimization
Extracardiac stimulation	• The IFU indicates the lead as MR conditional. In addition, the IFU indicates warning / precautions related to use of lead under MRI. • Model 093000 design verification and reliability analysis ensuring freedom from failure under MRI condition as prescribed per IFU.
Thermal hazard for implanted product heating	• The IFU indicates the lead as MR conditional. In addition, the IFU indicates warning / precautions related to use of lead under MRI. • Model 093000 design verification and reliability analysis ensuring freedom from failure under MRI condition as prescribed per IFU.
System revision	• Model 093000 design verification and reliability analysis ensuring freedom from failure as specified. • Instruction provided in IFU for implant procedure; specifically, with the usage selection of anchoring sleeve and lead fixation using helix. • The CIP requires that the Model 093000 implant procedure is to be performed by an investigator who has received timely hands-on training on all aspects of the implant procedure.
Product integrity/functionality failure from environment influence	• The IFU indicates the lead as MR conditional. In addition, the IFU indicates warning / precautions related to use of lead under MRI. • Model 093000 design verification and reliability analysis ensuring freedom from failure under MRI condition as prescribed per IFU.
Septal wall perforation	• IFU states implant technique. Coil stiffness requirement based on field data of predicate leads. • Availability of multiple delivery systems length (catheters).
RV lead dislodgement post-implant	• Dislodgement rates may be higher in LBBAP compared to a non-LBBAP RV configuration. The stability performance will be evaluated as part of product development activities.

Potential risk	Risk Minimization
Loss of capture	• Auto-adjusting capture management feature adjusts therapy outputs in response to increasing thresholds. • Capture threshold diagnostics/testing allows clinicians to diagnose risk of losing capture and adjust parameters accordingly. • Clinical study subject monitoring will include monitoring of capture threshold performance and any necessary interventions to ensure sufficient capture over time.

10.3.Potential Benefits

Potential transvenous ICD lead benefits

The potential benefits of having the Next Generation ICD Lead implanted are consistent with the benefits of ICD/CRT-D therapy and similar market-approved transvenous ICD leads, which include:

- Decreased mortality risk for both primary and secondary prevention of SCD
- Appropriate therapy application (cardioversion and defibrillation) via anti-tachycardia pacing (ATP) or shock
- Preservation or improvement of quality of life
- Ease of transvenous implantation
- Lower rate of complications compared to epicardial leads

Additional Next Generation ICD Lead specific potential benefits may include:

- Long term reliability
- Ease of extraction
- Potential to target specifically selected sites with the use of a catheter delivery system
- MR Conditional capabilities allow for safe use in an MRI environment
- Reduce inflammation and enhance electrical performance as a result of the steroid, (e.g., reduce peaking and variation in pacing thresholds at the electrode interface with the myocardium)

Potential benefits of LBBAP

The target LBBAP location is the intra-septal part of the left bundle fascicles. Reaching this area requires a deeper lead location moving from the right side of the ventricular septum and securing the lead near the left side of the ventricular septum. The Next Generation ICD intra-septal lead is intended to reach the deeper layers of the myocardium. The first publication on LBBAP occurred in 2017 by Huang et al.[19] Since then, numerous publications have reported benefits including low thresholds and high sensing amplitudes, and benefits relative to RV pacing including less dyssynchrony, shorter paced QRS duration, higher LVEF and maintenance of LVEF over time, lower LVEDD over time, and fewer HF hospitalizations and/or the composite of HF hospitalization and either upgrade to BiV pacing or mortality.[18, 24-28]

Additionally, 2021 ESC Guidelines on Pacing and CRT noted LBBAP as an alternative pacing strategy stating that electrical parameters are usually excellent. Benefits of LBBAP are suspected to apply to the adolescent pediatric patient as well as adult. LBBAP is a physiological pacing opportunity that could potentially overcome some of the limitations for pediatric patients, e.g., detrimental long-term effect of unnecessary traditional RV pacing in some patients, leading to reduction of HF. In a total of 16 pediatric patients reported in the literature with an average age of 11.0 ± 3.6 years (range, 2.9-18 years), the pacing threshold of LBBAP ranged from 0.3 to 1.0V.[30-39]

Potential benefits of using the Next Generation ICD Lead in the LBBAP location[2]

- Catheter delivery and small lumenless lead body provides precise lead placement to target LBB site supporting successful implant.
- Fixed helix design increases helix stability to reduce fracture risks and overall reliability.
- Reduced prevalence of RV pacing may reduce shock burden and death leading to improved long-term outcomes.
- Minimizing the number of leads and complex configurations overall by utilizing only one lead at the LBBAP site.
- Low and stable thresholds for left bundle area pacing and high sensing amplitude.
- LBBAP may support maintenance of LVEF and a reduction in heart failure hospitalizations.

Potential LOT-CRT benefits

LOT-CRT may provide greater electrical resynchronization as compared with BiV-CRT. In a study including 112 patients who underwent LOT-CRT, LOT-CRT resulted in significant narrowing of QRS complex which was better than narrowing obtained with BiV-CRT or LBBAP alone.[29] Without a defibrillation lead for use in the LBBAP location, physicians are implanting complex system configurations for LOT-CRT in patients requiring CRT-D. By combining the RV, LBBAP and defibrillation leads into a single lead location, use of the Next Generation ICD Lead would remove the need for an additional defibrillation lead to be implanted in patients undergoing LOT-CRT.

- Improved electrical resynchronization with increased narrowing of QRS complex
- Minimizing the number of leads and complex configurations for LOT-CRT by utilizing only one lead at the LBBAP site

Next Generation ICD Lead potential benefits in adolescent pediatric patients

The Next Generation ICD Lead is designed for long term reliability, reduced defibrillation lead diameter, and ease of extraction. These are important characteristics in adolescent pediatric patients, who are expected to undergo more system revisions or system upgrades during their life. The Next Generation ICD Lead is based on the platform of the Medtronic Model 3830 bradycardia lead, which is reported to

[2] Additional supportive citations can be found within Section 3.1 Background

be associated with low or reduced venous occlusion in pediatric patients[40, 41] and reduced lead explant complications including partial extractions, femoral approach, and use of additional tools in pediatric patients.[42, 43] In a study comparing outcomes associated with epicardial vs. transvenous ICDs in 122 pediatric patients, ICD lead dysfunction occurred more frequently in patients with an epicardial ICD vs. patients with a transvenous ICD and was associated with a higher incidence of ICD-related reintervention.[44] A smaller more reliable transvenous ICD lead may provide an alternative option to epicardial lead placement in pediatric patients and may minimize surgical interventions.
The Next Generation ICD Lead potential benefits in adolescent pediatric patients may include:

- Minimization of surgical interventions
- Reduction of venous occlusion due to smaller lead diameter
- Reduction of lead explant complication due to smaller lead diameters

The information gained from this study could result in the improved management of other ICD or CRT-D patients. Additionally, information collected from this study may assist in the design of new product(s)/therapy(ies), development of future training and/or education materials and/or instructions for use.

10.4.Risk-Benefit Rationale

In addition to the extensive pre-clinical testing, bench testing, and computational modeling, a formal risk analysis and risk assessment for the Next Generation ICD Lead was performed according to EN ISO 14971:2019 and were used to ensure that the level of risk is acceptable prior to starting clinical investigations. The risk management activities reduced the risks to as low as possible and concluded that the residual risks associated with these hazards are acceptable when weighed against the benefits. The risk management file for the Next Generation ICD Lead will be updated periodically for impact to the product's overall residual risk for issues that are identified during the clinical investigational study and following market release, in accordance with EN ISO 14971:2019.
A risk management plan/report establishes the strategy for performing systematic and comprehensive evaluation of potential safety risks associated with the use or performance of the Next Generation ICD Lead for the investigational study, in accordance with EN ISO 14971:2019.
The risk management plan describes inputs to the hazard analysis as well as the structure of the hazard analysis activities performed for the Next Generation ICD Lead project. The chosen strategy was to perform hazard analysis for the therapy to capture potential risks associated with design inputs and then also perform hazard analyses for the new lead to capture potential risks associated with the design outputs (i.e., finished devices). The hazard analysis leverages the relevant risk analysis inputs such as failure analysis and use error analysis. Furthermore, the hazard analysis captures the pertinent risk controls that serve to minimize the residual risk to as low as possible. This plan may be updated in future phases of the device development lifecycle.

A systematic process is in place to continuously collect, analyze, and assess data relevant to the safety performance of the system during human use. Furthermore, the information gained during the investigational study will be leveraged during the planning and execution of the risk management activities throughout all phases for this project and for commercial release.
In summary, the anticipated risks of the Next Generation ICD Lead placed in the LBBAP location are consistent with the risks of similar market-approved transvenous ICD and catheter-delivered pacing leads. The potential benefits of having the Next Generation ICD Lead implanted in the LBBAP location are also consistent with the benefits of ICD therapy and similar market-approved transvenous ICD leads. Additionally, due to the smaller lead diameter of the Next Generation ICD Lead and the novel catheter delivery in tachycardia application, potential benefits may be seen in long term reliability, the ease of extraction and the potential to target specifically selected sites with the use of a catheter delivery system. The Next Generation ICD Lead may also be an alternative for subjects with small vasculature anatomies. Furthermore, the benefits for pediatric subjects, described in detail in section 10.3, outweigh the risks based on lower body mass. Therefore, it is concluded that the potential benefits related to the use of the Next Generation ICD Lead placed in the LBBAP location have been determined to outweigh any potential risks and justify the implementation of this investigation.

10.5.Risk Determination

The LEADR LBBAP study will be conducted under the existing US FDA Investigational Device Exemption (IDE) for the Next Generation ICD Lead in compliance with 21 Code of Federal Regulations (CFR) Parts 11, 50, 54, 56, and 812. The study was determined to be a significant risk thus a supplement to the Original IDE (under G210150) will be made to the US FDA.

11. 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. Reporting and analysis of safety data are mandated by regulatory authorities worldwide. Medtronic has established procedures in conformity with worldwide regulatory requirements to ensure appropriate reporting of safety information. The study is conducted in accordance with these procedures and regulations.
Since the safety reporting requirements and classification systems vary for each regulatory agency, requirements from all geographies are taken into account for the collection and reporting of safety information.

11.1.Adverse Events

AE definitions are provided in Table 13. All AEs will be collected throughout the study duration, starting at the time the ICF is signed. For purposes of reporting, events shall be captured on an AE eCRF.

All instances of shocks delivered via the Next Generation ICD Lead will be considered associated with a reportable AE. Shocks delivered appropriately to treat a ventricular arrhythmia should be noted as treatment delivered within the AE for the ventricular arrythmia(s) experienced. If device therapy (shocks and/or ATP) are delivered inappropriately due to a Next Generation ICD Lead issue, the issue should be reported as the underlying system related AE. The delivery of appropriate ATP therapy alone does not imply an untoward medical occurrence for the subject, but should be evaluated for a reportable AE if determined to be associated with a new or worsened condition (e.g. arrhythmia resulting in symptoms). Reporting of these events to Medtronic will occur on an AE eCRF. Each event must be reported separately.

Documented pre-existing conditions are not considered AEs unless the nature or severity of the condition has worsened. Worsening may be identified if there is a change in frequency, associated symptoms, or the need for new/additional treatment (e.g., ventricular arrhythmias would be considered worsened if there are new associated symptoms or treatment/shock is warranted).

Unavoidable Adverse Events, listed in Table 13 do not need to be reported unless the AE worsens or is present outside the stated timeframe post-implant procedure. Note: Pacing sensation or discomfort observed during device testing will not be considered a reportable AE.

For AEs that require immediate reporting, initial reporting may be done by phone, or on the eCRF by completing as much information as possible. The completed AE eCRF must be submitted to Medtronic as soon as possible.

Any medication/treatment associated with the treatment of an AE must be reported.

Subject deaths are also required to be reported. Refer to section 11.6 for Subject Death collection and reporting requirements.

Heart failure related hospitalization will be collected as part of the AE eCRF, if applicable. Refer to Table 13 for definition.

11.2.Device Deficiency

The DD definition is provided in Table 13. DD information will be collected throughout the study and reported to Medtronic. An eCRF should be completed for each device deficiency that did not lead to an AE. Note that a DD that results in an AE to the subject should be captured as an AE only.

DDs 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 15).

Examples of instances that may be considered DDs in the absence of an untoward clinical occurrence to the subject may include, but are not limited to:

- Damaged components observed out of packaging
- Unsuccessful Next Generation ICD Lead implant and/or Failed defibrillation testing
- Product insufficiency (e.g. catheter length, lead handling difficulties, etc.)

- Pervasive/persistent sensing issues occurring outside of device testing deficiency that did not lead to an AE and resulted in device reprogramming

11.3.Processing Updates and Resolution

For any changes in status of a previously reported AE or DD (i.e., change in actions taken, change in outcome, change in relatedness), information needs to be updated on, or added to the original AE or DD form. All AEs must be followed until the AE has been resolved, the subject dies or exits the study, or until study closure, whichever occurs first.
In the event that a subject is exited from the study prior to study completion, all efforts should be made to continue following subjects until all unresolved system or procedure related AEs, as classified by the investigator, are resolved. Once the ongoing system or procedure AE(s) is/are resolved, or the subject has been followed for 30 days, whichever occurs first, the subject should be exited.
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 updates provided, as applicable.

11.4.Adverse Event and Device Deficiency Definitions

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. In Japan, the definitions include events related to the investigational medical device, the comparator or the concomitant devices, etc. For this study, any component of the system under investigation, or any market-released component or accessory listed in Table 1 is applicable.

Table 13: Adverse Event and Device Deficiency definitions

General	
Adverse Event (AE)	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 and whether anticipated or unanticipated. Note 1: This definition includes events related to the investigational medical device or the comparator. Note 2: This definition includes events related to the procedures involved. Note 3: For users or other persons, this definition is restricted to events related to investigational medical devices or comparators. (ISO 14155)
Adverse Event (AE) – China Definition*	Untoward medical occurrence during the clinical study, whether or not related to investigational medical devices. (China GCP 2022 Article 64) * The ISO 14155 definition is equivalent to AE under China GCP 2022.
Adverse Device Effect (ADE)	AE related to the use of an investigational medical device.

	Note 1: This definition includes AEs resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device. Note 2: This definition includes any event resulting from use error or from intentional misuse of the investigational medical device. Note 3: This includes 'comparator' if the comparator is a medical device. (ISO 14155)
Device Deficiency (DD)	Inadequacy of a medical device with respect to its identity, quality, durability, reliability, usability, safety or performance. Note 1: Device deficiencies include malfunctions, use errors, and inadequacy in the information supplied by the manufacturer including labeling. Note 2: This definition includes device deficiencies related to the investigational medical device or the comparator. (ISO 14155)
Device Deficiency (DD) – China Definition*	Any unreasonable risk caused by a medical device in normal use during clinical study that may endanger human health or life safety, such as label error, quality issues, malfunction and etc. (China GCP 2022 Article 64) * The ISO 14155 definition is equivalent to DD under China GCP 2022.
Relatedness	
Procedure Related	An adverse event that is directly related to the implantation or modification of the system. Note: In general, this excludes events that are inherent to any surgical procedure (e.g., anesthesia complications, anticoagulation interruption) as well as indirect subsequent consequences of the procedure (e.g., reaction to pain medication).
Outside Standard of Care Procedure Related	Outside Standard of Care is any procedure that is required per the study CIP and is in addition to the standard of care for the system (e.g., which the subject would not get if receiving an ICD or CRT-D device outside of participation to the study). Outside Standard of Care procedures for this study may include: • Defibrillation testing • 12-lead ECG • KCCQ • Echocardiography • Subject Global Assessment • Sensing, Impedance & Pacing Tests • Fluoroscopy of final lead position (motion picture in LAO, RAO, AP and, if performed, sheath ventriculography) • Chest radiographs (PA & Lateral) • Holter recording (Troubleshooting) Any adverse event that may occur after these procedures will be assessed for relatedness to outside standard of care CIP procedures by the site and sponsor. Note: these procedures might be standard of care at participating sites, but the timing, specific settings and/or measurements might not be standard of care.

System Related	An adverse event that results from the presence or performance of any component of the system. Device Related: An adverse event that results from the presence or performance (intended or otherwise) of the device. RA Lead Related: An adverse event that results from the presence or performance (intended or otherwise) of the RA lead. Next Generation ICD Lead Related: An adverse event that results from the presence or performance (intended or otherwise) of the Next Generation ICD Lead. Other RV ICD Lead Related: An adverse event that results from the presence or performance (intended or otherwise) of the non-Next Generation ICD RV lead. LV Lead Related: An adverse event that results from the presence or performance (intended or otherwise) of the LV lead. Other Lead Related: An adverse event that results from the presence or performance (intended or otherwise) of an other lead.
Accessory Related	Catheter Related: An adverse event that results from the presence or performance (intended or otherwise) of the catheter used with the Next Generation ICD Lead.
Heart Failure Related Hospitalization	Hospitalization due to heart failure will be defined as a therapeutic admission lasting >24hrs that occurred primarily because of the documented presence of: • Use of additional or increased pharmacologic or mechanical interventions directed at the treatment of heart failure, and at least 1 of the following 2 criteria: o Clinical manifestations of heart failure o Biomarker or radiographic evidence consistent with heart failure Clinical manifestations of heart failure include the following new or worsening signs and symptoms: • Dyspnea • Orthopnea • Paroxysmal nocturnal dyspnea • Edema • Pulmonary rales • Jugular venous distension • Third heart sound or gallop rhythm • Hypotension or cardiogenic shock not occurring in the context of an acute myocardial infarction or as the consequence of an arrhythmia, or • Other clinical evidence of new or worsening heart failure, e.g., weight gain, or confinement to bed predominantly due to heart failure symptoms Biomarker or radiographic evidence consistent with heart failure • Biomarker results consistent with heart failure include documented increased or increasing levels of a natriuretic peptide (BNP or NTproBNP). • Radiographic evidence consistent with heart failure includes documented worsening pulmonary congestion or pulmonary edema on chest X-ray or echocardiographic evidence of heart failure (reduced ejection fraction, regional/global wall mobility abnormality, etc.) or other generally recognized imaging pattern.

