ExtraVascular Implantable Cardioverter Defibrillator (EV ICD) Japan Study

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Medtronic

Statistical Analysis Plan

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1. Version History

Version	Summary of Changes	Author(s)/Title
1.0	• Not Applicable, New Document	Gregory Hilleren, Sr Statistician

2. List of Abbreviations and Definitions of Terms

Abbreviation	Definition
AE	Adverse Event
ATP	Antitachycardia pacing
CEC	Clinical Events Committee
CIP	Clinical Investigation Plan
DMC	Data Monitoring Committee
EV ICD	ExtraVascular Implantable Cardioverter Defibrillator
MHLW	Ministry of Health, Labour, and Welfare
ICD	Implantable Cardioverter Defibrillator
PHD	Pre-hospital Discharge Visit
SAP	Statistical Analysis Plan
S-ICD	Subcutaneous Implantable Cardioverter Defibrillator
SSVA	Sustained shockable ventricular arrhythmia

3. Introduction

This Statistical Analysis Plan (SAP) has been designed to document, before data are analyzed, the rationale for the study design, and the planned analyses that will be included in study reports. This SAP does not limit the analysis in reports. Additional analysis of the study data beyond this plan may be needed. This SAP is developed for the EV ICD Japan study, based on the Clinical Investigation Plan (CIP) version 3.0 dated October 17, 2022.

Today, implantable cardioverter defibrillator (ICD) therapy is the treatment of choice for subjects who are at risk for sudden cardiac death due to life-threatening ventricular arrhythmias. Traditional ICD systems with transvenous leads are considered standard of care for primary or secondary prevention of tachyarrhythmic death. However, these systems have limitations. Short- and long-term complications arising from ICD systems with transvenous leads, such as infection, pneumothorax, venous thrombosis, lead dislodgement, lead malfunction, and lead perforation, have persisted for decades as impediments

to ICD usage. As a result, there is demand for novel ICD systems that circumvent the potential disadvantages of transvenous ICD systems by preserving the heart and vasculature.

Medtronic has developed an extravascular ICD system which uses a substernal lead rather than a transvenous or a subcutaneous lead. The EV ICD System has similar capabilities to a single-chamber transvenous system while avoiding leads in the heart or vasculature. Compared to current market-released non-transvenous subcutaneous ICDs, the EV ICD System includes a smaller device that uses less defibrillation energy which may result in longer battery life and has the additional capabilities to deliver pacing therapies such as antitachycardia pacing (ATP) and backup asystole pacing from a single device.

In order to develop and evaluate a newly designed system for the substernal space, Medtronic completed pre-clinical research evaluations of substernal defibrillation, pacing, and sensing, and subsequently initiated three acute human clinical research feasibility studies with combined 121 implants to explore the potential development of a future chronic implantable extravascular defibrillation system with a lead implanted in the substernal space. Later, a first-in-human chronic pilot study was initiated based on the assurance from acute feasibility data. The acute feasibility and pilot studies contributed to the advancement of the EV ICD program, including refinement of the device, algorithm and implant procedure. Based on the results of this pilot study, a pivotal study with 356 enrollments with 316 subjects with an EV ICD implant procedure attempt was conducted to demonstrate the safety and efficacy of the EV ICD system: a complete single-chamber extravascular ICD system with the lead implanted substernally. Results of this study showed both primary endpoints were met; the defibrillation testing success rate at implant was 98.7% and the freedom from major complications related to the system and/or procedure at 6 months post-implant was 92.6%. At the time of this protocol being written, patients are still in follow-up and the study is undergoing regulatory review.

The EV ICD Japan study aims to supplement the pivotal analysis and provide additional data to support the safety and efficacy of the EV ICD system within a Japanese population.

4. Study Objectives

4.1 Primary Objectives

The first primary objective is to characterize the freedom from major complications related to the EV ICD System and/or procedure at 2 weeks post-implant. The endpoint is defined as a subject's first occurrence of a major complication related to the EV ICD System and/or procedure, as determined by an independent Clinical Events Committee (CEC), that occurs on or prior to 2 weeks (14 days) post-implant.

For an adverse event to meet the endpoint, the event must have occurred within 14 days (inclusive) of the EV ICD System implant and be adjudicated by the CEC as being a major complication related (causal relationship) to the EV ICD System and/or procedure. Major complications are those complications resulting in:

- Death
- Permanent loss of defibrillation function (specifically shock) due to mechanical or electrical dysfunction of the device
- Hospitalization
- Prolongation of an existing hospitalization by at least 48 hours
- System revision (reposition, replacement, explant)

The second primary objective is to characterize the defibrillation efficacy at implant of the EV ICD System. The endpoint, defibrillation testing success, is defined as:

- Single sustained shockable ventricular arrhythmia (SSVA) conversion at 20J, or
- Conversion of two consecutive episodes of SSVA at 30J in final system configuration.

Notes:

- In one of the two consecutive SSVA episodes, up to two 30J shocks are permitted.
- To achieve final system configuration, changing the position of the ICD generator and/or the lead, or changing shock polarity is permitted.
- Subjects can return for testing on another day if testing is not fully completed on the day of implant.
- If SSVA cannot be induced, the EV ICD System must be removed (refer to CIP section 8.5.8).
- For more information on the rationale behind these objectives, refer to section 7.7 (i.e., CIP section 12).

4.2 Ancillary Objectives

- Characterize appropriate and inappropriate shocks
- Characterize electrical performance (pacing capture thresholds, pacing impedance, sensing amplitudes) over time
- Characterize extracardiac pacing sensation
- Characterize asystole pacing
- Summarize ATP performance with spontaneous arrhythmias
- Summarize adverse events
- Characterize EV ICD defibrillation testing conducted per physician discretion

5. Investigation Plan

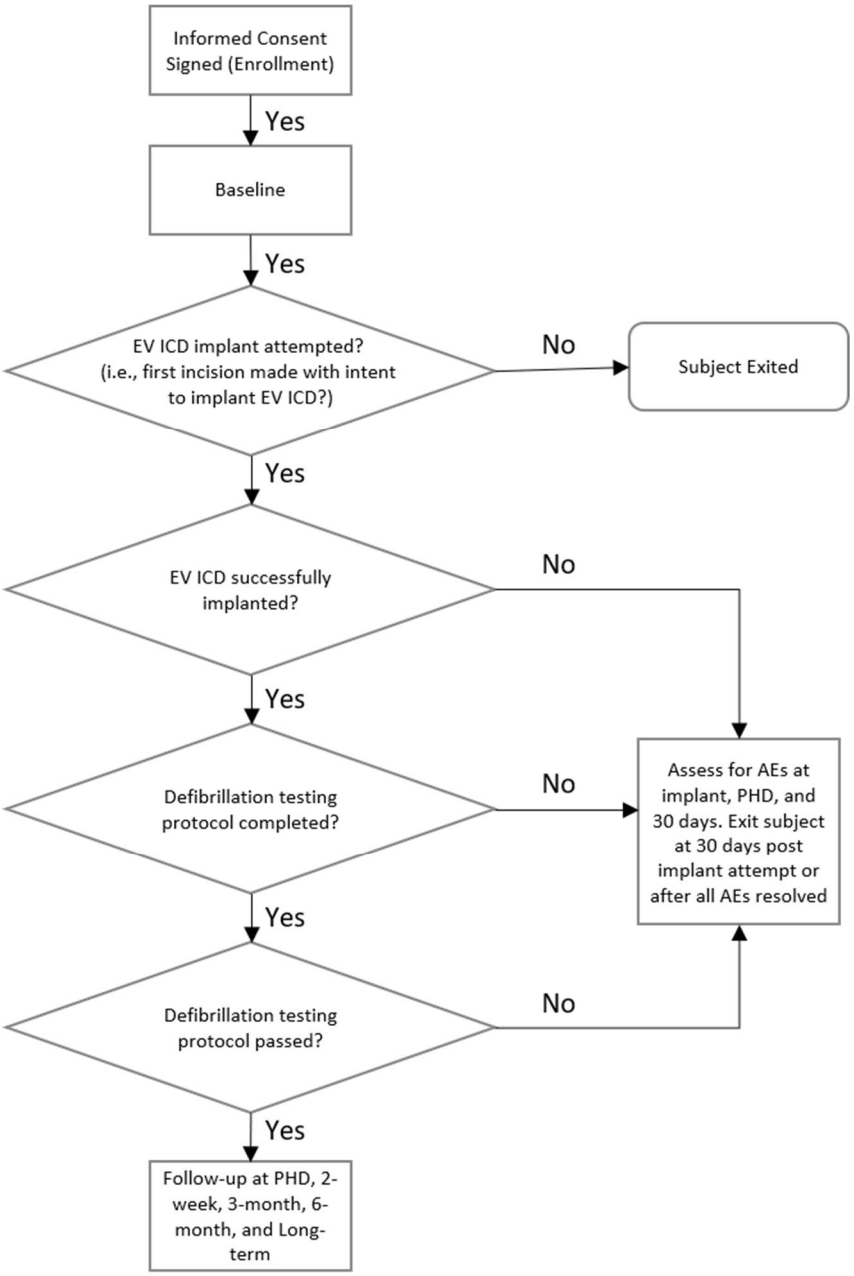
The EV ICD Japan Study is a prospective, multi-center, single-arm, non-randomized, pre-market clinical study. Enrollment will include about 15 and up to 25 subjects at up to 3 sites in Japan. Subject inclusion/exclusion criteria can be found in CIP section 7.