	The use of additional or increased pharmacologic or mechanical interventions directed at the treatment of heart failure includes: • Initiation of intravenous diuretic, inotropic, or vasodilator therapy • Significant addition or increase in oral heart failure therapy • Up-titration of intravenous therapy, if already on therapy • Initiation of mechanical or surgical intervention (mechanical circulatory or ventilatory support, heart transplantation or ventricular pacing to improve cardiac function), or the use of ultrafiltration, hemofiltration, or dialysis that is specifically directed at treatment of heart failure.
Not Related	Relationship can be excluded when: • the event has no temporal relationship with the use of the device or procedure; • the event does not follow a known response pattern to the device (if the response pattern is previously known) and is biologically implausible; • the discontinuation of device application or the reduction of the level of activation/e–posure - when clinically feasible – and reintroduction of its use (or increase of the level of activation/exposure), do not impact on the event; • the event involves a body-site or an organ not expected to be affected by the device or procedure; • the 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; 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
Possible	The relationship 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 where relatedness cannot be assessed or no information has been obtained should also be classified as possible.
Probable	The relationship seems relevant and/or the event cannot reasonably explained by another cause.
Causal Relationship	The event is associated 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 o the device or procedures are applied to; o the device or procedures have an effect on; • the event follows a known response pattern to the device (if the response pattern is previously known);

	• the discontinuation of 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 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 event.
Seriousness	
Serious Adverse Event (SAE)	Adverse event that led to any of the following a) Death, b) Serious deterioration in the health of the subject, users or other persons as defined by one or more of the following: 1) a life-threatening illness or injury, or 2) a permanent impairment of a body structure or a body function including chronic diseases, 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, or c) fetal distress, fetal death or a congenital abnormality or birth defect including physical or mental impairment 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. (ISO 14155)
Serious Adverse Event (SAE) – China Definition*	Any untoward medical occurrence during the clinical study: results in death or serious deterioration in health; life-threatening diseases or injuries; causing permanent damage to the body structure or function; requires hospitalization or prolongation of hospitalization; requires medical measures to prevent from persistent or significant disability/incapacity; results in fetal distress, fetal death, or congenital anomaly/birth defect. (China GCP 2022 Article 64) * The ISO 14155 definition is equivalent to SAE under China GCP 2022.
Serious Adverse Device Effect (SADE)	ADE that has resulted in any of the consequences characteristic of a SAE. (ISO 14155)
Unanticipated Adverse Device Effect (UADE)	Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death, was not previously identified in 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. (21 CFR 812.3(s))
Unanticipated Serious Adverse Device Effect (USADE)	SADE which by its nature, incidence, severity or outcome has not been identified in the current risk assessment. Note 1: Anticipated Serious Adverse Device Effect (ASADE) is an effect which by its nature, incidence, severity or outcome has been identified in the risk assessment. (ISO 14155)

Serious Health Threat	A signal from any adverse event or device deficiency that indicates an imminent risk of death or a serious deterioration in the health in subjects, users or other persons, and that requires prompt remedial action for other subjects, users or other persons. Note 1: This would include events that are of significant and unexpected nature such that they become alarming as a potential serious health hazard or possibility of multiple deaths occurring at short intervals. (ISO 14155)
Significant Safety Issue– (SSI) - Australia	A safety issue that could adversely affect the safety of participants or materially impact on the continued ethical acceptability or conduct of the trial. (NHMRC Safety monitoring and reporting in clinical trials involving therapeutic goods November 2016)
Urgent Safety Measure– (USM) - Australia	A measure required to be taken in order to eliminate an immediate hazard to a participant's health or safety. Note: This type of significant safety issue can be instigated by either the investigator or sponsor and can be implemented before seeking approval from Human Research Ethics Committee (HRECs) or institutions. (NHMRC Safety monitoring and reporting in clinical trials involving therapeutic goods November 2016).
Complication	An adverse event that includes the following is considered a complication: • Results in death, • Involves any termination of significant device function (i.e., defibrillation therapy), or • Requires an invasive intervention Non-invasive (21 CFR 812.3(k)): when applied to a diagnostic device or procedure, means one that does not by design or intention: • Penetrate or pierce the skin or mucous membranes of the body, the ocular cavity, or the urethra, or • Enter the ear beyond the external auditory canal, the nose beyond the nares, the mouth beyond the pharynx, the anal canal beyond the rectum, or the vagina beyond the cervical os Where "penetrate" means: to pass, extend, pierce, or diffuse into or through something; to enter by overcoming resistance; to gain entrance to, and "pierce" means to force a way into or through something Note (FDA): Blood sampling that involves simple venipuncture is considered non-invasive, and the use of surplus samples of body fluids or tissues that are left over from samples taken for non-investigational purposes is also considered non-invasive. Note: Only system or procedure related AEs will be classified as complication (major, minor) or observation.
Major complication	A system or procedure-related complication which results in: • Death • Lead Fracture • Hospitalization • Prolongation of an existing hospitalization by at least 48 hours • System revision (reposition, replacement, explant) Note: Only system or procedure related AEs will be classified as complication (major, minor) or observation.

<table>
<tr><td>Minor complication</td><td>Any complication that is not a major complication (e.g., event classified as a complication solely based on intravenous drug administration).
Note: Only system or procedure related AEs will be classified as complication (major, minor) or observation.</td></tr>
<tr><td>Observation</td><td>Any AE that is not a complication.
Note: Only system or procedure related AEs will be classified as “complication” (major, minor) or “observation”.</td></tr>
<tr><td colspan="2">Timing</td></tr>
<tr><td>Pre-Implant Procedure</td><td>Occurs after the ICF has been signed but before the skin incision during the Model 093000 implant procedure.</td></tr>
<tr><td>During Implant Procedure</td><td>Occurs during the Model 093000 implant procedure, after skin incision and prior to completion of skin closure.</td></tr>
<tr><td>Post-Implant Procedure</td><td>Occurs after the completion of skin closure for the Model 093000 implant procedure.</td></tr>
<tr><td colspan="2">Other</td></tr>
<tr><td>Unavoidable Adverse Event</td><td>An AE inherent to a surgical procedure that is expected to occur in all subjects for a projected duration according to the Investigator’s opinion, including, but not limited to:
<table>
<tr><th>Event Description</th><th>Timeframe (hours) from the Surgical Procedure</th></tr>
<tr><td>Anesthesia related nausea / vomiting</td><td>24</td></tr>
<tr><td>Low-grade fever (oral temperature >98.6°F (>37°C) but <100.4°F (<38.0°C))</td><td>48</td></tr>
<tr><td>Pocket site / Incisional pain</td><td>72</td></tr>
<tr><td>Mild to moderate bruising / ecchymosis</td><td>168</td></tr>
<tr><td>Sleep problems (insomnia)</td><td>72</td></tr>
<tr><td>Back pain related to laying on table</td><td>72</td></tr>
<tr><td>Shoulder pain/discomfort/stiffness related to shoulder immobilization during procedure</td><td>72</td></tr>
</table></td></tr>
<tr><td>Hospitalization</td><td>A therapeutic inpatient hospitalization (excludes observation unit, emergency room and outpatient visits) lasting greater than or equal to 24 hours.</td></tr>
<tr><td>Lead Fracture</td><td>A lead failure that results from a fracture of one or more of the conductors (visual, electrical with visual and/or fluoroscopic evidence, and/or radiographic evidence of mechanical break within the lead conductor).</td></tr>
</table>

11.5.Reporting of Adverse Events and Device Deficiencies

11.5.1. Adverse Event and Device Deficiency Classification

All reportable AEs and DDs will be reviewed by a Medtronic representative. AEs will be classified according to the definitions provided in section 11.4. For the purposes of the clinical report, Medtronic will classify each AE according to ISO 14155.

Upon receipt of AEs at Medtronic, a Medtronic representative will review the AE/DD 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 AE based on the information provided by the investigator.

Regulatory reporting of AEs and DDs will be completed according to local regulatory requirements. Refer to Table 15 for a list of required investigator and Medtronic reporting requirements and timeframes. It is the responsibility of both to abide by any additional AE reporting requirements stipulated by the EC responsible for oversight of the study.

Appendix D: Foreseeable Adverse Event List contains the list of Foreseeable Adverse Events, which is a list of AEs related to the system or procedure that have been observed in previous studies and may be experienced by subjects. This list may help to assess if an AE is unanticipated by nature.

For emergency contact regarding a UADE, USADE, SAE and/or SADE, contact a study representative immediately (refer to the study contact list provided in the study site's study documents binder/investigator site file or refer to the Sponsor contact information provided on the title page).

AEs and Deaths will be classified according to the standard definitions as outlined in Table 13.

Table 14: Adverse Event classification responsibilities

What is classified?	Who classifies?	Classification Parameters
Timing of the Event	Investigator	Pre-implant procedure, During procedure, Post-implant procedure
Relatedness	Investigator	Procedure (Index Procedure, System Modification), Outside Standard of Care Procedure, System (Device, RA Lead, Next Generation ICD Lead, LV Lead, Other RV ICD Lead, Other Lead), Accessory (Catheter, Implant Tool, Programmer), Heart Failure Related Hospitalization
	Sponsor	Procedure (Index Procedure, System Modification), Outside Standard of Care Procedure, System (Device, RA Lead, Next Generation ICD Lead, LV Lead, Other RV ICD Lead, Other Lead), Accessory (Catheter, Implant Tool, Programmer), Heart Failure Related Hospitalization
Seriousness	Investigator	SAE, DD with SADE potential
	Sponsor	SAE, UADE/USADE, DD with SADE potential
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

An independent CEC will review and adjudicate, at a minimum, all events classified by the investigator or Medtronic as procedure or system related to determine relatedness and complication (major, minor) or observation classifications. In addition, the CEC will also review and adjudicate all AEs resulting in death. A hospitalization due to heart failure will be determined by the investigator and confirmed by Medtronic. An attempt will be made to resolve any discrepancies with the investigator determination. When determining whether a USADE has occurred, where the sponsor's causality assessment conflicts with the assessment made by the site investigator, the site investigator's assessment cannot be downgraded by the sponsor (i.e., altered from 'related' to 'not related'). In this case, if an investigator's judgment triggers the reporting of a USADE, the opinion of both the investigator and the sponsor should be provided with any report sent to regulatory reporting as required.

11.5.2. Adverse Event and Device Deficiency Reporting Requirements

Regulatory reporting of AEs and DDs will be recorded and reported according to local regulatory requirements. It is the responsibility of the Investigator and the sponsor to abide by the AE reporting requirements stipulated by local law and the study site's EC. In countries following European Union Medical Device Regulation (EU MDR) 2017/745, AEs will be reported according to EU MDR 2017/745 Art. 80(2) and Medical Device Coordination Group (MDCG) 2020-10/1 guidance. Reporting requirements in Table 15 have been summarized at the time of CIP creation; however, changes may occur during the course of the study. Updates may be provided under separate cover and it is the investigator's responsibility to comply with current local regulatory and institutional reporting requirements.

Table 15: Reporting requirements

SAEs	
Investigator shall submit to:	
Medtronic	**Australia:** Without unjustified delay. (The National Health and Medical Research Council (NHMRC) Safety monitoring and reporting in clinical trials involving therapeutic goods November 2016 section C.2.b). **China:** Report to the sponsor, GCP office and the Ethics Committee within 24 hours of first acknowledge. Follow SAE per CIP requirements and submit a follow-up report (if applicable) (China GCP 2022 Article 32) **United Kingdom:** To the sponsor in acceptable timely conditions, but not later than 3 calendar days after investigational site study personnel's awareness of the event, including new information in relation to an already reported event (MEDDEV 2.7/3). **Japan:** Immediately (no later than 72 hours) (Japan GCP Article 68). **All geographies:** Report to the sponsor, without unjustified delay, all serious adverse events.
Regulatory Authority	**All geographies:** Submit to Regulatory Authority per local reporting requirement.
EC	**China:** Report to the sponsor, GCP office and the Ethics Committee within 24 hours of first acknowledge. Follow SAE per CIP requirements and submit a follow-up report (if applicable)

	(China GCP 2022 Article 32) **All geographies:** Submit to EC per local reporting requirement.
Head of Medical Institution (HOMI)	**Japan:** Immediately (Japan GCP Article 68).
GCP Offices	**China:** Report to the sponsor, GCP office and the Ethics Committee within 24 hours of first acknowledge. Follow SAE per CIP requirements and submit a follow-up report (if applicable) (China GCP 2022 Article 32)
Sponsor shall submit to:	
Investigators	**Japan:** Annually (Japan GCP Article 28).
Regulatory Authority	**Europe – countries not following EU MDR**: Immediately, but no later than 7 calendar days after awareness. **Europe – countries following EU MDR (device and/or procedure related SAEs)** see SADE section **Japan:** Annually (Enforcement Regulation of the PMDL Article 274- 2). **All geographies:** Submit to Regulatory Authority per local reporting requirement.
EC	**All geographies:** Submit to EC per local reporting requirement.
HOMI	**Japan:** Annually (Japan GCP Article 28).
ADEs	
Investigator shall submit to:	
Medtronic	**All geographies:** Submit in a timely manner after the investigator first learns of the effect.
Regulatory Authority	**All geographies:** Submit to Regulatory Authority per local reporting requirement.
EC	**All geographies:** Submit to EC per local reporting requirement.
Sponsor shall submit to:	
Regulatory Authority	**All geographies:** Submit to Regulatory Authority per local reporting requirement.
EC	**All geographies:** Submit to EC per local reporting requirement.
SADEs, UADEs, USADEs	
Investigator shall submit to:	
Medtronic	**All geographies:** Immediately after the investigator learns of the event or of new information in relation to an already reported event. **Canada (SADEs, USADEs):** SADEs and USADEs on the patient, the user or any other person must be reported to the regulator and to the Sponsor within 72 hours after it comes to the attention of the qualified investigator. **Europe (SADEs, USADEs):** To the sponsor in acceptable timely conditions, but not later than 3 calendar days after investigational site study personnel's awareness of the event, including new information in relation to an already reported event. (MDCG 2020-10/1, MEDDEV 2.7/3)

	Japan (SADEs, UADEs, USADEs): Immediately (no later than 72 hours) (Japan GCP Article 68). **Malaysia**: Within 48 hours of the occurrence of awareness. (NOTIFICATION OF EXEMPTION FROM REGISTRATION OF MEDICAL DEVICES FOR THE PURPOSE OF CLINICAL RESEARCH OR PERFORMANCE EVALUATION (MDA/GD/0016)) **US (UADEs, USADEs):** An investigator shall submit to the sponsor and to the reviewing EC a report of any UADE occurring during an investigation as soon as possible, but in no event later than 10 working days after the investigator first learns of the effect. (21 CFR 812.150(a))
Regulatory Authority	**All geographies:** Submit to Regulatory Authority per local reporting requirement **Canada (SADEs, USADEs):** SADEs and USADEs on the patient, the user or any other person must be reported to the regulator and to the Sponsor within 72 hours after it comes to the attention of the qualified investigator.
EC	**All geographies:** Submit to EC per local reporting requirement. **US (UADEs, USADEs):** An investigator shall submit to the sponsor and to the reviewing EC a report of any UADE occurring during an investigation as soon as possible, but in no event later than 10 working days after the investigator first learns of the effect. (21 CFR 812.150(a))
Institution	**Australia (USADEs):** Report USADE to their institution without undue delay and no later than 72 hours of the Principal Investigator becoming aware of the event. (NHMRC Safety monitoring and reporting in clinical trials involving therapeutic goods November 2016 section C.2.g)
HOMI	**Japan (SADEs):** Immediately (Japan GCP Article 68).
Sponsor shall submit to:	
Regulatory Authority	**All geographies:** Submit to Regulatory Authority per local reporting requirement. **Australia (USADEs):** Fatal or life-threatening Australian USADE – No later than 7 calendar days after being made aware of the case with any follow up information within a further 8 calendar days. Other Australian USADEs- No later than 15 calendar days after being made aware of the case. (NHMRC Safety monitoring and reporting in clinical trials involving therapeutic goods November 2016 section C.1.f) **Canada (SADEs, USADEs):** For USADE, as soon as possible to meet regulatory reporting requirements within 10 days after the date the sponsor becomes aware. (Immediately following confirmation a USADE notice is required and before any communication is sent). For SADEs and Device deficiencies that has resulted in SAE, as soon as possible to meet regulatory reporting requirements within 10 days after the date Medtronic becomes aware. **China:** **a) Investigational device related SAEs - death or life-threatening:** Report to competent authority within 7 days upon being informed, including - the drug regulatory departments in the province, autonomous region or municipality directly under the Central Government where the sponsor is located, - the drug regulatory departments and health administration departments in the provinces, autonomous regions or municipalities directly under the

	Central Government where the clinical trial institutions are located (China GCP 2022 Article 44) **b) Investigational device related SAEs – non death or life-threatening:** Report to competent authority within 7 days upon being informed, including - the drug regulatory departments in the province, autonomous region or municipality directly under the Central Government where the sponsor is located, - the drug regulatory departments and health administration departments in the provinces, autonomous regions or municipalities directly under the Central Government where the clinical trial institutions are located (China GCP 2022 Article 44) **c) large scale investigational device related SAEs or other serious safety issues that led to clinical study suspension or termination:** Report to competent authority, including – the drug regulatory departments in the province, autonomous region and municipality directly under the Central Government where the sponsor is located, - to the drug regulatory departments and health administration departments in the provinces, autonomous regions and municipalities directly under the Central Government where all clinical trial institutions are located. (China GCP 2022 Article 44) **Europe – countries following EU MDR (SADEs):** Any device and/or procedure related SAE immediately, but no later than 7 calendar days after awareness **Europe (SADEs with imminent risk):** Report immediately, but no later than 2 calendar days after awareness by sponsor for any device and/or procedure related SAE which indicates an imminent risk of death, serious injury, or serious illness and that requires prompt remedial action for other patients/subjects, users or other persons or a new finding to it (occurred in the study under same CIP). (EU MDR 2017/745) **Japan (SADEs):** [Life threatening or death] Individual reporting within 15 calendar days after awareness, and [All SADEs] Annually (Enforcement Regulation of the PMDL Article 274- 2) **Japan (USADEs)**: [Life-threatening or death] Individual reporting within UNECE calendar days after awareness, [Nonlife threatening or death] Individual reporting within 15 calendar days after awareness, and [All USADE] Annually. (Enforcement Regulation of PMDL Article 274-2) **US (UADEs):** Notification as soon as possible to FDA, but not later than 10 working days after the sponsor first receives notice of the effect. (21 CFR 812.150(b))
EC	**All geographies:** Submit to EC per local reporting requirement. **China:** **a) Investigational device related SAEs - death or life-threatening:** Report to other clinical trial institutions (GCP offices), the Ethics Committees and principal investigators involved in the clinical trial within 7 days upon being informed (China GCP 2022 Article 44) **b) Investigational device related SAEs – non death or life-threatening:** Report to other clinical trial institutions (GCP offices), the Ethics Committees and principal investigators involved in the clinical trial within 15 days upon being informed (China GCP 2022 Article 44)

	c) large scale investigational device related SAEs or other serious safety issues that led to clinical study suspension or termination: Report to the management department of all clinical trial institutions (common known as GCP offices), the Ethics Committees and principal investigators (China GCP 2022 Article 44) **Japan (SADEs):** Annually (Japan GCP Article 28) **Japan (USADEs):** Immediately (Japan GCP Article 28) **US (UADEs):** Notification as soon as possible, but not later than 10 working days after the sponsor first learns of the effect. (21 CFR 812.150(b))
Investigators	**All geographies:** Submit per local reporting requirement. **Japan (SADEs):** Annually (Japan GCP Article 28). **Japan (USADEs):** Immediately (Japan GCP Article 28) **US (UADEs,):** Notification as soon as possible, but not later than 10 working days after the sponsor first learns of the effect. (21 CFR 812.150(b))
GCP Offices	**China:** **a) Investigational device relate–d SAEs - death or life-threatening:** Report to other clinical trial institutions (GCP offices), the Ethics Committees and principal investigators involved in the clinical trial within 7 days upon being informed (China GCP 2022 Article 44) **b) Investigational device related SAEs – non death or life-threatening:** Report to other clinical trial institutions (GCP offices), the Ethics Committees and principal investigators involved in the clinical trial within 15 days upon being informed (China GCP 2022 Article 44) **c) large scale investigational device related SAEs or other serious safety issues that led to clinical study suspension or termination:** Report to the management department of all clinical trial institutions (common known as GCP offices), the Ethics Committees and principal investigators (China GCP 2022 Article 44)
HOMI	**Japan (SADEs):** Annually (Japan GCP Article 28) **Japan (USADEs):** Immediately (Japan GCP Article 28)
All other reportable AEs	
Investigator shall submit to:	
Medtronic	**All geographies:** Submit in a timely manner after the investigator first learns of the event.
Regulatory Authority	**All geographies:** Submit to Regulatory Authority per local reporting requirement.
EC	**All geographies:** Submit to EC per local reporting requirement.
DDs with SADE potential	
Investigator shall submit to:	
Medtronic	**All other geographies:** Submit or report as required per local reporting requirements.

	Australia: Without unjustified delay. (NHMRC Safety monitoring and reporting in clinical trials involving therapeutic goods November 2016 section C.2.b) **Canada:** DDs that have resulted in any of the consequences characteristic of an SAE on the patient, the user or any other person or could do so were it to reoccur must be reported to the regulator and the Sponsor within 72 hours after it comes to the attention of the qualified investigator. **Europe:** To the sponsor in acceptable timely conditions, but not later than 3 calendar days after investigational site study personnel's awareness of the event, including new information in relation to an already reported event. (MDCG 2020-10/1,MEDDEV 2.7/3) **Japan:** Within 30 calendar days after awareness (Enforcement Regulation of PMDL Article 274-2, section 3)
Regulatory Authority	**All geographies:** Submit to Regulatory Authority per local reporting requirement. **Canada:** DDs that have resulted in any of the consequences characteristic of an SAE on the patient, the user or any other person or could do so were it to reoccur must be reported to the regulator and the Sponsor within 72 hours after it comes to the attention of the qualified investigator.
EC	**All geographies:** Submit to EC per local reporting requirement.
HOMI, EC, PI	**Japan:** Immediately, if requested by PMDA (Japan GCP Article 68)
Sponsor shall submit to:	
Regulatory Authority	**All geographies:** Submit to Regulatory Authority per local reporting requirement. **Canada:** As soon as possible to meet regulatory reporting requirements within 30 days after the date the sponsor becomes aware. **Europe:** Immediately, but no later than 7 calendar days after awareness; Report immediately, but no later than 2 calendar days after awareness by sponsor for any DD that may have led to a SADE which indicates an imminent risk of death, serious injury, or serious illness and that requires prompt remedial action for other patients/subjects, users or other persons or a new finding/update to it (occurred in the study under same CIP). **Japan:** Within 30 calendar days after awareness and annually (Enforcement Regulation of PMDL Article 274-2)
EC	**All geographies:** Submit to EC per local reporting requirement.
Investigator	**All geographies:** Submit to investigators per local reporting requirement. **Japan:** Immediately per the direction of Pharmaceuticals and Medical Devices Agency (PMDA) and/or annually (Japan GCP Article 28)
HOMI	**Japan:** Immediately per the direction of PMDA and/or annually (Japan GCP Article 28)
All other Device Deficiencies	
Investigator shall submit to:	
Medtronic	**All geographies:** Submit in a timely manner after the investigator first learns of the deficiency.

Regulatory Authority	**All geographies:** Submit to Regulatory Authority per local reporting requirement.
EC	**All geographies:** Submit to EC per local reporting requirement.
Significant Safety Issues	
Investigator shall submit to:	
Sponsor	**Australia:** Urgent Safety Measure (USMs): Within 24 hours (NHMRC Safety monitoring and reporting in clinical trials involving therapeutic goods November 2016 section C.2.c)
EC, Institution	**Australia:** All other significant safety issues: without undue delay and no later than 72 hours of the principal investigator becoming aware of the event (NHMRC Safety monitoring and reporting in clinical trials involving therapeutic goods November 2016 section C.2.g)
Sponsor shall submit to:	
TGA	**Australia:** Urgent Safety Measure (USMs): within 24 hours (where possible) and in any case, no later than 72 hours of the measure being taken. - Reasons for the urgent safety measure, Measures taken, Further actions planned - Reasons for the termination, Measures taken, Further actions planned (NHMRC Safety monitoring and reporting in clinical trials involving therapeutic goods November 2016 section C.1.k)

11.6.Subject Death

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

In the event of a subject's death, it is recommended that the implanted system be interrogated (full interrogation), explanted, and returned to Medtronic for analysis whenever possible per local process. Local laws and procedures must be followed where applicable. 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 pseudonymized copy of the death certificate, if available and allowed by state/local law, should be sent to Medtronic. When a death occurs in a hospital, a pseudonymized copy of the death summary report and all relevant hospital records, if available, should be sent to the Medtronic clinical study team. If an autopsy is conducted, a pseudonymized copy of the autopsy report should also be sent to the Medtronic clinical study team if available and allowed by state/local law. When the death occurs at a remote study site, it is the investigative study 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 information/reports and Save-to-Media information/reports (if available)
- Device disposition information
- Pseudonymized death summary/hospital records (if available and allowed by state/local law)
- Pseudonymized autopsy report (if available and allowed by state/local law)
- Pseudonymized death certificate (if available and allowed by state/local law)

11.6.1. 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: 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 time of onset cannot be determined, Sudden Cardiac Death 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 Death Classification: Unknown death classification is intended for use only when there is insufficient or inadequate information to classify the death.

The CEC will review deaths and provide a final adjudication of the cardiac classification. See section 12.1 for handling events where the adjudication of the investigator and the CEC differ.
Regulatory reporting of Subject Deaths will be completed according to local regulatory requirements.

11.7.Product Complaint Reporting

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.
The reporting of product complaints is not part of the LEADR LBBAP study and should be done in addition to the AE/DD reporting requirements. 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. The reporting of product complaints by the clinical team must be done according to the local Standard Operating Procedures. Medtronic will notify

the Regulatory Authorities (e.g., CA) as applicable for the following incidents immediately upon learning of them and is not limited to AEs and DDs only:

- 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 withdrawal of a device from the market by the manufacturer.
- Any serious deterioration in the state of health, including:
  - Life-threatening illness or injury
  - Permanent impairment of a body function or permanent damage to a body structure
  - A condition necessitating medical or surgical intervention to prevent permanent impairment of a body function or permanent damage to a body structure

12. Data Review Committees

12.1. Clinical Events Committee Review

The study will utilize an independent CEC. The CEC Member list will be under a separate cover and available upon request. At regular intervals, the independent CEC will review and adjudicate at a minimum all system and procedure-related AEs as classified by investigator or Medtronic. Additionally, the CEC will provide an adjudication of the death classification for all reported deaths.
The CEC will consist of a minimum of three (3) non-Medtronic employed physicians whose site is not participating in the study, including a CEC chairperson.
Medtronic personnel may facilitate and participate in CEC meetings but will be non-voting members.
For AEs and deaths reviewed by the CEC, Medtronic will provide the CEC with the Investigator's description and supportive documentation (when available). The CEC is responsible for reviewing the Investigator's description, assessment and supportive documentation (when available), reviewing applicable definitions, and determining final classifications for all adjudication parameters. For AEs, classification includes system/procedure relatedness and complication (major, minor) or observation.
The CEC may use diagnostic information contained on device interrogation files as well as source data such as diagnostic tests (e.g., X-rays, Holter data), clinician notes, and data collected on eCRFs in making their classifications.
Additionally, the CEC will provide an adjudication for all reported deaths, including system/procedure relatedness and cardiac relatedness.
If the CEC disagrees with the investigator's classification of the event, the rationale will be provided to the investigator. If the investigator agrees with the CEC's adjudication, the eCRF documenting the AE will be updated accordingly.

If the investigator does not agree with the CEC's adjudication classification, both determinations will be provided within the final report; however, the CEC's adjudication will be used for data analysis. The disagreement will also be included in reporting to Ethics Committees and regulatory authorities, if required.

12.2.CRO/Core Lab(s)

This information may be subject to change during the course of the study. Periodic updates to study contact information will be sent to study sites as needed.

Table 16: CRO and Core Laboratory Information

Contact Information	Role
Echo Core Lab (contact information will be provided under separate cover upon request)	Review and analyze echocardiographic data

12.3.Episode Review Committee

An Episode Review Committee (ERC) will be established to evaluate device-treated ventricular episodes according to an ERC Charter. Committee membership, meeting frequency, roles and responsibilities and procedures will also be described in the ERC Charter. Device-treated ventricular episodes in the device episode log with EGM will be reviewed by the ERC and adjudicated based on appropriateness of therapy (shocks and ATP) delivered to subjects and success of the therapy. Inappropriate therapy will be identified based on adjudication rhythm truth and device episode log information.
This committee may include independent physicians and/or Medtronic personnel. The ERC Member list will be under a separate cover and available upon request.

12.4. Data Monitoring Committee

Ongoing oversight for this study will be provided by an independent DMC. The DMC will have one statistician, at least one physician specializing in cardiology and electrophysiology and at least one physician specializing in LBBAP. None of the DMC members are participating in the LEADR LBBAP study. A chairperson from among those members will be identified and the DMC will operate according to a charter, which is available upon request.
The DMC will be responsible for safeguarding the scientific integrity of the study and assessing the accumulating data on safety of the device/therapy and interventions during the study in the interest of study participants. To enhance the integrity of the study, the DMC may also formulate recommendations related to the selection, recruitment, and retention of subjects, their management, improvement of adherence to protocol-specified regimens and procedures for data management and quality control.

The DMC will be advisory to the sponsor. The DMC may provide recommendations for early termination of the study. In order to recommend early termination of the study for efficacy, data contributing to primary efficacy will be evaluated for futility. In addition, other considerations for early stopping for efficacy will include, but are not limited to, the magnitude of effect, primary safety and ancillary objectives, data quality, and consistency of results across subgroups. Review and consensus by the entire committee is required in order to recommend that the study should be stopped.

The DMC will monitor the AE rates of the study.

13. Statistical Design and Methods

13.1. General Aspects of Analysis

Data analysis will be performed by a Medtronic statistician or designee.

A Statistical Analysis Plan will be developed and kept under separate cover and will include a comprehensive description of the statistical methods and reports, as well as a description of how missing, unused, and spurious data will be accounted. Any change to the data analysis methods described in the CIP will require an amendment only if it changes a principal feature of the CIP. Any other change to the data analysis methods described in the CIP, and the justification for making the change, will be described in the clinical study report.

Descriptive statistics will be used to summarize the subject demographic including age, sex at birth, race, ethnicity and clinical characteristics at baseline. Data for qualitative variables will be presented as incidence rates (total number of subjects, number of events, and percent). Data for continuous variables will be summarized using measures of central tendency and dispersion.

Subject disposition will be illustrated in a CONSORT diagram. Subject visits will be tabulated and compliance to visit schedule and visit windows will be summarized. Summaries of safety data will be compiled including summaries of AEs and any subject deaths.

No imputation of missing data is planned, but missingness will be summarized as a binary variable.

Hypothesis tests will be conducted at a two-sided alpha level of 0.05 unless otherwise stated.

Analysis sets (which subjects/data are to be included in which analysis) are defined below for each objective.

Poolability assessments for sex at birth, age groups (i.e., 12- 18, 19-65 and 65+), and geographic region will be assessed for both primary objectives based on data availability. For the efficacy objective, the effect of each of these factors on defibrillation efficacy may be summarized separately using Fisher's exact tests. A Cox proportional hazards model may be carried out to evaluate the safety objective for

the subgroups. Additionally, the estimated complication rate through 6 months will be determined for each investigational site with at least five subjects.

13.2.Data Reporting

Analysis for the LEADR LBBAP study will occur when the first 150 subjects have undergone an implant attempt for LBBAP with the Next Generation defibrillation lead and have had an opportunity to have a 3-month visit, and at least 160 subjects have completed the defibrillation protocol. Analysis will include the primary efficacy and safety objectives. Ancillary objectives will be addressed based on available data.

An additional analysis will be performed once 150 subjects have undergone a LOT-CRT implant attempt for LBBAP with the Next Generation defibrillation lead and have had an opportunity to have a 6-month visit. Analysis will include the primary safety objective and all ancillary objectives, based on available data. The primary efficacy objective will not be updated for this report.

A final report will be prepared at study closure. This report will provide updated data summaries, including safety data and ancillary objectives, but inferential analysis for the primary objectives will not be updated.

DMC reports will be developed as needed for DMC meeting. Reporting to the DMC might include an open report available to the steering committee and study team. In addition, a closed report might be developed and made available only for privileged viewers.

Other reports may be generated at the request of regulatory bodies and/or for other business purposes if appropriate.

Study reports will be used for global regulatory submissions as needed.

13.3.Sample Size Determination

There are two primary objectives (safety and efficacy). The safety primary objective sample size requirement will refer to subjects who undergo an implant attempt of the Next Generation ICD Lead in the LBBAP location, while the efficacy primary objective samples size will be defined as subjects with the lead successfully implanted in the LBBAP location who complete the implant defibrillation testing protocol. Approximately 300 subjects will enroll, and final study sample size will depend on enrollment rate and timing of enrollment closure. Medtronic may decide to stop or pause ICD or LOT-CRT enrollments (in all or in specific regions), for example to manage sample size.

13.3.1. Safety Objective Sample Size Determination

The primary safety objective is to estimate the Next Generation ICD Lead-related major complication-free rate at 3 months. The sample size for this objective is not driven by formal hypothesis testing. Rather, it is sized to allow the complication-free rate to be estimated within a desired level of precision. Table 17 provides summaries of the expected confidence interval width and absolute error for these

estimates at a variety of sample sizes. The summaries are Monte Carlo approximations based on 10,000 simulations for each sample size. Complications were simulated using a piecewise exponential distribution where the assumed complication-free rate (shown in Figure 6) was 95.5% at one month and 95.0% at three months. Attrition was simulated using a Weibull distribution where the assumed attrition rate was 4% at one month and 6% at three months.

In over 80% of the simulated samples containing 150 subjects undergoing an LBBAP implant attempt, the confidence interval for the complication-free rate at 3 months was less than 10% wide and the absolute error (the distance from the point estimate to the true value of 95%) was less than 2.5%. Therefore, a sample of at least 150 subjects will be used for this objective.

Table 17: Summary of estimation performance for LBBAP-related major complication-free rate at 3 months

Number of subjects undergoing LBBAP implant attempts	Median confidence interval width	20^{th} percentile confidence interval width	80^{th} percentile confidence interval width	Median absolute error	20^{th} percentile absolute error	80^{th} percentile absolute error
100	8.67%	6.46%	10.08%	1.32%	0.78%	2.94%
150	6.98%	5.92%	7.98%	1.2%	0.46%	2.27%
200	6.08%	5.25%	6.82%	1.09%	0.37%	1.93%
250	5.45%	4.79%	6.05%	0.88%	0.38%	1.71%

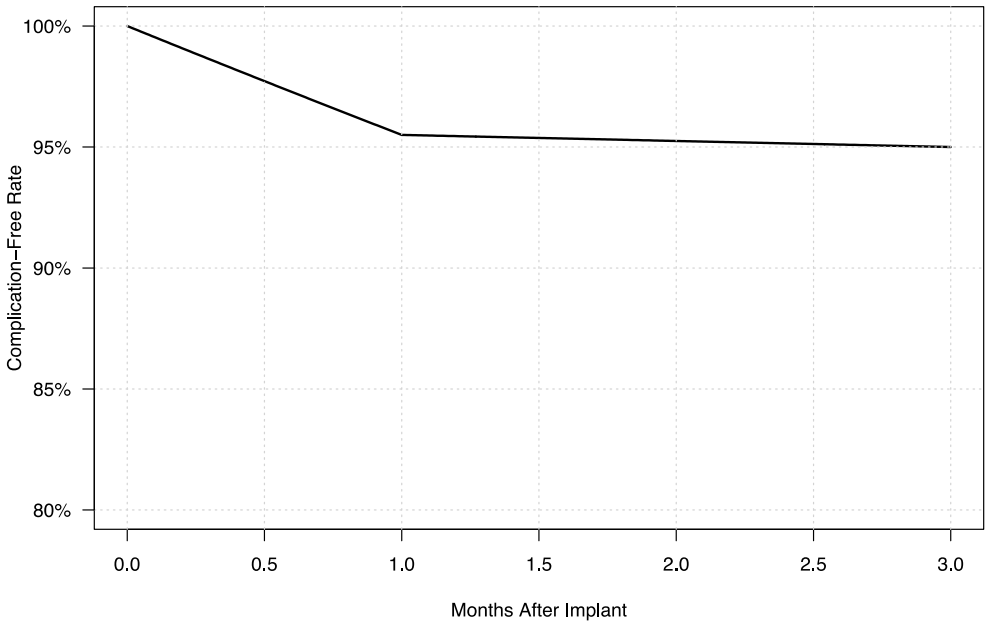


Figure 6. Assumed rate for LBBAP lead-related major complications using the Next Generation defibrillation lead.

13.3.2. Efficacy Objective Sample Size Determination

A performance goal of 88% was chosen to evaluate the primary efficacy objective metric of implant testing success defined as successfully terminating one or more induced SSVA episodes (see section 13.4.4 for more details). Each subject included in the efficacy objective analysis who completes the defibrillation protocol will be counted as a success or failure. Figure 7 shows the relationship between sample size and statistical power to pass the objective. The calculated powers are Monte Carlo approximations based on 10,000 simulations for each approximation. The assumed true defibrillation success rate is either 97.0% or 95.5%. Defibrillation success samples were generated from a Binomial distribution.

As can be seen in Figure 7, statistical power does not increase monotonically as sample size increases. However, a sample size of at least 160 subjects undergoing defibrillation testing will provide at minimum 90.4% power assuming the true success rate is 95.5% (this minimum occurs with a sample of 170 subjects). Therefore, a sample size of at least 160 subjects will be used for this objective.

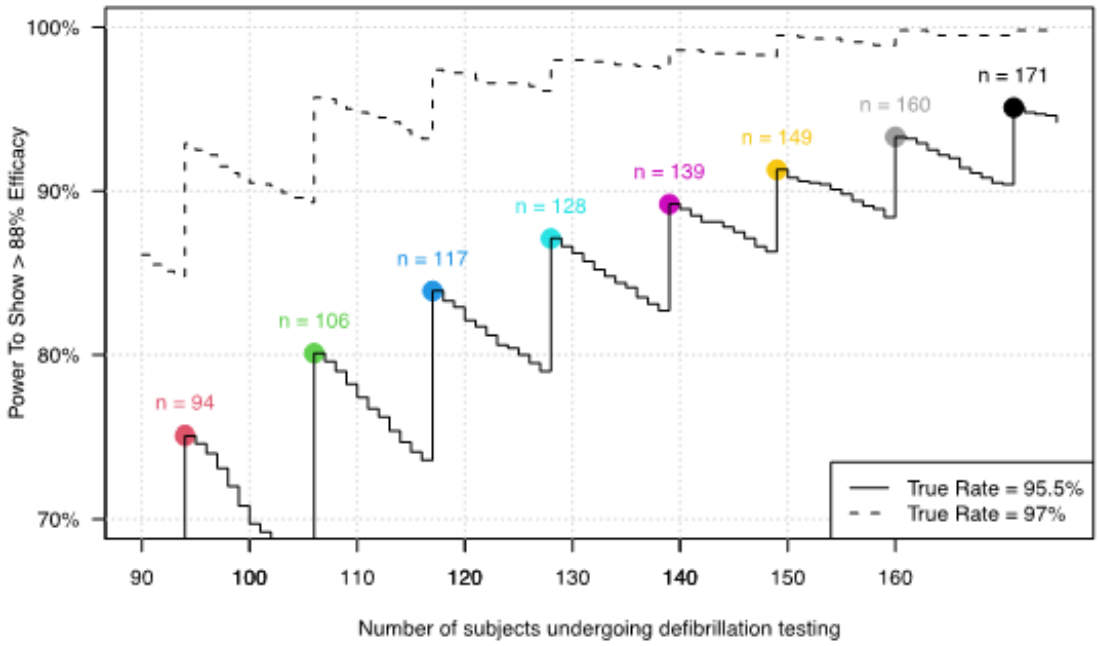


Figure 7. Power calculations for defibrillation efficacy objective.

13.4.Primary Objective #1: Efficacy

Demonstrate the percentage of patients successfully defibrillated at implant with the Next Generation ICD Lead when placed in the LBBAP location exceeds a pre-specified threshold of 88%.

13.4.1. Hypothesis

H_0: The percentage of patients successfully defibrillated at implant with the Next Generation ICD Lead when placed in the LBBAP location is ≤ 88%

H_A: The percentage of patients successfully defibrillated at implant with the Next Generation ICD Lead when placed in the LBBAP location is >88%

13.4.2. Endpoint Definition

The endpoint, defibrillation success, is defined as:

- First induced SSVA episode successfully terminated with an 18J or maximum output minus 10 Joule (M-10J) shock, or
- First therapy of the second induced SSVA episode successfully terminated with a M-10J shock, or
- First therapy after a system reposition of an induced SSVA episode successfully terminated with a M-10J shock, or
- Two consecutively induced SSVA episodes successfully terminated with a M-10J shock.

Additional requirements that must be observed during the defibrillation testing protocol are defined in Section 9.9.4.2.

13.4.3. Performance Requirements

This objective will be met if the lower bound of the two-sided 95% confidence interval for defibrillation success rate is larger than 88%.

13.4.4. Rationale for Performance Requirement

Defibrillation implant success for transvenous devices, though no longer routinely performed, has historically been shown to be as low as 88% (Table 18). Literature and other studies show multiple sources in which the defibrillation rates were less than 92%.