Participating sites that enroll faster than others will be allowed to do so to maintain an adequate enrollment rate. However, to ensure a reasonable distribution of experience and minimize site bias in study results, the maximum number of subjects enrolled at each site will be capped at 12 (approximately 50% of 25 total enrollments).

The expected study duration is approximately 1.5 years from the study's first enrollment. The enrollment period is expected to take approximately 5 months. Individual subjects may be participating in the study for a period of minimum 1.5 to approximately 2.5 years. The duration of individual subject participation will vary based on timing of site activation, timing of enrollment and enrollment rate. Subjects will undergo assessments at Baseline, Pre-Hospital Discharge, 2 Weeks, 3 Months, 6 Months, and every 6 months thereafter until official study closure. Official study closure is defined as when Medtronic and/or Ministry of Health, Labour, and Welfare (MHLW) requirements have been satisfied per the CIP and/or by a decision by Medtronic or regulatory authority to stop or close the study. Official study closure is expected to occur after the EV ICD System is approved by the MHLW, anticipated in 2024.

The following diagram provides an overview of the EV ICD Japan Study. This can also be found in CIP section 5.

Figure 1: Overview of the EV ICD Japan Study



6. Determination of Sample Size

As stated in the CIP, about 15 and up to 25 subjects will be implanted with the investigational EV ICD system. Enrollment is stopped once 15 subjects have completed the defibrillation protocol testing at

implant; but any previously scheduled implant procedures will be allowed to occur. There are no hypotheses for both primary safety and efficacy objectives in this study. The sample size is not pre-specified to satisfy any statistical requirements, but rather to allow for multiple investigational sites enrolling patients and implanting the EV ICD system.

7. Statistical Methods

The CIP version 3.0 dated October 17, 2022 is the currently approved version as of the approval date of this document. Should there be any additional CIP updates, the impacts of it on the integrity of the study will be evaluated; if such impacts are confirmed, the data collected before and after the amendment will be analyzed statistically per ISO 14155:2020 to assess the effect of the amendment on the safety and efficacy analysis.

7.1 Study Subjects

7.1.1 Disposition of Subjects

This is a single-arm study. After subjects sign the informed consent form, they are enrolled in the study. Screening logs are not used in this study as historically they have typically been found to have poor compliance. Extensive inclusion/exclusion criteria have been chosen in this study to restrict the target population to those thought to be best served by this EV ICD system and mitigate the risk of selection bias. Enrollment can be a stand-alone visit or can occur on the same day as the baseline visit. After that, subjects will undergo implant of the EV ICD system, with required defibrillation, sensing, impedance and pacing testing. Subjects will then return for follow-up visits at 2 Weeks, 3 Months, 6 Months, and every 6 months thereafter. Subject disposition will be presented using a flow diagram where completed visits, missed visits, and attrition due to exit and death will be indicated.

7.1.2 Clinical Investigation Plan (CIP) Deviations

A study deviation is an event within a study that did not occur according to the CIP or the Clinical Trial Agreement. Study deviations will result in corresponding Study Deviation eCRFs being completed. These deviations will be summarized with descriptive statistics including, for each type of deviation, how many occurrences there were in the study, and the number of subjects experiencing each type of deviation. Inclusion/exclusion violations will not result in subjects being excluded from analysis of objectives. Of particular importance will be required testing not completed at implant or follow-up. If it is discovered there were subjects not meeting the inclusion/exclusion criteria who underwent an implant attempt and possibly defibrillation testing, additional analyses may be performed with these subjects excluded.