Table 18: Historical Transvenous ICD Defibrillation Testing Success Rates

Reference	Sample Size	Defibrillation Implant Success
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
Leong-Sit AMJ: 2006; 152:1104-8	N=168	90.5%
Pires JCE 2006; 17:1-6	Defibrillation Testing at implant (N=129) Safety Margin Testing at Implant (N=503) No Testing at Implant (N=203)	77% 93% N/A
Michowitz Europace 2011; 13:683-88	N=204	91.7%
SIMPLE Study Lancet 2015; 385:785-91	Safety Margin Testing at Implant (N=1218) No Testing at Implant (N=1227)	91.8% N/A

The threshold of 88% has also been used in pivotal trials for alternative defibrillation devices (S-ICD and EV ICD) and for the Next Generation ICD lead via the LEADR study that is also used in this study, so there is precedent for an OPC of 88% being considered an acceptable criterion for evaluating termination of induced ventricular rhythms at implant. The S-ICD literature shows acute defibrillation testing results less than 93% when testing at 65J (applying a 15J safety margin), and the results of the EV ICD study show an estimated 98.7% defibrillation success rate based on 302 subjects completing defibrillation testing.[45]

13.4.5. Analysis Methods

The point estimate of the success rate will be calculated by dividing the number of subjects meeting the endpoint defined in Section 13.4.2 by the number of subjects included in the analysis as defined in Section 13.4.6. A two-sided 95% confidence interval of the defibrillation success rate will be constructed using the exact Binomial method.

Descriptive statistics will also be used to summarize the results, including summaries based on when a patient was successfully defibrillated, i.e. during the first episode, during the second episode, etc.

Finally, a tipping point analysis will be performed to assess the robustness of the result to missing data. Subjects, who attempted defibrillation testing (i.e. had at least one induced episode) but did not complete defibrillation testing, will be included in the tipping point analysis. Subjects that did not undergo defibrillation testing will not be included in this analysis.

13.4.6. Determination of Subjects for Analysis

The primary evaluation of this objective will include all subjects that:

- Are implanted with the Next Generation ICD lead in the LBBAP location throughout defibrillation testing as determined by the LBBAP implant success criteria described in 9.9.2, and
- Complete the defibrillation testing protocol per section 9.9.4.

It is expected that, based on physician discretion, not all enrolled subjects with a successful LBBAP implant will complete defibrillation testing.

Subjects who start but cannot complete the defibrillation protocol for reasons such as an insufficient number of episodes being inducible will be reported separately. However, these subjects will be included in a tipping point analysis as described above.

13.5.Primary Objective #2: Safety

Estimate the Next Generation ICD Lead-related major complication rate at 3-months post implant when the Next Generation ICD Lead implant is attempted in the LBBAP location.

13.5.1. Hypothesis

This objective does not involve testing a hypothesis.

13.5.2. Endpoint Definition

The endpoint is defined as a subject's first occurrence of a major complication related to the Next Generation ICD Lead placed in the LBBAP location or the implant attempt at the LBBAP location as determined by an independent CEC, that occurs on or prior to 3 months (90 days) post-implant.

For an AE to meet the endpoint, the event must have occurred within 90 days (inclusive) of the Next Generation ICD Lead implant attempt and be adjudicated by the CEC as being a major complication related (causal relationship) to the Next Generation ICD Lead placed in the LBBAP location or the implant attempt at the LBBAP location. Major complications are those complications resulting in:

- Death
- Lead Fracture
- Hospitalization (in-patient)
- Prolongation of an existing hospitalization by at least 48 hours
- System Revision (reposition, replacement, explant)

13.5.3. Analysis Methods

The point estimate for the complication rate will be based on a Kaplan-Meier curve, generated using each subject's time to first Next Generation ICD Lead -related major complication or time to last exposure to the Next Generation ICD Lead if a subject does not have a major complication, in which case the subject will be censored. Last exposure to the Next Generation ICD Lead will be defined as the date of their pre-hospital discharge visit, last follow-up visit, study exit date (if exited for reason other than lost-to-follow-up), or date of death, whichever is last. Additionally, if a subject has an explant of the Next Generation ICD Lead that is not related to a Next Generation ICD Lead major complication the subject will have their last exposure date set to their explant date. All subjects undergoing an implant attempt of the Next Generation ICD Lead will be included in the analysis.

Results will also be summarized in aggregate using descriptive statistics, including the total number of major complications experienced by subjects for whom an implant is attempted. Kaplan-Meier curve estimates will be provided for follow-up time points past 3 months based on availability of data if number at risk is greater than 30.

13.5.4. Determination of Subjects for Analysis

All subjects attempting an implant with the Next Generation ICD Lead in the LBBAP location will be included.

13.6. Ancillary Objective(s)

There are no hypotheses for the ancillary objectives. They are descriptive in nature and intended to provide additional information about the Next Generation ICD lead.

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13.7. Minimization of Bias

Selection of subjects, treatment of subjects, and evaluation of study data are potential sources of bias. Methods incorporated in the study design to minimize potential bias include (but are not limited to):

- Subject demographics and comorbidities will be collected at baseline to later assess possible characteristics that may influence endpoints
- Data collection requirements and study procedures will be standardized
- A statistical analysis plan will be developed prior to analyzing data which will document all prespecified analyses and analysis methods
- All study clinicians will be trained on and required to follow the CIP
- All study clinicians and Medtronic personnel will be trained on their respective aspects of the study using standardized training materials
- An independent CEC will be utilized to regularly review and adjudicate reported AEs
- An ERC containing independent reviewers will be utilized to review and adjudicate device-treated episodes to determine appropriateness of therapy (shocks and ATP) delivered to subjects
- An independent Data Monitoring Committee (DMC) will be utilized to review accumulating data, help safeguard the interests of study subjects, and monitor the overall conduct of the study
- All sites will use the same version of the CIP and standardized eCRFs when possible
- All study investigators will be required to meet 21 CFR Part 54, Financial Disclosure by Clinical Investigators
- Monitoring visits will be conducted to verify adherence to the CIP and source data

In summary, potential sources of bias that may be encountered in this study have been considered and minimized by careful study design.

14. Ethics

14.1.Statement(s) of Compliance

The LEADR LBBAP study was designed to reflect the Good Clinical Practice (GCP) principles outlined in ISO 14155 and other international clinical requirements outlined below. These include the protection of the rights, safety and well-being of human subjects, controls to ensure the scientific conduct and credibility of the clinical investigation and the definition of responsibilities of the sponsor and investigators. In accordance with ISO 14155, the sponsor shall avoid improper influence on, or inducement of, the subject, monitor, any investigator(s) or other parties participating in, or contributing to, the clinical investigation. All investigators shall avoid improper influence on or inducement of the subject, sponsor, monitor, other investigator(s) or other parties participating in or contributing to the clinical investigation. AE and DD handling in the LEADR LBBAP study is ISO 14155 compliant for all participating geographies.

The principles of the Declaration of Helsinki (DoH) have been implemented through the IC process, EC approval, study training, clinical trial registration, pre-clinical testing, risk-benefit assessment and publication policy.

Ultimately, all study sites in all geographies will follow and comply with:

- Principles of DoH
- 21 CFR Part 11 (Electronic Records, Electronic Signatures)
- 21 CFR Part 54 (Financial Disclosure by Clinical Investigators)
- The CTA, MSA, or MCTA with associated WO
- The procedures described within this CIP
- Local EC Requirements
- Local regulations

In addition to the regulatory requirements outlined above, the study will be conducted according to federal, national and local laws, regulations, standards, and requirements of the countries/geographies where the study is being conducted. These include but are not limited to:

- In Australia the study will be conducted in compliance with:
  - ISO 14155
- In Canada the study will be conducted in compliance with:
  - SOR/98-282, Medical Device Regulations
- In Mainland China the study will be conducted in compliance with:
  - China GCP 2022

- Announcement of CFDA on Filing of the Medical Device Clinical Trial (2015, No.87)
- In Europe, Middle East and Africa the study will be conducted in compliance with:
  - ISO 14155
  - Local regulations
- In Hong Kong the study will be conducted in compliance with:
  - ISO 14155
- In Japan the study will be conducted in compliance with:
  - Ministerial Ordinance Concerning Good Clinical Practice for Medical Devices (The Ministry of Health, Labour and Welfare (MHLW) Ministerial Ordinance No.36 in 2005)
- In Malaysia the study will be conducted in compliance with:
  - ISO 14155
  - Notification of Exemption from Registration of Medical Devices for the Purpose of Clinical Research or Performance Evaluation (MDA/GD/0016)
- In the US, the study will be conducted under an FDA IDE-S in compliance with 21 CFR Parts:
  - 50: Protection of Human Subjects
  - 54: Financial Disclosure by Clinical Investigators
  - 56: IRBs
  - 812: IDEs

The study will be referenced under the existing LEADR IDE public registration prior to subject recruitment in accordance with the 2007 Food and Drug Administration Amendments Act (FDAAA) and DoH on http://clinicaltrials.gov (PL 110-85, section 810(a)). In addition, the study may be registered in local regulatory databases where required by local law.

For US sites, the LEADR LBBAP protocol will be submitted as an supplement to the LEADR study (G210150) as part of Continued Access. The LEADR LBBAP study will remain separate from LEADR in terms of reporting requirements and follow the reporting requirements as described within this CIP.

Approval of the CIP and CIP amendments is required from the following groups prior to any study procedures at a study site:

- Medtronic
- Principal Investigators (where required by local law/regulations)
- Geography-specific regulatory authorities (if regulatory approval is required)
- An independent medical EC

Similarly, approval of subsequent revisions to the CIP is required at each study site from the above-mentioned groups prior to implementation of the revised CIP at the study site.

15. Study Administration

15.1. 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 or remote to ensure the study is conducted in accordance with the CIP, the CTA, MSA, or MCTA with associated WO, and the applicable regulatory and local requirements. Medtronic, or delegates, must therefore be allowed direct access to the subjects' case histories (clinic and hospital records, and other source data/documentation) upon request as per the ICF, Research Authorization to Use and Disclose Personal Health Information/Research Authorization/HIPAA/other privacy language (where applicable) and the CTA, MSA, or MCTA with associated WO. The Principal Investigator should also be available during monitoring visits.

15.1.1. Monitoring Visits

Frequency of monitoring visits may be based upon subject enrollment, study compliance, number of AEs, number of deviations, observations from previous monitoring visits and any suspected inconsistency in data that requires investigation. Regulatory documents will be reviewed for each study site. Monitoring for the study, including site initiation visits, interim monitoring visits, and closeout visits, will be done in accordance with the study-specific monitoring plan.

Monitoring visits may be conducted periodically to assess study site progress, the investigator's adherence to the CIP, regulatory compliance including but not limited to EC approval and review of the study, maintenance of records and reports, and review of source documents against subject eCRFs in accordance with the study-specific monitoring plan. Monitors review site regulatory and study compliance by identifying observations of non-compliance and communicating those observations 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.

15.2. Data Management

Data will be collected using an electronic data management system for 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 study 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 in accordance with applicable regulations.

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 pseudonymize for instance, where the subject's name cannot be removed from the data carrier, such as fluoroscopy images.
Procedures in the CIP require source documentation. Source documentation will be maintained at the study site. Source documents, which may include subject worksheets, subject medical records, programmer printouts, and interrogation files, must be maintained by the investigational study site team.
The investigator will clearly mark clinical records to indicate that the subject is enrolled in this clinical investigation.
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. See section 9.22 for eCRFs and data collection elements that may be considered source.
Device data from transmissions will be uploaded to secure servers. Save-to-media/Save Reports files and other non-eCRF data such as radiographs and fluoroscopies collected via electronic media at office visits will be sent to Medtronic. Upon receipt, via transmission or electronic media, non-eCRF data will be maintained and stored, and retrieved for analysis and reporting.

15.3.Direct Access to Source Data/Documents

Medtronic may conduct audits at participating study sites. The purpose of an audit is to verify the performance of the monitoring process and the study conduct, independently of the personnel directly involved in the study. Regulatory Authorities, such as the FDA, may also perform inspections at participating study sites. The investigator and/or institution shall permit Medtronic, ECs and Regulatory Authorities direct access to source data and documents during monitoring, audits and regulatory inspections.

15.4.Confidentiality

All information and data sent to parties involved in study conduct concerning subjects or their participation in this study will be considered confidential. Study sites will be provided a unique SID to each subject. Records of the SID relationship will be maintained by the study site. The SID number is to be recorded on all study documents to link them to the subject's medical records at the study site. Confidentiality of data will be observed by all parties involved at all times throughout the clinical investigation. All data shall be secured against unauthorized access. The privacy of each subject and confidentiality of their information shall be preserved in reports, when publishing any data, and when developing potential future training/education materials. In the US, "Protected Health Information" (PHI) will be maintained in compliance with the HIPAA of 1996. To maintain confidentiality, the subject's name or any other PHI should not be recorded on any study document other than the ICF. This scenario will be covered in the ICF. In the event a subject's name/PHI is included for any reason, it will be blinded as applicable. In the event of inability to blind the identification (e.g., digital media), it will be handled in a confidential manner by the authorized personnel. Data relating to the study might be made available

to third parties (for example in case of an audit performed by Regulatory Authority), provided the data are treated as confidential and that the subject's privacy is guaranteed. No identifiable subject information will be published.

15.5.Liability/Insurance Information

15.5.1. Insurance (Australia)

Medtronic Australasia Pty Ltd is a wholly owned subsidiary of Medtronic, which as the parent company of such entity maintains appropriate clinical study 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 Study insurance statement/certificate will be provided to the EC.

15.5.2. Insurance (Canada)

Medtronic Canada ULC is a wholly owned subsidiary of Medtronic, which as the parent company of such entity maintains appropriate general 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 General Liability insurance statement/certificate will be provided to the EC.

15.5.3. Insurance (China)

Medtronic (Shanghai) Management Co., Ltd is a wholly owned subsidiary of Medtronic, which as the parent company of such entity maintains appropriate clinical study 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 General Liability insurance statement/certificate will be provided to the EC.

15.5.4. Insurance (Europe, Middle East, Africa)

Medtronic Bakken Research Center B.V. is a wholly owned subsidiary of Medtronic, which as the parent company of such entity maintains appropriate clinical study 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 EC.

15.5.5. Insurance (Hong Kong)

Medtronic Hong Kong Medical Ltd. is a wholly owned subsidiary of Medtronic, which as the parent company of such entity 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 EC.

15.5.6. Insurance (Japan)

Medtronic Japan Co., Ltd. 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. A documentation explaining compensation to the subjects in the event of study-related injuries and if required, a Clinical Trial insurance statement/certificate will be provided to the study site for the review of EC.

15.5.7. Insurance (Malaysia)

Medtronic Malaysia Sdn Bhd is a wholly owned subsidiary of Medtronic, which as the parent company of such entity 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 EC.

15.5.8. Insurance (US)

Medtronic maintains appropriate clinical study 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 study insurance statement/certificate will be provided to the EC.

15.6.CIP Amendments and Addenda

Any revisions or amendments to the CIP or ICF, along with a statement of justification for the changes, will be submitted to all affected Regulatory Authorities (e.g., FDA, Competent Authority (CA)) and governing ECs, according to applicable regulations. All amendments to the CIP shall be agreed upon between Medtronic and the principal investigator(s), or the coordinating investigator. Approval by regulatory agencies and ECs (where applicable) must be obtained prior to implementing a revision at the study site.

Requests from ECs and/or CAs can be stipulated in an addendum applicable to a site or country upon mutual agreement between sponsor and the EC and/or CA.

15.7.Record Retention

All study-related documents must be retained for a period of at least 2 years after market-release in each region and after study closure (or longer if required by local law). Medtronic will inform the investigator/study site about the document retention period at site closure.

No study document or image will be destroyed without prior written agreement between Medtronic and the investigator. The investigator should take measures to prevent accidental or premature

destruction of documents. Should the investigator wish to assign the study records to another party or move them to another location, advance written notice must be given to Medtronic.
Medtronic will retain the study records according to Medtronic corporate policy and record retention schedule.
For China, clinical study institutions shall keep the clinical study data for at least ten years after the completion of clinical studies, and the sponsor shall keep clinical studies essential documents till no such medical device is used.

15.7.1. Investigator Records

The investigator (or in Japan the study site) is responsible for the preparation and retention of the records cited below. All of the below records, with the exception of case history records and eCRFs, should be kept in the ISF (e.g., the study binder provided to the investigator or electronic equivalent provided to the investigator through Veeva SiteVault if used by the site) or Subject Study Binder. eCRFs must be maintained and signed electronically within the electronic data capture system during the study. The following records are subject to inspection and must be retained for a period of two years (or longer as local law or hospital administration requires) after product approval or the date on which the investigation is terminated:

- All correspondence between the EC, sponsor, monitor, FDA, Regulatory Authority and the investigator that pertains to the investigation, including required reports.
- Subject's case history records, including:
    - Signed and dated ICF in accordance with local requirements
    - Observations of AEs/ADEs/DDs
    - Medical history
    - Implant and follow-up data (if applicable)
    - Documentation of the dates and rationale for any deviation from the CIP
- Subject Identification and Enrollment Log (if applicable)
- List of investigation study sites
- Financial disclosure
- All approved versions of the CIP, ICF and other information given to the subject, and Investigator's Brochure
- Electronically signed and dated eCRFs and a blank set of CRFs when required by local regulations
- Signed and dated CTA, MSA, or MCTA with associated WO
- Current CV of Principal Investigator and key members of the investigation study site team (as required)
- Documentation of delegated tasks
- Ethics Committee approval documentation. Written information that the investigator or other study staff, when member of the Ethics Committee, did not participate in the approval

process. Approval documentation must include the Ethics Committee composition, where required per local law.

- Regulatory authority notification, correspondence and approval, where required per local law
- Study training records for study site staff
- Insurance certificate (if applicable per local law)
- Shipping records of investigational devices
- Equipment maintenance records, if applicable
- Any other records that FDA and local regulatory agencies require to be maintained
- Final Study Report including the statistical analysis

15.7.2. Sponsor Records

Medtronic shall maintain the following accurate, complete, and current records:

- All correspondence which pertains to the investigation
- Investigational device traceability records
- Sample of label attached to investigational device
- Signed CTA, MSA, or MCTA with associated WO
- Financial disclosure
- Current CV of Principal Investigator and key members of the investigation study site team (as required)
- Delegated task list
- All approved ICF templates, and other information provided to the subjects such as advertisement, including translations
- Copies of all Ethics Committee approval letters, relevant Ethics Committee correspondence and Ethics Committee voting list/roster/letter of assurance
- Names of the institutions in which the clinical study will be conducted
- Regulatory authority correspondence, notification and approval as required by national legislation
- Insurance certificates (if applicable per local law)
- Names/contact addresses of monitors
- Monitoring visit reports
- Statistical analyses and underlying supporting data
- Final report of the study
- The CIP, Investigator's Brochure and study related reports, and revisions
- eCRFs, including AE and DD forms and eCRF corrections
- Study training records for site personnel and Medtronic personnel involved in the study
- Any other records that local regulatory agencies require to be maintained

Medtronic records and reports will be maintained in a password-protected document management system, and paper documents (where applicable) will be stored in secured file cabinets at Medtronic during the course of this study.
After closure of the study, Medtronic will archive records and reports per Medtronic procedures and applicable regulations.

15.8.Reporting Requirements

15.8.1. Investigator Reports

The investigator is responsible for the preparation (review and signature) and submission to the sponsor of all eCRFs, including AEs and adverse device effects (reported per the country-specific collection requirements), device deficiencies, deaths, and any deviations from the CIP. If any action is taken by an Ethics Committee with respect to this clinical study, copies of all pertinent documentation must be forwarded to Medtronic in a timely manner. Reports are subject to inspection and to the retention requirements as described above for investigator records.
Safety data investigator reporting requirements are listed in section 11.5.2. The investigator shall prepare and submit in a complete, accurate and timely manner the reports listed in this section.

Table 19: Investigator reports applicable for all geographies per Medtronic requirement

Report	Submit to	Description/Constraints
Withdrawal of EC approval	Sponsor and Relevant Authorities	The investigator must report a withdrawal of approval by the reviewing EC of the investigator's part of the investigation within 5 working days.
Study Deviations	Sponsor and EC	Any deviation from the clinical investigational plan shall be recorded together with the explanation of the deviation. Notice of deviations from the CIP to protect the life or physical well-being 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.
Final Report	ECs and Relevant Authorities	This report must be submitted within 3 months of study completion or termination.

Table 20: Investigator reports applicable to the United States per FDA regulations

Report	Submit to	Description/Constraints
Withdrawal of EC approval (either suspension or termination)	Sponsor	The investigator must report a withdrawal of approval by the reviewing EC of the investigator's part of the investigation within 5 working days. (21 CFR 812.150(a)(2))
Progress report	Sponsor and EC	The investigator must submit this report to the sponsor and EC at regular intervals, but in no event less than yearly intervals. (21 CFR 812.150 (a)(3)).
Study deviations	Sponsor and 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, the EC, and the FDA/applicable Regulatory Authority. If the deviation does not affect these issues then only Medtronic must approve it. (21 CFR 812.150(a)(4))
Failure to obtain IC prior to investigational device use	Sponsor and ECs	If an investigator uses a device without obtaining IC, the investigator shall report such use within 5 working days after device use. (21 CFR 812.150(a)(5))
Final report	Sponsor ECs Relevant Authorities	This report must be submitted within 3 months of study completion or termination of the investigation or completion or termination of the investigator's part of the investigation. (21 CFR 812.150(a)(6))
Other	EC and FDA	An investigator shall, upon request by a reviewing EC, FDA or any other Regulatory Authority, provide accurate, complete, and current information about any aspect of the investigation. (21 CFR 812.150(a)(7))

Table 21: Investigator reports applicable to Europe, Middle East and Africa per ISO 14155

Report	Submit to	Description/Constraints
Withdrawal of EC approval	Sponsor	Report if required by local law.
Progress Report	Sponsor and EC	Provide if required by local law or EC.
Study Deviations	Sponsor, Competent Authority and EC	Any deviation from the CIP shall be recorded together with an explanation for the deviation. Deviations shall be reported to the sponsor who is responsible for analyzing them and assessing their significance. Note: When relevant, ECs, CAs or the appropriate Regulatory Authorities should be informed. (ISO 14155)
Failure to obtain IC	Sponsor and ECs	IC shall be obtained in writing and documented before a subject is enrolled into the clinical investigation. (ISO 14155)

Table 22: Investigator (study site) reports applicable to Japan

Report	Submit to	Description/Constraints
Withdrawal of EC approval	Sponsor and the Principal Investigator	The Head of Institution shall notify the principal investigator and the sponsor, including promptly issuing written instructions and decision based on the EC, along with a copy of the dated cancellation document of the EC. In addition, the Head of Institution shall explain in detail and in writing the decision of the EC to the principal investigator and the sponsor. (MHLW Ordinance 36, Article 51)
Progress Report	The Head of Institutions	The investigator shall submit written summaries of the status of the clinical study to the Head of Institution annually, or more frequently if requested by the EC. The Head of Institution shall submit to the EC for the appropriateness of continuing the clinical study. (MHLW Ordinance 36, Article 68)
Study Deviations	Sponsor and the Head of Institutions	The investigator may implement a deviation from, or a change in, the protocol to eliminate an immediate hazard(s) to study subjects without prior EC approval. In this case, the investigator shall immediately submit to the sponsor, the Head of Institution, and to the EC via the Head of Institution, the description and reason for the deviation and the proposed revision to the protocol, if one is necessary, to receive agreement. It is the document submitted to the EC via the Head of Institute to discuss the appropriateness of continuing the clinical study. All deviations, regardless of the reason, shall be recorded. (MHLW Ordinance 36, Article 66)
Suspension, Termination and Completion Report	The Head of Institutions	When suspending or terminating a clinical study at his or her discretion, the principal investigator shall promptly report thereof and submit the details therefore in writing to the Head of Institution. Upon completion of a clinical study, the principal investigator shall report thereof in writing and submit a summary of the results of the clinical study to the Head of Institution. (MHLW Ordinance 36, Article 69)

Table 23: Investigator reports applicable to China per China GCP 2022

Report	Submit to	Description/Constraints
Progress reports	EC	Principal investigators shall report the progress of clinical trials of medical devices to the Ethics Committee on time. (China GCP 2022 Article 34)
Suspension, termination	GCP office, Sponsor and EC	Investigators shall promptly report safety information in clinical trials of medical devices: (II) When the risks in clinical trials of medical devices are identified to outweigh the possible benefits and it is indeed necessary to suspend or terminate the clinical trials, principal investigators shall report to the sponsor, the regulatory department of the clinical trial institution of medical devices and the Ethics Committee. In addition to informing the subjects in time, they shall also ensure that the subjects could receive appropriate treatment and follow-up visits. (China GCP 2022 Article 32(II))
Protocol deviation	EC	Principal investigators shall report any deviation from the clinical trial protocol in time. (China GCP 2022 Article 34)
Site-specific summary	Sponsor	For multi-site studies: The site-specific summary of each sub-site shall be signed and dated by the principal investigator of the site, reviewed and signed by the clinical trial institution of medical device of the site, and then submitted to the sponsor. The site-specific summary of clinical trials in sub-sites mainly includes personnel information, information of investigational medical devices and control medical devices (if applicable), trial overview, case inclusion, implementation of clinical trial protocol, summary and descriptive analysis of trial data, quality management of clinical trials of medical devices, occurrence and treatment of adverse events and device defects, description of deviation from the protocol, etc. (China GCP 2022 Article 56)

Table 24: Investigator reports for Australia

Report	Submit to	Description/Constraints
Study Deviations	Sponsor and EC	Report any suspected breaches to the sponsor and confirmed serious breaches to their institution (research governance office) within 72 hours of being aware or notified of the same; provide any follow-up information as required and work with the institution or sponsor, as appropriate, to implement any corrective and preventative actions. Australia - Serious Breach: A breach of Good Clinical Practice or the protocol that is likely to affect to a significant degree: a) The safety or rights of a trial participant, or b) The reliability and robustness of the data generated in the clinical trial. Note: this guidance's definition of serious breach differs from the definition in the Australian Code for the Responsible Conduct of Research and is about deviations from the requirements of Good Clinical Practice or the clinical trials protocol. (NHMRC Reporting of Serious Breaches of Good Clinical Practice (GCP) or the Protocol for Trials Involving Therapeutic Goods 2018

15.8.2. Sponsor Reports

Medtronic shall prepare and submit the following complete, accurate, and timely reports listed in the tables below (by geography). In addition to the reports listed below, Medtronic shall, upon request of the reviewing EC, Regulatory Authority or FDA, provide accurate, complete and current information about any aspect of the investigation. Safety data Medtronic reporting requirements are listed in section 11.5.2.

Table 25: Sponsor reports for Australia

Report	Submit to	Description/Constraints
Premature termination or suspension of the clinical investigation	Investigators, EC, and relevant authorities	Provide prompt notification of termination or suspension and reason(s). (ISO 14155)
Recall and device disposition	Investigators, Head of Institution, EC, relevant authorities, and FDA	Notification as per local requirements.
Study deviation	Investigators, EC	Ensure that all deviations from the CIP are reviewed with the appropriate clinical investigator(s), are reported on the CRFs and the final report of the clinical investigation. (ISO 14155) Study site specific study deviations will be submitted to investigators periodically. Report serious breaches to the reviewing HREC and PI within 7 calendar days of confirming a serious breach has occurred and provide follow-up when required. (NHMRC Reporting of Serious Breaches of Good Clinical Practice (GCP) or the Protocol for Trials Involving Therapeutic Goods 2018)
Withdrawal of approval by TGA or HREC or approving authority	TGA, HREC	Notify TGA of withdrawal of ethics approval. In case of revocation of CTN or CTX approval status by TGA, sponsor to notify HREC and sites. In case of withdrawal of authorization from approving authority, communicate information to the HREC and to TGA (Australian Clinical Trial Handbook, version 2.4, Aug 2021)
Completion of clinical trial	TGA	Notify TGA of the completion of a clinical trial after the trial has been completed at all sites along with the reason the clinical trial ceased (e.g., concluded normally, insufficient recruits, etc.) (Australian Clinical Trial Handbook, version 2.4 Aug 2021)
Annual safety reports, single case adverse events, clinical study report	TGA	Submit upon request from TGA (Australian Clinical Trial Handbook, version 2.4, Aug 2021)

Report	Submit to	Description/Constraints
USADEs for Australia and international / safety report / updated IB / approved product information	Investigator and HREC	Per EC requirements, but at least annually: • Annual safety report including: a summary of the evolving safety profile of the trial, a brief description and analysis of new/relevant findings, implications of safety data to the risk-benefit ratio for the trial, a description of any measures taken or proposed to minimize risks (NHMRC Safety monitoring and reporting in clinical trials involving therapeutic goods, November 2016, section C.1.i) • An updated/addenda of IB or IFU, if appropriate (e.g., when an IB is no longer maintained) (NHMRC Safety monitoring and reporting in clinical trials involving therapeutic goods, November 2016, section C.1.h)
Action with respect to safety that has been taken by another country's regulatory agency (relevant to an ongoing clinical trial in Australia)	TGA	Without undue delay and no later than 72 hours of the trial sponsor becoming aware of the action (Australian Clinical Trial Handbook, version 2.4, Aug 2021)

Table 26: Sponsor reports Canada

Report	Submit to	Description/Constraints
Premature termination or suspension of the clinical investigation	Investigators and EC, relevant authorities	In the event of the premature discontinuation of a study in its entirety or at a study site for which an ITA or ITA revision has been issued in Canada, the manufacturer or importer should notify Health Canada as soon as possible, but no later than fifteen (15) calendar days after the date of discontinuation.
Resumption of trial	Investigators and relevant authorities	Submit to Health Canada prior to resumption of trial or site.
Recall and device disposition	Investigators, Head of Institution, EC, relevant authorities, and Health Canada	Notification within 30 working days and will include the reasons for any request that an investigator return, repair, or otherwise dispose of any devices.
Study deviation	Investigators	Ensure that all deviations from the CIP are reviewed with the appropriate clinical investigator(s), are reported on the CRFs and the final report of the clinical investigation. Study site specific study deviations will be submitted to investigators periodically.

Report	Submit to	Description/Constraints
Final report	Investigators, EC, and Health Canada	A final report will be submitted to investigators, ECs, and Health Canada after completion or termination of the clinical study.

Table 27: Sponsor reports for China per China GCP 2022

Report	Submit to	Description/Constraints
Closeout, premature termination or suspension of the clinical investigation	PIs, EC, GCP office, Relevant authorities	The sponsor shall report in writing to all principal investigators, regulatory departments of clinical trial institutions of medical devices and the Ethics Committee within 10 working days after the suspension, termination or completion of the clinical trial. The sponsor shall report to the drug regulatory departments of the province, autonomous region or municipality directly under the Central Government where the sponsor is located within 10 working days after the termination or completion of the clinical trial of medical devices. (China GCP 2022 Article 48) The sponsor shall evaluate and report the safety information during clinical trials of medical devices: (II) In case of any serious adverse events on the medical device under clinical trial on a large scale or any other major safety problems, the sponsor shall suspend or terminate clinical trials of medical devices and report to the regulatory department of all clinical trial institutions of medical devices, the Ethics Committees and principal investigators, to the drug regulatory departments in the province, autonomous region and municipality directly under the Central Government where the sponsor is located, and to the drug regulatory departments and health administration departments in the provinces, autonomous regions and municipalities directly under the Central Government where all clinical trial institutions of medical devices are located. (China GCP 2022 Article 44(II))

Table 28: Sponsor reports for Europe, Middle East and Africa

Report	Submit to	Description/Constraints
Premature termination or suspension of the clinical investigation	Investigators, EC, Relevant authorities and Head of the Institution	Provide prompt notification of termination or suspension and reason(s). (ISO 14155) For EU MDR compliant countries and Switzerland only: Competent Authorities will be notified in case of a temporary halt or early termination of the clinical investigation within 15 days (24 hours if based on safety grounds).
Withdrawal of EC approval	Investigators, Head of Institution, EC and relevant authorities	Investigators, ECs will be notified only if required by local laws or by the EC.
Withdrawal of CA approval	Investigators, Head of Institution, EC, and relevant authorities	Investigators, ECs will be notified only if required by local laws or by the EC.
Progress Reports	EC and regulatory authorities	This will be submitted to the EC and/or regulatory authorities (if required).
Final report	Investigators, EC, and regulatory authorities if required	For ISO 14155 compliant countries: • 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 principal Investigator in each study site should be obtained. (ISO 14155) For EU MDR compliant countries and Switzerland only: This report must be submitted within one year of the end of the clinical investigation or within 3 months of early trial termination or temporary halt. The report shall be accompanied by a summary that is easily understandable to the intended user.
Study deviation	Investigators and CA (if required)	Ensure that all deviations from the CIP are reviewed with the appropriate clinical investigator(s), are reported on the CRFs and the final report of the clinical investigation. (ISO 14155) Study site specific study deviations will be submitted to investigators periodically.

Report	Submit to	Description/Constraints
Study deviations (UK only)	MHRA	All deviations relating to UK study sites only must be reported to the MHRA (medicines and Healthcare products Regulatory Agency) by the manufacturer (Sponsor) as soon as they have been made aware of them. Details about the nature of the deviation, when it occurred and any proposed corrective and preventive actions should be provided.
End of clinical investigation	Investigators, Regulatory authorities	This will be notified to the IRB/EC/CA only if required by the IRB/EC/CA. For EU MDR compliant countries: notify the end of the clinical investigation that is defined as global study data base lock within 15 days to the CAs.

Table 29: Sponsor Reports for Hong Kong

Report	Submit to	Description/Constraints
Premature termination or suspension of the clinical investigation	Investigators, EC, Relevant authorities, and Head of the Institution	Provide prompt notification of termination or suspension and reason(s).
Recall and device disposition	Investigators, Head of Institution, EC, relevant authorities, and FDA	Notification within 30 working days and will include the reasons for any request that an investigator return, repair, or otherwise dispose of any devices.
Study deviation	Investigators	Ensure that all deviations from the CIP are reviewed with the appropriate clinical investigator(s), are reported on the CRFs and the final report of the clinical investigation. Study site specific study deviations will be submitted to investigators periodically.

Table 30: Sponsor reports for Japan

Report	Submit to	Description/Constraints
Premature termination or suspension of the clinical investigation	PMDA and the Head of Institution	When the sponsor suspends or discontinues the clinical study, he or she shall promptly notify thereof and the detailed reason(s) thereof in writing to the Heads of Institutions and the regulatory authorities. (MHLW Ordinance 36, Article 32)

Report	Submit to	Description/Constraints
Suspension of development of investigational device	PMDA, the Head of Institution and the related facilities	When the sponsor decides not to attach the documents concerning clinical study records collected in the clinical study to the authorization application, he or she shall promptly notify thereof and the detailed reason therefor in writing to the Heads of Institutions and related facilities. (MHLW Ordinance 36, Article 32)
Important information concerning the quality, efficacy, and safety of the investigational device	Investigators, Regulatory Authority, the Head of Institution, and EC as applicable	Information of affecting subjects' safety, affecting clinical studies performance, or possibility changing the appropriateness of continuing clinical study judged by EC shall be submitted to all Principal Investigators and The Head of Institutions. The sponsor annually notifies Safety Periodic Report to the Principal Investigators and the Heads of Institutions since initial CTN submission to the regulatory authority. When the sponsor recognizes safety information that is NOT been expecting from the Investigator's brochure (IB), he/she immediately notify thereof to the Principal Investigators and the Heads of Institutions. The sponsor may directly notify above thereof to the ECs in addition to the Principal Investigators and the Heads of Institutions based on the agreement with the ECs and the Heads of Institutions. When new, important information is obtained, the sponsor shall revise the IB. In addition, prior to revising the Investigator's brochure, the sponsor shall report the information to the principal investigator, the Heads of Institutions, and the regulatory authority. (MHLW Ordinance 36, Article 28)
Final report	PMDA upon request	The sponsor shall prepare, according to the procedure, a clinical study report that summarizes the results, etc., of a clinical study when it is completed or discontinued. The final report should be stored to be submitted upon request from the regulatory authority. (MHLW Ordinance 36, Article 33)
Study deviation	The Investigators and the Heads of investigation, as necessary	When the monitor confirms deviation as a result of monitoring, the monitor shall notify the principal investigator and, as necessary, the Head of Medical Institution thereof. The monitor shall also request for appropriate measures to be taken to prevent such deviation in the future. (MHLW Ordinance 36, 2005 Article 30)

Table 31: Sponsor reports for Malaysia

Report	Submit to	Description/Constraints
Study closeout	Regulatory Authority	Upon completion of the clinical research /performance evaluation, the Applicant shall make a declaration using the form in Annex E of MDA/GD/0016. This declaration shall be submitted to the Authority within 30 days after the date of completion. (MDA/ GD/ 0016, NOTIFICATION OF EXEMPTION FROM REGISTRATION OF MEDICAL DEVICES FOR THE PURPOSE OF CLINICAL RESEARCH OR PERFORMANCE EVALUATION)
Early termination	Regulatory Authority	Should the clinical research /performance evaluation terminate earlier than the proposed date or temporarily suspended, Medical Device Authority shall be notified of the reasons for termination or suspension within two (2) weeks of the clinical research /performance evaluation being discontinued using the form in Annex E of MDA/GD/0016. (MDA/ GD/ 0016, NOTIFICATION OF EXEMPTION FROM REGISTRATION OF MEDICAL DEVICES FOR THE PURPOSE OF CLINICAL RESEARCH OR PERFORMANCE EVALUATION)
Progress report	Regulatory Authority	Applicant shall submit a progress report every 6 months, following template as per form in Annex F of MDA/GD/0016. (MDA/ GD/ 0016, NOTIFICATION OF EXEMPTION FROM REGISTRATION OF MEDICAL DEVICES FOR THE PURPOSE OF CLINICAL RESEARCH OR PERFORMANCE EVALUATION)
Clinical research changes	Regulatory Authority	Applicant shall inform Authority on the changes on clinical research under clinical research notification using form in Annex G of MDA/GD/0016. The changes involved may include: a) Change to principal investigator; b) Change in site name; c) Change in site address; d) Subsequent notification of additional clinical research notification site; e) Change to ethic committee; f) Changes of device (e.g.: quantity of device and type of device used); or g) Others (e.g.: change in protocol/CIP, protocol title, subject recruitment) (MDA/ GD/ 0016, NOTIFICATION OF EXEMPTION FROM REGISTRATION OF MEDICAL DEVICES FOR THE PURPOSE OF CLINICAL RESEARCH OR PERFORMANCE EVALUATION)

Table 32: Sponsor reports for the United States

Report	Submit to	Description/Constraints
Withdrawal of EC approval	Investigators, EC, FDA, and relevant authorities	Notification within five working days. (21 CFR 812.150(b)(2))
Withdrawal of FDA approval	Investigators, EC, and relevant authorities	Notification within five working days. (21 CFR 812.150(b)(3))
Investigator List	FDA	Submit at 6-month intervals, a current list of the names and addresses of all investigators participating in the investigation. (21 CFR 812.150(b)(4))
Progress Reports	EC and FDA	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, EC, relevant authorities, and FDA	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, EC, Regulatory Authorities upon request, and FDA	Medtronic will notify FDA within 30 working days of the completion or termination of the investigation. A final report will be submitted to the FDA, investigators, and ECs within six months after completion or termination of this clinical study. (21 CFR 812.150(b)(7))
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))
Study deviation	Investigators	Ensure that all deviations from the CIP are reviewed with the appropriate clinical investigator(s), are reported on the CRFs and the final report of the clinical investigation. Study site specific study deviations will be submitted to investigators periodically.
Other	EC, FDA	Accurate, complete, and current information about any aspect of the investigation. (21 CFR 812.150(b)(10))
Premature termination or suspension of clinical study	EC, Investigators, and regulatory authorities, where applicable	Medtronic will provide prompt notification of termination or suspension and reason(s) to investigator and where required to EC and Regulatory Authorities.

15.9.Publication and Use of Information

Publications from the LEADR LBBAP study will be handled according to the Standard Operating Procedures and as indicated in the CTA, MSA, or MCTA with associated WO.

15.9.1. Publication Committee

The Steering Committee will serve as the LEADR LBBAP Publication Committee. Medtronic personnel may serve as members of the committee. This committee will manage study publications with the goal of publishing findings from the data. The Publication Committee will develop the final Publication Plan as a separate document.

The Publication Committee's role is to: 1) manage elements addressed in the publication plan as outlined in this appendix, 2) develop the final Publication Plan under separate cover, 3) execute the Publication Plan, 4) oversee the publication of primary and ancillary study results, 5) review and prioritize publication proposals, 6) provide input on publication content, and 7) determine authorship. In addition, the committee will apply and reinforce the authorship guidelines set forth in the Publication Plan.

Membership in the Publication Committee does not guarantee authorship. The committee will meet as needed.

15.9.2. Management of Primary and Ancillary Publications

The Publication Committee reviews, prioritizes, and manages all publications including primary, secondary and ancillary publications. Primary and secondary publications are those that address analyses of any or all primary objectives, respectively, as specified in the CIP.

An ancillary publication is any publication that does not address the study objectives identified in the CIP. They include publications proposed and developed by other Medtronic departments or entities, clinicians participating in this study, and clinicians not participating in this study. The committee will work with Medtronic to ensure that requests do not present conflicts with other proposals, are not duplicative, and to determine which ancillary publication proposals, if any, will be supported.

The committee may decide that no publications, including abstracts, will be published prior to the end of the study or with individual study site data. Requests for publications on study objectives utilizing subset data (e.g., regional) will be evaluated for scientific validity and the ability of Medtronic to provide resources.

15.9.3. Criteria for Determining Authorship

Publications will adhere to authorship criteria defined by the International Committee of Medical Journal Editors (ICMJE, Uniform requirements for manuscripts submitted to biomedical journals, www.icmje.org). Individual authorship criteria defined by the target journal or conference will be followed when it differs from ICMJE criteria.

Authors, including Medtronic personnel, must at a minimum meet all of the conditions below:

- Substantial contributions to conception and design of the work, or the acquisition, analysis, or interpretation of data for the work; AND

- Drafting the work or revising it critically for important intellectual content; AND
- Final approval of the version to be published; AND
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Decisions regarding authorship and contributor-ship will be made by the committee. The selected authors will be responsible for drafting the publication. All selected authors must fulfill the authorship conditions stated above to be listed as authors, and all contributors who fulfill the conditions must be listed as authors.
All investigators not listed as co-authors will be acknowledged as the "Medtronic LEADR LBBAP Study Investigators" and will be individually listed according to the guidelines of the applicable scientific journal when possible and affiliation. Any other contributors will be acknowledged by name with their specific contribution indicated.

15.9.4. Transparency

Transparency of clinical study results will be maintained by the following means:

- A final report, describing the results of all objectives and analysis, will be distributed to all investigators, ECs and CAs of participating countries when required by local law
- Registering and posting the study results on publicly accessible database, e.g., ClinicalTrials.gov based on the posting rules stipulated
- Submitting for publication the primary study results after the study ends
- Disclosing conflicts of interest (e.g., financial) of the co-authors of publications according to the policies set forth by the corresponding journals and conferences
- Making an individual study site's study data accessible to the corresponding investigator after the completion of the study, if requested

15.10. Suspension or Early Termination

15.10.1. Planned Study Closure

Study Closure is a process initiated by distribution of a study closure letter. Study closure is defined as closure of a study that occurs when Medtronic and/or regulatory requirements have been satisfied per the CIP and/or by a decision by Medtronic or Regulatory Authority, whichever occurs first. The study closure process is complete upon distribution of the Final Report. For active sites, ongoing EC oversight is required until the overall study closure process is complete. Refer to section 9.24 for additional information regarding study exit procedures. Following closure of the clinical study, subjects will be provided with standard medical care by their (personal) physician.

15.10.2. Early Termination or Suspension

Early Termination is the closure of a study that occurs prior to meeting defined endpoints. This is possible for the whole study or a single study site. Following closure of the clinical study subjects will be provided with standard medical care by their (personal) physician. 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 study site.

15.10.3. Study-wide termination or suspension

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

- AEs 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 or Regulatory Authority (where the study is operating under Regulatory Authority)
- Recommendation of early termination by the DMC based on interim analyses
- Technical issues during the manufacturing process

15.10.4. Investigator/study site termination or suspension

Possible reasons for investigator or study site termination or suspension include but are not limited to:

- Failure to obtain initial 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 to regulations and the terms of the CTA, MSA, or MCTA with associated WO (e.g. failure to submit data in a timely manner, failure to follow-up on data queries and monitoring observations in a timely manner, etc.)
- EC suspension of the study 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)

15.10.5. Procedures for Termination or Suspension

Below procedures will apply in addition to any other specific requirement per local regulations.

15.10.6. Medtronic-initiated and regulatory authority-initiated

- Medtronic will promptly inform the clinical investigators of the termination or suspension and the reasons and inform the Regulatory Authorities where required
- In the case of study termination or suspension for reasons other than a temporary EC approval lapse, the investigator will promptly inform the EC. A written explanation of the termination or suspension will be provided, where required per regulatory requirements.
- 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

15.10.7. 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 EC, along with a written explanation of the termination or suspension (where required per regulatory requirements)
- The investigator will promptly inform the regulatory authorities (when applicable per local regulations)
- 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

15.10.8. Ethics Committee-initiated

- The investigator will inform Medtronic and provide a detailed written explanation of the termination or suspension within 5 business days, or sooner if required per local requirements
- Subject enrollment must stop until the suspension is lifted
- Subjects already enrolled should continue to be followed in accordance with 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, or legal parent(s)/guardians, and/or the personal physician of the subjects, with the rationale for the study termination or suspension to ensure appropriate care and follow-up is provided

- The investigator will promptly inform the regulatory authorities (when applicable per local regulations)

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17. Appendices

Appendix A: List of Compatible ICD and CRT-D Devices

A complete list of compatible ICD and CRT-D devices that can be utilized as part of the study will be distributed under separate cover upon request.

Appendix B: User Manual and Instructions for Use

The LEADR LBBAP Study User Manual for placement of the Next Generation ICD Lead in the LBBAP location is provided under separate cover. The 093000 Technical Manual for the Next Generation ICD Lead and IFU for catheters are provided with each component under separate cover.

Appendix C: Informed Consent

Medtronic approved Informed Consent Form Templates for each geography where the study will be conducted will be distributed under separate cover.

Appendix D: Foreseeable Adverse Event List

The information provided in this section pertains to foreseeable adverse events that may be observed in the LEADR LBBAP study and may collectively assist in identifying those events for a given device or therapy that are unexpected in nature. The foreseeable adverse events information consists of three parts: 1) observed adverse device effect(s) in similar Medtronic studies, 2) adverse events reported in published literature, and 3) additional foreseeable adverse events. An evaluation of potentially anticipated events, adverse device effects observed in previous clinical studies, and reported events in literature may be used in combination with device labeling, current event reporting information, and other published data to assess for an unexpected occurrence.

The implantation of the Next Generation ICD Lead and the associated ICD system involves surgery, therefore, standard adverse events associated with a surgical procedure may be experienced (e.g. anesthesia complications, injury, infections, bleeding, exacerbation of pre-existing conditions, healing complications, etc.). However, the focus of this section is to address in more detail, those events that are foreseeable due to the implantation, use, performance, and/or presence of the system under investigation.

Potential risks associated with the implantation of the Next Generation ICD Lead, as well as risk minimization are discussed within section 10 Risks and Benefits. Treatment required for procedure and/or system related adverse events may include medication, device reprogramming, device modification (e.g. repositioning, surgical abandonment, surgical removal), or other surgical and medical remedies. The remainder of this section provides examples of adverse event data from previous Medtronic clinical studies and literature. Evaluation of potentially anticipated events may involve data in this section as well as a thorough review of all available information (e.g. labeling, current event reporting, published data, etc.).

Observed Adverse Device Effect in Previous Clinical Studies

Table 33 to Table 36 below provide examples of adverse events associated with the use of ICD, CRT-D and IPG systems reported in four previous Medtronic studies. The BLOCK HF, Evera MRI and REVERSE studies were selected as a reference as they were IDE studies using ICD and CRT-D devices and used adverse event definitions consistent with those utilized in this study. The 3830 Lead IDE study was selected as a reference as the Next Generation ICD Lead is built off the SelectSecure Model 3830 bradycardia lead. For the BLOCK HF, Evera MRI and REVERSE study adverse events were classified utilizing MedDRA, the Medical Dictionary for Regulatory Activities, to allow coding to a standard set of medical terms.

The MedDRA Preferred Terms (PT) are provided in Table 33 through Table 36. The four predicate Medtronic studies collected adverse event data from 1396 subjects that underwent an ICD/CRT-D or IPG implant. The average follow-up within the studies ranged from 10 to 54 months. Kaplan-Meier estimates and associated 95% confidence intervals of the adverse event rates are provided in the tables below at 30 days and 12-months (365 days) post-implant to characterize both peri-

procedural and long-term adverse events related to the procedure or system. Table 33 displays the adverse event rates classified as related to the system and/or procedure for CRT-D devices (BLOCK HF and REVERSE study) while Table 34 shows the adverse event rate as related to the system and/or procedure for ICD devices (Evera MRI). Table 35 shows the procedure and system-related adverse events for IPG devices with a catheter delivered lead (3830 Lead IDE study). Table 36 shows RV lead related adverse events for all four studies.

Table 33: System and Procedure-Related AEs from Previous Medtronic Studies with CRT-D Devices (n=771)

MedDRA Preferred Term	Within 30-days of Implant		Within 12-months of Implant	
	No. Events (No. Subjects, %)	95% CI	No. Events (No. Subjects, %)	95% CI
ACUTE MYOCARDIAL INFARCTION	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
ACUTE PULMONARY OEDEMA	2 (2, 0.26%)	0.06% - 1.03%	2 (2, 0.26%)	0.06% - 1.03%
ADVERSE DRUG REACTION	5 (5, 0.52%)	0.20% - 1.38%	5 (5, 0.52%)	0.20% - 1.38%
ANGINA UNSTABLE	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
ANXIETY	0 (0, 0%)	--	1 (1, 0.14%)	0.02% - 1.00%
ARRHYTHMIA SUPRAVENTRICULAR	1 (1, 0.13%)	0.02% - 0.92%	2 (1, 0.13%)	0.02% - 0.92%
ATELECTASIS	3 (3, 0.39%)	0.13% - 1.20%	3 (3, 0.39%)	0.13% - 1.20%
ATRIAL FIBRILLATION	14 (13, 1.69%)	0.98% - 2.89%	15 (14, 1.83%)	1.09% - 3.07%
ATRIAL FLUTTER	6 (6, 0.78%)	0.35% - 1.73%	6 (6, 0.78%)	0.35% - 1.73%
ATRIOVENTRICULAR BLOCK COMPLETE	3 (2, 0.26%)	0.06% - 1.03%	3 (2, 0.26%)	0.06% - 1.03%
ATRIOVENTRICULAR BLOCK THIRD DEGREE	6 (6, 0.78%)	0.35% - 1.72%	6 (6, 0.78%)	0.35% - 1.72%
BODY TEMPERATURE INCREASED	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
BRADYCARDIA	2 (2, 0.26%)	0.06% - 1.03%	2 (2, 0.26%)	0.06% - 1.03%
BRONCHITIS	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
CARDIAC FAILURE	15 (15, 1.95%)	1.18% - 3.22%	15 (15, 1.95%)	1.18% - 3.22%
CARDIAC FAILURE ACUTE	2 (2, 0.26%)	0.07% - 1.04%	2 (2, 0.26%)	0.07% - 1.04%
CARDIAC FAILURE CHRONIC	1 (1, 0.13%)	0.02% - 0.92%	2 (2, 0.27%)	0.07% - 1.06%
CARDIAC PERFORATION	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
CARDIAC PROCEDURE COMPLICATION	2 (2, 0.26%)	0.06% - 1.03%	2 (2, 0.26%)	0.06% - 1.03%
CARDIAC TAMPONADE	1 (1, 0.13%)	0.02% - 0.92%	2 (2, 0.27%)	0.07% - 1.06%
CEREBROVASCULAR ACCIDENT	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
CHEST PAIN	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
COMPLICATION OF DEVICE INSERTION	2 (2, 0.26%)	0.06% - 1.03%	2 (2, 0.26%)	0.06% - 1.03%
CONTRAST MEDIA REACTION	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
CORONARY SINUS DISSECTION	9 (9, 1.17%)	0.61% - 2.23%	9 (9, 1.17%)	0.61% - 2.23%
DECREASED RV SENSING	0 (0, 0%)	--	2 (2, 0.29%)	0.07% - 1.14%
DEEP VEIN THROMBOSIS	2 (2, 0.26%)	0.07% - 1.03%	4 (4, 0.53%)	0.20% - 1.42%
DEFIBRILLATION THRESHOLD INCREASED	1 (1, 0.13%)	0.02% - 0.92%	2 (2, 0.27%)	0.07% - 1.06%
DEHYDRATION	2 (2, 0.26%)	0.07% - 1.04%	2 (2, 0.26%)	0.07% - 1.04%
DEVICE ELECTRICAL FINDING	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
DEVICE LEAD DAMAGE	1 (1, 0.13%)	0.02% - 0.92%	2 (2, 0.27%)	0.07% - 1.08%
DEVICE MIGRATION	1 (1, 0.13%)	0.02% - 0.92%	2 (2, 0.26%)	0.07% - 1.06%
DEVICE RELATED INFECTION	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
DIZZINESS	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%

MedDRA Preferred Term	Within 30-days of Implant		Within 12-months of Implant	
	No. Events (No. Subjects, %)	95% CI	No. Events (No. Subjects, %)	95% CI
DIZZINESS POSTURAL	0 (0, 0%)	--	1 (1, 0.14%)	0.02% - 0.96%
DRUG HYPERSENSITIVITY	2 (2, 0.26%)	0.07% - 1.03%	2 (2, 0.26%)	0.07% - 1.03%
DYSPNOEA	4 (4, 0.52%)	0.20% - 1.38%	4 (4, 0.52%)	0.20% - 1.38%
DYSPNOEA EXERTIONAL	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
ELECTRICAL RESET OF DEVICE	0 (0, 0%)	--	2 (2, 0.28%)	0.07% - 1.10%
ELECTROMECHANICAL DISSOCIATION	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
ELEVATED PACING THRESHOLD	2 (2, 0.26%)	0.07% - 1.03%	5 (5, 0.68%)	0.28% - 1.62%
ENTERITIS	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
EXTRASYSTOLES	1 (1, 0.13%)	0.02% - 0.93%	1 (1, 0.13%)	0.02% - 0.93%
FAILURE TO CAPTURE	3 (3, 0.39%)	0.13% - 1.21%	5 (5, 0.67%)	0.28% - 1.60%
FATIGUE	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
FLUID RETENTION	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
GASTROINTESTINAL HAEMORRHAGE	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
HAEMATOMA	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
HAEMOPNEUMOTHORAX	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
HAEMORRHAGE	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
HYPOTENSION	8 (8, 1.04%)	0.52% - 2.07%	8 (8, 1.04%)	0.52% - 2.07%
HYPOXIA	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
IMPAIRED HEALING	1 (1, 0.13%)	0.02% - 0.92%	2 (2, 0.26%)	0.07% - 1.05%
IMPLANT SITE CELLULITIS	0 (0, 0%)	--	1 (1, 0.14%)	0.02% - 0.96%
IMPLANT SITE EROSION	0 (0, 0%)	--	2 (2, 0.27%)	0.07% - 1.08%
IMPLANT SITE HAEMATOMA	21 (21, 2.73%)	1.79% - 4.15%	23 (23, 3.00%)	2.00% - 4.48%
IMPLANT SITE HAEMORRHAGE	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
IMPLANT SITE INFECTION	8 (8, 1.04%)	0.52% - 2.07%	13 (13, 1.72%)	1.00% - 2.94%
IMPLANT SITE INFLAMMATION	0 (0, 0%)	--	1 (1, 0.14%)	0.02% - 0.97%
IMPLANT SITE PAIN	10 (10, 1.30%)	0.70% - 2.40%	18 (17, 2.26%)	1.41% - 3.61%
IMPLANT SITE RASH	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
INAPPROPRIATE DEVICE STIMULATION OF TISSUE	39 (36, 4.68%)	3.40% - 6.43%	66 (56, 7.41%)	5.75% - 9.52%
INAPPROPRIATE DEVICE THERAPY	1 (1, 0.13%)	0.02% - 0.93%	6 (6, 0.82%)	0.37% - 1.82%
INCISION SITE HAEMORRHAGE	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
INFLUENZA	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
IODINE ALLERGY	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
JUGULAR VEIN THROMBOSIS	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
KELOID SCAR	0 (0, 0%)	--	1 (1, 0.14%)	0.02% - 0.98%
LV LEAD DISLODGEMENT	28 (27, 3.51%)	2.42% - 5.07%	39 (36, 4.75%)	3.45% - 6.53%
MEDICAL DEVICE CHANGE	0 (0, 0%)	--	1 (1, 0.14%)	0.02% - 0.99%
MEDICAL DEVICE COMPLICATION	0 (0, 0%)	--	1 (1, 0.14%)	0.02% - 0.97%
MEDICAL DEVICE DISCOMFORT	0 (0, 0%)	--	1 (1, 0.14%)	0.02% - 0.97%
MUSCLE SPASMS	1 (1, 0.13%)	0.02% - 0.92%	2 (2, 0.27%)	0.07% - 1.08%
MUSCLE STRAIN	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
MUSCULOSKELETAL PAIN	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
MYOCARDIAL INFARCTION	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
OEDEMA PERIPHERAL	3 (3, 0.39%)	0.13% - 1.20%	4 (4, 0.53%)	0.20% - 1.39%

MedDRA Preferred Term	Within 30-days of Implant		Within 12-months of Implant	
	No. Events (No. Subjects, %)	95% CI	No. Events (No. Subjects, %)	95% CI
ORTHOSTATIC HYPOTENSION	2 (2, 0.26%)	0.07% - 1.04%	2 (2, 0.26%)	0.07% - 1.04%
OVERSENSING	1 (1, 0.13%)	0.02% - 0.92%	4 (4, 0.55%)	0.21% - 1.45%
OXYGEN SATURATION DECREASED	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
PAIN IN EXTREMITY	2 (2, 0.26%)	0.07% - 1.03%	2 (2, 0.26%)	0.07% - 1.03%
PERICARDIAL EFFUSION	8 (8, 1.04%)	0.52% - 2.07%	9 (9, 1.17%)	0.61% - 2.24%
PERICARDITIS	0 (0, 0%)	--	1 (1, 0.14%)	0.02% - 0.96%
PHANTOM SHOCK	1 (1, 0.13%)	0.02% - 0.93%	1 (1, 0.13%)	0.02% - 0.93%
PLEURAL EFFUSION	7 (7, 0.91%)	0.43% - 1.90%	8 (8, 1.04%)	0.52% - 2.08%
PLEURITIC PAIN	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
PNEUMONIA	2 (2, 0.26%)	0.06% - 1.03%	2 (2, 0.26%)	0.06% - 1.03%
PNEUMOTHORAX	4 (4, 0.52%)	0.20% - 1.38%	4 (4, 0.52%)	0.20% - 1.38%
PNEUMOTHORAX TRAUMATIC	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
PROCEDURAL HYPOTENSION	2 (2, 0.26%)	0.06% - 1.03%	2 (2, 0.26%)	0.06% - 1.03%
PULMONARY OEDEMA	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
PUNCTURE OF PERIOSTEUM	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
PYREXIA	2 (2, 0.26%)	0.07% - 1.03%	2 (2, 0.26%)	0.07% - 1.03%
RA LEAD DISLODGEMENT	13 (13, 1.69%)	0.99% - 2.89%	16 (15, 1.96%)	1.19% - 3.24%
RENAL FAILURE	3 (3, 0.39%)	0.13% - 1.20%	3 (3, 0.39%)	0.13% - 1.20%
RENAL FAILURE ACUTE	3 (3, 0.39%)	0.13% - 1.21%	3 (3, 0.39%)	0.13% - 1.21%
RV LEAD DISLODGEMENT	13 (13, 1.69%)	0.98% - 2.89%	19 (19, 2.51%)	1.61% - 3.90%
SHOULDER PAIN	4 (4, 0.52%)	0.20% - 1.38%	4 (4, 0.52%)	0.20% - 1.38%
SLEEP APNOEA SYNDROME	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
SUBCLAVIAN VEIN THROMBOSIS	2 (2, 0.26%)	0.07% - 1.03%	2 (2, 0.26%)	0.07% - 1.03%
SUPRAVENTRICULAR TACHYCARDIA	0 (0, 0%)	--	2 (2, 0.28%)	0.07% - 1.12%
SUTURE RELATED COMPLICATION	0 (0, 0%)	--	2 (2, 0.27%)	0.07% - 1.07%
SYNCOPE VASOVAGAL	2 (2, 0.26%)	0.06% - 1.03%	2 (2, 0.26%)	0.06% - 1.03%
THERMAL BURN	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
UNDERSENSING	1 (1, 0.13%)	0.02% - 0.92%	2 (2, 0.27%)	0.07% - 1.06%
UPPER RESPIRATORY TRACT INFECTION	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
URINARY RETENTION POSTOPERATIVE	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
VENTRICULAR ASYSTOLE	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
VENTRICULAR FIBRILLATION	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
VERTIGO CNS ORIGIN	1 (1, 0.13%)	0.02% - 0.92%	1 (1, 0.13%)	0.02% - 0.92%
WHEEZING	2 (2, 0.26%)	0.06% - 1.03%	2 (2, 0.26%)	0.06% - 1.03%

Table 34: System and Procedure-Related AEs from a Previous Medtronic Study with Single and Dual Chamber ICD Devices (n=264)

MedDRA Preferred Term	Within 30-days of Implant		Within 12-months of Implant	
	No. Events (No. Subjects, %)	95% CI	No. Events (No. Subjects, %)	95% CI
ABDOMINAL PAIN UPPER	1 (1, 0.38%)	0.05% - 2.66%	1 (1, 0.38%)	0.05% - 2.66%
ATRIAL TACHYCARDIA	0 (0, 0%)	--	2 (2, 0.77%)	0.19% - 3.04%

MedDRA Preferred Term	Within 30-days of Implant		Within 12-months of Implant	
	No. Events (No. Subjects, %)	95% CI	No. Events (No. Subjects, %)	95% CI
ATRIAL THROMBOSIS	0 (0, 0%)	--	1 (1, 0.41%)	0.06% - 2.90%
BACK PAIN	0 (0, 0%)	--	1 (1, 0.39%)	0.05% - 2.73%
BACTERAEMIA	0 (0, 0%)	--	1 (1, 0.39%)	0.05% - 2.72%
BURNING SENSATION	0 (0, 0%)	--	1 (1, 0.38%)	0.05% - 2.70%
CARDIAC FAILURE	1 (1, 0.38%)	0.05% - 2.66%	1 (1, 0.38%)	0.05% - 2.66%
CARDIAC PERFORATION	1 (1, 0.38%)	0.05% - 2.66%	1 (1, 0.38%)	0.05% - 2.66%
CARDIAC TAMPONADE	1 (1, 0.38%)	0.05% - 2.66%	1 (1, 0.38%)	0.05% - 2.66%
CEREBROVASCULAR ACCIDENT	1 (1, 0.38%)	0.05% - 2.66%	1 (1, 0.38%)	0.05% - 2.66%
CHEST DISCOMFORT	1 (1, 0.38%)	0.05% - 2.66%	1 (1, 0.38%)	0.05% - 2.66%
CHEST PAIN	1 (1, 0.38%)	0.05% - 2.66%	1 (1, 0.38%)	0.05% - 2.66%
CHRONIC OBSTRUCTIVE PULMONARY DISEASE	3 (1, 0.38%)	0.05% - 2.66%	3 (1, 0.38%)	0.05% - 2.66%
CONFUSIONAL STATE	1 (1, 0.38%)	0.05% - 2.66%	1 (1, 0.38%)	0.05% - 2.66%
DEEP VEIN THROMBOSIS	0 (0, 0%)	--	1 (1, 0.39%)	0.05% - 2.72%
DEVICE LEAD DAMAGE	0 (0, 0%)	--	1 (1, 0.51%)	0.07% - 3.53%
DEVICE MALFUNCTION	0 (0, 0%)	--	1 (1, 0.41%)	0.06% - 2.89%
DEVICE PACING ISSUE	1 (1, 0.38%)	0.05% - 2.66%	1 (1, 0.38%)	0.05% - 2.66%
ECCHYMOSIS	1 (1, 0.38%)	0.05% - 2.66%	1 (1, 0.38%)	0.05% - 2.66%
HYPOTENSION	1 (1, 0.38%)	0.05% - 2.66%	1 (1, 0.38%)	0.05% - 2.66%
IMPLANT SITE HAEMATOMA	2 (2, 0.76%)	0.19% - 2.99%	2 (2, 0.76%)	0.19% - 2.99%
IMPLANT SITE INFECTION	1 (1, 0.38%)	0.05% - 2.66%	2 (2, 0.79%)	0.20% - 3.12%
IMPLANT SITE PAIN	2 (2, 0.76%)	0.19% - 2.99%	5 (4, 1.52%)	0.57% - 4.01%
IMPLANT SITE WARMTH	0 (0, 0%)	--	2 (2, 0.78%)	0.19% - 3.06%
INCISION SITE VESICLES	0 (0, 0%)	--	1 (1, 0.38%)	0.05% - 2.70%
INJURY	1 (1, 0.38%)	0.05% - 2.66%	1 (1, 0.38%)	0.05% - 2.66%
OVERSENSING	1 (1, 0.38%)	0.05% - 2.66%	3 (3, 1.15%)	0.37% - 3.52%
PERICARDIAL EFFUSION	1 (1, 0.38%)	0.05% - 2.66%	1 (1, 0.38%)	0.05% - 2.66%
PERICARDITIS	1 (1, 0.38%)	0.05% - 2.66%	1 (1, 0.38%)	0.05% - 2.66%
PNEUMONIA	1 (1, 0.38%)	0.05% - 2.66%	1 (1, 0.38%)	0.05% - 2.66%
PNEUMONIA ASPIRATION	1 (1, 0.38%)	0.05% - 2.66%	1 (1, 0.38%)	0.05% - 2.66%
POSTOPERATIVE WOUND INFECTION	0 (0, 0%)	--	1 (1, 0.38%)	0.05% - 2.68%
PROCEDURAL NAUSEA	1 (1, 0.38%)	0.05% - 2.66%	1 (1, 0.38%)	0.05% - 2.66%
PULMONARY EMBOLISM	0 (0, 0%)	--	1 (1, 0.40%)	0.06% - 2.81%
RA LEAD DISLODGEMENT	2 (2, 0.76%)	0.19% - 2.99%	2 (2, 0.76%)	0.19% - 2.99%
RV LEAD DISLODGEMENT	1 (1, 0.38%)	0.05% - 2.66%	1 (1, 0.38%)	0.05% - 2.66%
VENOUS OCCLUSION	1 (1, 0.38%)	0.05% - 2.66%	2 (2, 0.77%)	0.19% - 3.03%
VENTRICULAR TACHYCARDIA	2 (2, 0.76%)	0.19% - 2.99%	2 (2, 0.76%)	0.19% - 2.99%

Table 35: System and Procedure-Related AEs from a Previous Medtronic Study with a Catheter-Delivered Lead and IPGs (n=361)

Key Term	Within 30-days of Implant		Within 12-months of Implant	
	No. Events (No. Subjects, %)	95% CI	No. Events (No. Subjects, %)	95% CI
ABNORMAL LABS	1 (1, 0.28%)	0.04% - 1.95%	1 (1, 0.28%)	0.04% - 1.95%
AFIB/AFLUTTER	4 (4, 1.16%)	0.44% - 3.07%	4 (4, 1.16%)	0.44% - 3.07%
AIR EMBOLISM	4 (4, 1.11%)	0.42% - 2.93%	4 (4, 1.11%)	0.42% - 2.93%
ANXIETY	1 (1, 0.29%)	0.04% - 2.01%	1 (1, 0.29%)	0.04% - 2.01%
ATELECTASIS	2 (2, 0.56%)	0.14% - 2.23%	2 (2, 0.56%)	0.14% - 2.23%
ATRIAL TACHYCARDIA	4 (4, 1.15%)	0.43% - 3.03%	4 (4, 1.15%)	0.43% - 3.03%
BLEEDING AT INCISION SITE	1 (1, 0.29%)	0.04% - 2.05%	1 (1, 0.29%)	0.04% - 2.05%
CARDIAC PERFORATION	1 (1, 0.28%)	0.04% - 1.95%	1 (1, 0.28%)	0.04% - 1.95%
CATHETER KINKING	4 (4, 1.11%)	0.42% - 2.93%	4 (4, 1.11%)	0.42% - 2.93%
CELLULITIS	1 (1, 0.28%)	0.04% - 1.95%	1 (1, 0.28%)	0.04% - 1.95%
CHEST PAIN / ANGINA PECTORIS	7 (6, 1.71%)	0.77% - 3.78%	8 (7, 2.03%)	0.97% - 4.22%
CONFUSION /DISORIENTATION	1 (1, 0.29%)	0.04% - 2.05%	1 (1, 0.29%)	0.04% - 2.05%
CORONARY ARTERY DISEASE	1 (1, 0.30%)	0.04% - 2.08%	1 (1, 0.30%)	0.04% - 2.08%
DECREASED RANGE OF MOTION	1 (1, 0.29%)	0.04% - 2.06%	1 (1, 0.29%)	0.04% - 2.06%
DEVICE MIGRATION	0 (0, 0%)	--	1 (1, 0.31%)	0.04% - 2.18%
DIARRHEA	1 (1, 0.29%)	0.04% - 2.07%	1 (1, 0.29%)	0.04% - 2.07%
DIFFICULTY POSITIONING LEAD	3 (3, 0.83%)	0.27% - 2.55%	3 (3, 0.83%)	0.27% - 2.55%
DIZZINESS	2 (2, 0.59%)	0.15% - 2.32%	2 (2, 0.59%)	0.15% - 2.32%
DYSPNOEA	1 (1, 0.29%)	0.04% - 2.07%	3 (3, 0.95%)	0.31% - 2.92%
ECCHYMOSIS	2 (2, 0.58%)	0.15% - 2.30%	2 (2, 0.58%)	0.15% - 2.30%
EDEMA	6 (6, 1.74%)	0.79% - 3.84%	6 (6, 1.74%)	0.79% - 3.84%
ELEVATED PACING THRESHOLDS	9 (9, 2.56%)	1.34% - 4.87%	26 (25, 8.39%)	5.71% - 12.24%
EMPHYSEMA	1 (1, 0.28%)	0.04% - 1.95%	1 (1, 0.28%)	0.04% - 1.95%
FAILURE TO CAPTURE / LOSS OF CAPTURE	6 (6, 1.69%)	0.76% - 3.71%	7 (7, 1.99%)	0.95% - 4.12%
FAILURE TO SENSE / UNDERSENSING	3 (3, 0.85%)	0.27% - 2.61%	3 (3, 0.85%)	0.27% - 2.61%
FALL	1 (1, 0.29%)	0.04% - 2.01%	1 (1, 0.29%)	0.04% - 2.01%
FATIGUE / TIREDNESS	2 (2, 0.58%)	0.15% - 2.31%	3 (3, 0.92%)	0.30% - 2.85%
HEART FAILURE	2 (1, 0.29%)	0.04% - 2.05%	3 (2, 0.63%)	0.16% - 2.50%
HEART RATE VARIABILITY	1 (1, 0.29%)	0.04% - 2.05%	1 (1, 0.29%)	0.04% - 2.05%
HYPOTENSION	5 (5, 1.40%)	0.59% - 3.34%	5 (5, 1.40%)	0.59% - 3.34%
INAPPROPRIATE PROGRAMMING	4 (4, 1.16%)	0.44% - 3.06%	7 (6, 1.85%)	0.83% - 4.07%
INFECTION	1 (1, 0.28%)	0.04% - 1.95%	1 (1, 0.28%)	0.04% - 1.95%
LEAD INSERTION / ROUTE PROBLEM	5 (5, 1.39%)	0.58% - 3.32%	5 (5, 1.39%)	0.58% - 3.32%
LEAD INSULATION FAILURE	1 (1, 0.28%)	0.04% - 1.95%	1 (1, 0.28%)	0.04% - 1.95%
MEDICATION RELATED	8 (8, 2.26%)	1.14% - 4.48%	8 (8, 2.26%)	1.14% - 4.48%
MODE SWITCH	0 (0, 0%)	--	2 (2, 0.63%)	0.16% - 2.50%
MUSCLE STIMULATION	3 (3, 0.86%)	0.28% - 2.64%	4 (3, 0.86%)	0.28% - 2.64%
NAUSEA	1 (1, 0.28%)	0.04% - 1.95%	1 (1, 0.28%)	0.04% - 1.95%
NEAR SYNCOPE	1 (1, 0.28%)	0.04% - 1.95%	1 (1, 0.28%)	0.04% - 1.95%

Key Term	Within 30-days of Implant		Within 12-months of Implant	
	No. Events (No. Subjects, %)	95% CI	No. Events (No. Subjects, %)	95% CI
NON-CARDIAC PAIN	5 (5, 1.43%)	0.60% - 3.40%	5 (5, 1.43%)	0.60% - 3.40%
OVERSENSING	0 (0, 0%)	--	2 (2, 0.64%)	0.16% - 2.55%
PACEMAKER MEDIATED TACHYCARDIA	1 (1, 0.29%)	0.04% - 2.01%	1 (1, 0.29%)	0.04% - 2.01%
PACEMAKER SYNDROME	1 (1, 0.29%)	0.04% - 2.06%	1 (1, 0.29%)	0.04% - 2.06%
PAIN AT POCKET SITE	7 (7, 2.05%)	0.98% - 4.24%	12 (12, 3.83%)	2.18% - 6.68%
PALPITATIONS	2 (2, 0.59%)	0.15% - 2.33%	2 (2, 0.59%)	0.15% - 2.33%
PAROXYSMAL ATRIAL FLUTTER / FIBRILLATION	6 (6, 1.73%)	0.78% - 3.81%	6 (6, 1.73%)	0.78% - 3.81%
PERICARDIAL EFFUSION	8 (8, 2.24%)	1.13% - 4.43%	8 (8, 2.24%)	1.13% - 4.43%
PLEURAL EFFUSION	8 (8, 2.28%)	1.15% - 4.51%	8 (8, 2.28%)	1.15% - 4.51%
PNEUMOTHORAX	7 (7, 1.95%)	0.93% - 4.04%	7 (7, 1.95%)	0.93% - 4.04%
POCKET HEMATOMA	7 (7, 1.98%)	0.95% - 4.10%	9 (9, 2.58%)	1.35% - 4.89%
POCKET INFECTION	9 (9, 2.62%)	1.37% - 4.98%	14 (14, 4.15%)	2.48% - 6.92%
RA LEAD DISLODGEMENT	2 (2, 0.57%)	0.14% - 2.27%	4 (4, 1.29%)	0.48% - 3.42%
RASH	3 (3, 0.86%)	0.28% - 2.65%	3 (3, 0.86%)	0.28% - 2.65%
RENAL INSUFFICIENCY	1 (1, 0.29%)	0.04% - 2.01%	1 (1, 0.29%)	0.04% - 2.01%
RV LEAD DISLODGEMENT	4 (4, 1.13%)	0.43% - 2.99%	7 (7, 2.08%)	1.00% - 4.33%
SURGICAL COMPLICATION	1 (1, 0.29%)	0.04% - 2.05%	1 (1, 0.29%)	0.04% - 2.05%
SUTURE EXPOSED	1 (1, 0.29%)	0.04% - 2.06%	1 (1, 0.29%)	0.04% - 2.06%
SYNCOPE	1 (1, 0.28%)	0.04% - 1.95%	1 (1, 0.28%)	0.04% - 1.95%
TAMPONADE	3 (3, 0.83%)	0.27% - 2.55%	3 (3, 0.83%)	0.27% - 2.55%
UNABLE TO SLIT CATHETER	1 (1, 0.28%)	0.04% - 1.95%	1 (1, 0.28%)	0.04% - 1.95%
VENOUS THROMBOSIS	2 (2, 0.58%)	0.15% - 2.31%	2 (2, 0.58%)	0.15% - 2.31%
VENTRICULAR ECTOPY (INCLUDING PVCS)	1 (1, 0.29%)	0.04% - 2.03%	1 (1, 0.29%)	0.04% - 2.03%

Table 36: RV Lead Related AEs from Previous Medtronic Studies (n=1396)

Key Term	Within 30-days of Implant		Within 12-months of Implant	
	No. Events (No. Subjects, %)	95% CI	No. Events (No. Subjects, %)	95% CI
ATRIAL FIBRILLATION	1 (1, 0.07%)	0.01% - 0.51%	1 (1, 0.07%)	0.01% - 0.51%
ATRIAL THROMBOSIS	0 (0, 0%)	--	1 (1, 0.08%)	0.01% - 0.59%
ATRIOVENTRICULAR BLOCK COMPLETE	2 (2, 0.14%)	0.04% - 0.57%	2 (2, 0.14%)	0.04% - 0.57%
ATRIOVENTRICULAR BLOCK THIRD DEGREE	3 (3, 0.22%)	0.07% - 0.67%	3 (3, 0.22%)	0.07% - 0.67%
BACTERAEMIA	0 (0, 0%)	--	1 (1, 0.08%)	0.01% - 0.54%
CARDIAC FAILURE	1 (1, 0.07%)	0.01% - 0.51%	1 (1, 0.07%)	0.01% - 0.51%
CARDIAC PERFORATION	3 (3, 0.22%)	0.07% - 0.67%	3 (3, 0.22%)	0.07% - 0.67%
CARDIAC TAMPONADE	2 (2, 0.14%)	0.04% - 0.58%	3 (3, 0.22%)	0.07% - 0.68%
CHEST DISCOMFORT	1 (1, 0.07%)	0.01% - 0.51%	1 (1, 0.07%)	0.01% - 0.51%
COMPLICATION OF DEVICE INSERTION	1 (1, 0.07%)	0.01% - 0.51%	1 (1, 0.07%)	0.01% - 0.51%
DECREASED RV SENSING	0 (0, 0%)	--	2 (2, 0.21%)	0.05% - 0.83%
DEEP VEIN THROMBOSIS	2 (2, 0.15%)	0.04% - 0.58%	5 (5, 0.38%)	0.16% - 0.90%
DEFIBRILLATION THRESHOLD INCREASED	1 (1, 0.07%)	0.01% - 0.51%	2 (2, 0.15%)	0.04% - 0.59%
DEVICE ELECTRICAL FINDING	1 (1, 0.07%)	0.01% - 0.51%	1 (1, 0.07%)	0.01% - 0.51%
DEVICE LEAD DAMAGE	0 (0, 0%)	--	2 (2, 0.18%)	0.04% - 0.71%
DEVICE PACING ISSUE	1 (1, 0.07%)	0.01% - 0.52%	1 (1, 0.07%)	0.01% - 0.52%
DIFFICULTY POSITIONING LEAD	1 (1, 0.07%)	0.01% - 0.51%	1 (1, 0.07%)	0.01% - 0.51%
EDEMA	1 (1, 0.07%)	0.01% - 0.51%	1 (1, 0.07%)	0.01% - 0.51%
ELEVATED PACING THRESHOLD	0 (0, 0%)	--	2 (2, 0.16%)	0.04% - 0.63%
ELEVATED PACING THRESHOLDS	5 (5, 0.36%)	0.15% - 0.87%	20 (20, 1.61%)	1.04% - 2.49%
FAILURE TO CAPTURE	0 (0, 0%)	--	1 (1, 0.08%)	0.01% - 0.57%
FAILURE TO CAPTURE / LOSS OF CAPTURE	5 (5, 0.36%)	0.15% - 0.86%	6 (6, 0.43%)	0.20% - 0.96%
IMPLANT SITE INFECTION	1 (1, 0.07%)	0.01% - 0.52%	2 (2, 0.15%)	0.04% - 0.62%
INAPPROPRIATE DEVICE STIMULATION OF TISSUE	3 (3, 0.22%)	0.07% - 0.68%	4 (4, 0.29%)	0.11% - 0.78%
INAPPROPRIATE DEVICE THERAPY	0 (0, 0%)	--	1 (1, 0.08%)	0.01% - 0.54%
INAPPROPRIATE PROGRAMMING	0 (0, 0%)	--	1 (1, 0.08%)	0.01% - 0.56%
LEAD INSULATION FAILURE	1 (1, 0.07%)	0.01% - 0.51%	1 (1, 0.07%)	0.01% - 0.51%
MEDICAL DEVICE CHANGE	0 (0, 0%)	--	1 (1, 0.08%)	0.01% - 0.59%
MUSCLE STIMULATION	2 (2, 0.14%)	0.04% - 0.58%	2 (2, 0.14%)	0.04% - 0.58%
OEDEMA PERIPHERAL	1 (1, 0.07%)	0.01% - 0.51%	1 (1, 0.07%)	0.01% - 0.51%
OVERSENSING	2 (2, 0.14%)	0.04% - 0.57%	8 (8, 0.61%)	0.31% - 1.22%
PERICARDIAL EFFUSION	9 (9, 0.65%)	0.34% - 1.24%	9 (9, 0.65%)	0.34% - 1.24%
PERICARDITIS	1 (1, 0.07%)	0.01% - 0.51%	1 (1, 0.07%)	0.01% - 0.51%
PULMONARY EMBOLISM	0 (0, 0%)	--	1 (1, 0.08%)	0.01% - 0.56%
RV LEAD DISLODGEMENT	18 (18, 1.30%)	0.82% - 2.06%	27 (27, 1.99%)	1.37% - 2.89%
SUBCLAVIAN VEIN THROMBOSIS	2 (2, 0.15%)	0.04% - 0.58%	2 (2, 0.15%)	0.04% - 0.58%
TAMPONADE	2 (2, 0.14%)	0.04% - 0.57%	2 (2, 0.14%)	0.04% - 0.57%
VENOUS OCCLUSION	1 (1, 0.07%)	0.01% - 0.51%	2 (2, 0.15%)	0.04% - 0.59%
VENOUS THROMBOSIS	1 (1, 0.07%)	0.01% - 0.51%	1 (1, 0.07%)	0.01% - 0.51%
VENTRICULAR ECTOPY (INCLUDING PVCS)	1 (1, 0.07%)	0.01% - 0.51%	1 (1, 0.07%)	0.01% - 0.51%
VENTRICULAR TACHYCARDIA	2 (2, 0.15%)	0.04% - 0.58%	2 (2, 0.15%)	0.04% - 0.58%

Adverse Events Reported in Literature

Potential AEs associated with the implantation of ICD or CRT-D systems and additionally for LBBAP lead placement have been documented in various literature articles. A summary of those events and their published incidence are included below.

1. Haines DE, Wang Y, Curtis J. Implantable Cardioverter-Defibrillator Registry Risk Score Models for Acute Procedural Complications or Death After Implantable Cardioverter-Defibrillator Implantation. Circulation 2011;123:2069-2076.

The cohort of this study comprises patients undergoing ICD implantation from 1300 sites entering data in the National Cardiovascular Data Registry (NCDR) ICD Registry (USA) between January 1, 2006, and June 30, 2008. The rates of procedure related in-hospital complication and mortality were studied in patients from 268701 hospitalizations at 1300 hospitals.

Table 37: Prevalence of Procedure-Related Complications in the Overall Population (N=268701) as Well as in Patients Undergoing Elective ICD Implantation (N=179401)

Description	All Patients		Patients Undergoing Elective Implantation	
	N	%	N	%
Adverse Events				
Cardiac arrest	804	0.30	264	0.15
Drug reaction	249	0.09	152	0.08
Cardiac perforation	180	0.07	118	0.07
Cardiac valve injury	5	<0.01	4	<0.01
Conduction block	88	0.03	58	0.03
Coronary venous dissection	319	0.12	219	0.12
Hematoma	2509	0.93	1290	0.72
Lead dislodgement	2494	0.93	1542	0.86
Hemothorax	218	0.08	112	0.06
Pneumothorax	1126	0.42	677	0.38
Peripheral nerve injury	9	<0.01	8	<0.01
Peripheral embolus	75	0.03	26	0.01
Phlebitis, superficial	103	0.04	23	0.01
Phlebitis, deep	66	0.02	23	0.01
TIA	42	0.02	16	0.01
CVA/Stroke	154	0.06	52	0.03
MI	67	0.02	34	0.02
Pericardial tamponade	201	0.07	124	0.07
AV fistula	13	<0.01	0	<0.01
Infection related to device	76	0.03	33	0.02
Outcomes				
Any Complication	8182	3.05	4441	2.48
In-hospital death	1021	0.38	212	0.12

Description	All Patients		Patients Undergoing Elective Implantation	
	N	%	N	%
Any adverse events or in-hospital mortality	8589	3.20	4499	2.51
TIA indicates transient ischemic attack; CVA, cerebrovascular accident; MI, myocardial infarction; and AV, arterio-venous.				

2. Moore K, Ganesan A, Labrosciano C, et al. Sex Differences in Acute Complications of Cardiac Implantable Electronic Devices: Implications for Patient Safety. J Am Heart Assoc 2019;8

This study examined the influence of sex on acute complications. All patients aged >18 years from 2010 to 2015 who were a resident of Australia or New Zealand, undergoing a new pacemaker, ICD, or CRT implant were studied. A total of 81304 new implants (61658 pacemakers, 12097 ICDs, 7549 CRTs) were included.

Table 38: Risk of Complications After Cardiac Implantable Electronic Device Implantation

Primary Outcome	Pacemaker (N=61658)		ICD (N=12097)		CRT (N=7549)	
	N	%	N	%	N	%
Composite device-related complications	4702	7.6	1193	9.9	769	10.2
In hospital complications						
- Any in-hospital complication	2036	3.3	376	3.1	298	3.9
- Deaths	333	0.5	15	0.1	23	0.3
- Reoperation	1711	2.8	356	2.9	272	3.6
• Lead operation	981	1.6	209	1.7	163	2.2
◦ Removal	43	0.1	24	0.2	16	0.2
◦ Replacement	183	0.3	37	0.3	28	0.4
◦ Revision	787	1.3	153	1.3	124	1.6
• Generator operation	100	0.2	18	0.1	22	0.3
• Pocket reoperation	102	0.2	35	0.3	22	0.3
• Pericardial/pleural drainage	611	1.0	109	0.9	83	1.1
◦ Pericardial drainage	104	0.2	14	0.1	10	0.1
◦ Pleural drainage	522	0.8	95	0.8	74	1.0
Post-discharge complications						
- Any post-discharge complication	2802	4.5	859	7.1	505	6.7
- Deaths within 30 days	457	0.7	50	0.4	59	0.8
- Reoperation	1447	2.3	497	4.1	299	4.0
• Generator	348	0.6	150	1.2	84	1.1
• Lead	970	1.6	359	3.0	219	2.9
• Pocket reoperation	129	0.2	56	0.5	33	0.4
• Pleural/pericardial drainage	320	0.5	71	0.6	45	0.6
◦ Pleural drainage	73	0.1	20	0.2	12	0.2

Primary Outcome	Pacemaker (N=61658)		ICD (N=12097)		CRT (N=7549)	
	N	%	N	%	N	%
◦ Pericardial drainage	259	0.4	57	0.5	33	0.4
- Hospitalization for complications	1831	3.0	628	5.2	345	4.6
• Mechanical complication	1085	1.8	409	3.4	234	3.1
- Infection*	387	0.6	133	1.1	74	1.0
- Local perforation†	136	0.2	24	0.2	14	0.2
- Pocket complication‡	146	0.2	47	0.4	30	0.4
- VTE	110	0.2	31	0.3	8	0.1

VTE indicates venous thromboembolism.
*Infection includes device infection, endocarditis, or systemic infection.
†Local perforation includes admissions for perforation and/or inflammation such as a pneumothorax or a pericardial effusion.
‡Pocket complication includes hematoma or wound dehiscence.

3. Auricchio A, Schloss EJ, Kurita T, Meijer A, Gerritse B, Zweibel S, et al. Low inappropriate shock rates in patients with single- and dual/triple-chamber implantable cardioverter-defibrillators using a novel suite of detection algorithms: PainFree SST trial primary results. Heart Rhythm. 2015;12: 926–36.

The PainFree SST trial investigated new-generation ICDs to reduce inappropriate and unnecessary shocks through novel discrimination algorithms with modern programming strategies. This was a large, prospective, multi-site clinical trial that enrolled 2790 patients with approved indication for ICD implantation. Incidence of inappropriate therapy is summarized in Table 39.

Table 39: PainFree SST Inappropriate Therapy Incidence

Device Therapy	Inappropriate Therapy Incidence		
	1 year	2 years	3 years
Dual/triple-chamber device			
Inappropriate shock	1.5 % (CI 1.0%-2.1%)	2.8% (CI 2.1%-3.8%)	3.9% (CI 2.8%-5.4%)
Inappropriate therapy (shock or ATP)	2.3% (CI 1.7%-3.1%)	3.7% (CI 2.8%-4.8%)	5.7% (CI 4.0%-7.6%)
Single-chamber device			
Inappropriate shock	2.5% (CI 1.5%-3.9%)	3.7% (CI 2.2%-5.7%)	N/A
Inappropriate therapy (shock or ATP)	3.4% (CI 2.2%-5.0%)	4.8% (CI 3.2%-7.0%)	N/A

4. Medtronic SelectSecure™ MRI SureScan™ 3830 US Technical Manual, Medtronic plc, 2022 (14-16).

The technical manual for the Medtronic SelectSecure 3830 lead includes a section that describes the benefits and risks of pacing in the left bundle branch area using the Model 3830 lead. A total

of 58 articles were located that used the Model 3830 lead for left bundle branch area pacing and reported adverse events. Since not all articles reported events in all categories, the sample size for each category varies. Additionally, although articles may have reported events, the timing of the events was not always reported. The most commonly reported event was implant procedure-related conduction block, followed by septal perforation, and lead dislodgement. Of the 367 implant procedure-related conduction block events, 301 were transient events that resolved, 50 were persistent RBBB events, and 16 were persistent AV blocks. Of the 79 septal perforation events, 71 were observed during the implant procedure, and 8 were identified after the implant procedure (range: 2 days – 6 months). In all cases, leads were successfully repositioned to either an alternate site to achieve LBBAP or to RVP and no clinical sequelae or interventions were required other than lead repositioning. Of the 59 lead dislodgements reported, 26 occurred within the first 24 hours and there were 4 microdislodgements during follow-up that did not require revision as LV septal capture was obtained. See for the types of left bundle branch area lead-related adverse events reported.

Table 40: Left bundle branch area lead placement adverse events

Event	Number of studies reporting/sample size	Total Events
Elevated pacing thresholds	22/3129	16
Lead dislodgement	49/5753	59
Failure to capture/loss of capture/exit block	19/1534	12
Muscle stimulation	None reported	None reported
Pericardial effusion	12/2505	6
Venous occlusion	None reported	None reported
Septal perforation	43/5690	87
Cardiac tamponade	8/954	1
Pocket infection	26/4559	13
Procedure-related conduction block	10/1497	367
Undersensing	None reported	None reported
Oversensing	1/305	3

5. Jastrzebski M, Moskal P, Huybrechts W, et al. Left bundle branch-optimized cardiac resynchronization therapy (LOT-CRT): results from an international LBBAP collaborative study group. Heart Rhythm 2022; 19:13–21.table1

This study assessed the feasibility and outcomes of CRT based on left bundle branch area pacing (LBBAP, in lieu of the right ventricular lead) combined with coronary venous left ventricular pacing in an

international multi-site study. Of 91 patients with successful LOT-CRT, the following outcomes were reported:

- Lead dislodgement (n=2; 2.2%)
- Septal perforation (n=1; 1.1%)
- Pocket hematoma (n=2; 2.2%)
- Increased threshold (n=1; 1.1%)
- Infection (n=1; 1.1%)
- Death from heart failure (n=1; 1.1%)
- Death from non-cardiac issue (n=2; 2.2%)

Additional Adverse Events

The above incidences of each adverse event were reported from a collection of similar Medtronic studies or published papers. Other events that have been experienced in other studies or have the potential to be experienced by subjects, but were not recorded in these few Medtronic studies (or may have been reported with different terminology) also include:

Anemia, Aneurysm or pseudo-aneurysm, Angina pectoris, Aphasia, Arterio-venous fistula, Asystole, Atrial septal defect, Back pain, Blood or air embolism, Bruising, Cardiac dissection, Cardiogenic shock, Cellulitis, Constrictive pericarditis, Coronary artery constriction, Coronary artery disease, Coronary artery occlusion, Coronary vein occlusion, Device capture issue, Device connection issue, Device lead issue, Device pacing issue, Device protrusion, Device signal detection issue, Diaphoresis, Dressler's syndrome, Dysplasia, Ecchymosis, Edema, Electrical conduction disorders, Electrical shock, Electromagnetic interference, Endocarditis, Erythema, Exit block, Extravasation, Failure to terminate a ventricular tachycardia/ ventricular fibrillation, Fatigue, Fever, Headache, Heart block, Heart rate increase, Hematuria, Hyperkalemia, Hypertension, Impedance decreased, Impedance increased, Implant site abscess, Implant site complication, Implant site discomfort, Implant site drainage, Implant site seroma, Implant site swelling, Inappropriate device detection, Inappropriate device programming, Inflammation, Insomnia, Lead insertion tool delivery problem, Local swelling, Loss of consciousness, Mental status change, Musculoskeletal discomfort, Myocardial damage, Myocardial irritability, Neck pain, Necrosis, Neurological symptoms, Numbness at incision site, Numbness in hand, Panic attack, Paresthesia, Pericardial rub, Phlebitis, Poor hemodynamic recovery, Presyncope, Reduced cardiac output, Reduced perfusion, Respiratory failure, Restlessness, Retrosternal pain, Scar or scarring, Sepsis, Septic shock, Skin injuries, Skin reaction, Sleep apnea, Stroke, Subcutaneous emphysema, Sudden cardiac death, Thoracic pain, Thrombocytopenia, Thromboembolism, Thrombosis, Nerve damage, Transient ischemic attack, Urticaria, Valve damage, Vascular trauma, Vasovagal reaction, Venous insufficiency, Venous stenosis, Ventricular extrasystole, Vessel perforation or laceration, Vessel spasm, Vomiting, Weakness.

Appendix E: Participating Investigators and Institutions

A complete list of participating investigators and institutions will be provided under separate cover upon request.

Appendix F: Investigator Agreement and Signature Page (where applicable)

Study product Name	Model 093000 lead
Sponsor	**Sponsor:** **Medtronic, Inc.** 8200 Coral Sea Street NE Mounds View, MN 55112 United States of America +1 800 328 2518 **Local Sponsors:** **Australia** Medtronic Australasia Pty Ltd 2 Alma Road, Macquarie Park NSW, 2113 Australia +61 2 9857 9000 **Canada** Medtronic Canada ULC 99 Hereford Street Brampton Ontario, L6Y 0R3 Canada +1 905 460 3800 **Europe, Middle East, Africa** Medtronic, Bakken Research Center B.V. Endepolsdomein 5 6229 GW Maastricht The Netherlands +31 43 35 66 566 **Hong Kong** Medtronic Hong Kong Medical Ltd. 1104-11, 11/F, Tower 1, The Gateway, Harbour City, Kowloon Hong Kong SAR, China +852 2919 1300 **Japan** Medtronic Japan Co., Ltd. 1-2-70 Konan, Minato-ku, Tokyo Japan 108-0075 +81 3 6776 0105

	Mainland China Medtronic (Shanghai) Management Co., Ltd. 2106A, 21th Floor, No. 28. Maji Road, China (Shanghai) Pilot Free Trade Zone, 200131, Shanghai, P.R. China +86 215 866 9877 **Malaysia** Medtronic Malaysia Sdn. Bhd. B-23-1, Level 23 The Ascent, Paradigm No. 1 Jalan SS7/26A Kelana Jaya 47301 Petaling Jaya Selangor, Malaysia +603 7883 8000
Clinical Investigation Plan Identifier	MDT22048
Version Number/Date	2.0 / 23-JAN-2024

I have read the protocol, including all appendices and addenda as applicable, and I agree that it contains all necessary details for me and my staff to conduct this study as described. I will conduct this study as outlined herein and will make a reasonable effort to complete the study within the time designated.

I agree to comply with the Declaration of Helsinki, the Clinical Investigation Plan, and Good Clinical Practice, as well as local laws, regulations, and standards. I agree to ensure that the confidential information contained in this document will not be used for any purpose other than the evaluation and conduct of the clinical investigation without the prior written consent of Medtronic.

I will provide all study personnel under my supervision copies of the protocol and access to all information provided by Medtronic. I will discuss this material with them to ensure that they are fully informed about the products and the study.

Investigator's Signature:	
Investigator's Name:	
Institution:	
Date:	

Investigator Statement and Signature Page China

Investigator's statement

I agree that:

1. I will conduct this clinical trial in strict compliance with the Declaration of Helsinki, current laws and regulations of China, and the requirements of the Clinical Investigation Plan;
2. I will record all required data accurately on the Case Report Form (CRF) and assist to complete the final report of the clinical investigation;
3. The investigational medical device will be used only for this clinical investigation and the receipt and use of the investigational medical device will be recorded completely and accurately and the records will be retained during the process of the clinical investigation;
4. The monitors and auditors authorized or designated by the Sponsor and the regulatory authorities are allowed to conduct monitoring, audit and inspection for the clinical investigation;
5. The clinical investigation should be conducted in strict compliance with contract/articles of agreement signed by all parties.

I have already read the clinical study protocol, including the above statement and I fully agree all the above requirements.

Investigational Medical Device Information

Category of investigational medical device: Class III

Class III medical devices requiring clinical trial approval: Yes ☐ No ☒

Similar product in China: Yes ☒ No ☐

Principal Investigator: Signature: Date:

Medical device clinical trial institution: Signature (Stamp):

Date:

Sponsor:

Signature (Stamp):

Date:

Appendix G: Ethics Committee and Competent Authority List

Regulatory Bodies, Competent Authorities, and Ethics Committees and their Chairperson(s) that will be utilized as part of the study will be distributed under separate cover upon request.

Appendix H: EUDAMED Generated Unique Identifier

EUDAMED generated unique identifier once available will be provided under separate cover.

Version History

Version	Summary of changes	Justification of changes	Potential impact of the change on performance, effectiveness, or safety or other endpoints	Identification of the affected study documents	Author(s)/ Title
1.0	Not Applicable, New Document	Not Applicable, New Document	Not Applicable, New Document	Not Applicable, New Document	[redacted] Principal Clinical Research Specialist [redacted], Senior Principal Statistician

2.0	• Correction of typos and added minor clarifications • Added "Subjects from 12 years of age until adult also have a separate indication for pacing or CRT or are anticipated to develop one." to adolescent pediatric inclusion criterion • Updated Data collection table in 2.0 Synopsis and 9.2 Data Collection and Study Procedure Requirements to align with CIP language (i.e. removed medication collection at baseline, ECG collection at system modification and added note about permanent discontinue pacing therapy data collection) • Added "Other reports may be generated at the request of regulatory bodies and/or other business purposes if appropriate" in	• Adolescent pediatric inclusion criterion was updated on regulatory authority feedback • Other updates were corrections or clarifications • Updates to Table 28: Sponsor reports for Europe, Middle East and Africa to reflect current regulations	No impact	Informed Consent Form	[redacted], Principal Clinical Research Specialist [redacted] Senior Principal Statistician

Version	Summary of changes	Justification of changes	Potential impact of the change on performance, effectiveness, or safety or other endpoints	Identification of the affected study documents	Author(s)/ Title
	section 13.2 Data Reporting • Updated hypothesis language in section 13.4 Primary Objective #1: Efficacy to correct typo • Updated Table 28: Sponsor reports for Europe, Middle East and Africa				