7.1.3 Analysis Sets

All subjects with an implant attempt of the investigational product will be included in the primary analysis for the primary safety objective. All subjects who complete the defibrillation protocol will be included in the primary analysis for the primary efficacy objective.

7.2 General Methodology

Data analysis will be performed by Medtronic statisticians or designees.

The cohort will include all enrolled subjects who undergo the study procedures unless the subject does not complete the required testing, and there are no pre-specified subgroups for assessment. For endpoints involving only measurements collected at follow-up visits, only subjects who complete those visits will be included in the analysis of those endpoints.

7.3 Handling of Missing, Unused, and Spurious Data and Dropouts

All available data will be included in the data listings and tabulations. With regard to the primary safety objective, subjects who exit the study prior to experiencing a major system or procedure-related complication will be censored at the date of their exit (in the case of the subject being lost to follow-up or death of unknown classification, the subject will be censored at the date of last contact with the subject) in the calculation of any Kaplan-Meier freedom from complication rates.

7.4 Adjustments for Multiple Comparisons

There is no adjustment for multiple comparisons. Because a subject may be included in the analysis for the primary safety objective but not the efficacy objective if the subject does not complete the defibrillation protocol, the primary safety and efficacy objectives are not independent.

7.5 Demographic and Other Baseline Characteristics

Descriptive statistics will be used to summarize baseline and demographic characteristics. For categorical data, counts and percentages will be employed, while for continuous variables, means, standard deviation, quartiles, minimum, and maximum will be provided. These statistics will be provided both for all enrolled subjects and for the subset of subjects who undergo implant of the EV ICD system.

7.6 Treatment Characteristics

Descriptive statistics will be used to summarize all implant procedure information collected, including:

- Pre-procedure and substernal tunnel characteristics
- Sensing testing via analyzer and lead insertion
- Closure characteristics
- Operative time: Time of first incision to time of final device pocket suture

7.7 Evaluation of Objectives

7.7.1 Primary Objective #1: Safety

Characterize the freedom from major complications related to the EV ICD System and/or procedure at 2 weeks post-implant.

7.7.1.1 Hypothesis

There are no hypotheses for this objective.

7.7.1.2 Performance Requirements and Endpoint Definition

Performance requirements are not pre-specified for this objective. The endpoint is defined as a subject's first occurrence of a major complication related to the EV ICD System and/or procedure as determined by the independent Clinical Event Committee (CEC) that occurs on or prior to 2-weeks (14-days) post-implant.

For an adverse event to meet the endpoint, the event must have occurred within 14 days (inclusive) of the EV ICD System implant attempt and be adjudicated by the CEC as being a major complication related (causal relationship) to the EV ICD System and/or procedure. Major complications are those complications resulting in:

- Death
- Permanent loss of defibrillation function due to mechanical or electrical dysfunction of the device
- Hospitalization (see CIP Table 10 for Hospitalization definition)
- Prolongation of an existing hospitalization by at least 48 hours
- System revision (reposition, replacement, explant)

7.7.1.3 Rationale for Performance Criteria

This objective is for the purpose of gathering data pertaining to device safety over the first 2 weeks post-implant. There are no pre-specified performance criteria.

7.7.1.4 Analysis Methods

Results will be summarized in aggregate using descriptive statistics. The total number of major complications experienced by subjects for whom an implant is attempted will be summarized. The primary analysis for primary safety endpoint will be based on the endpoint definition described in section 7.7.1.2. Subjects not experiencing an event will be censored at their last point of contact. The 14-day freedom from major complication rate will be generated using the Kaplan-Meier method.

If any adverse events that occurred within 14 days (inclusive) of the EV ICD System implant attempt were adjudicated by the CEC as being major complications and the relatedness to the EV ICD System and/or procedure was determined by the CEC as "probable", a sensitivity analysis will be conducted with such adverse events included as having met the primary safety endpoint. An additional sensitivity

analysis may be performed including major complications with a system or procedure-relatedness classification of "possible", should there be any such major complications.

7.7.1.5 Determination of Subjects/Data for Analysis

All subjects with an implant attempt of the investigational product will be included in the analysis.

7.7.2 Primary Objective #2: Efficacy

Characterize the EV ICD defibrillation testing success rate at implant.

7.7.2.1 Hypothesis

There are no hypotheses for this objective.

7.7.2.2 Performance Requirements and Endpoint Definition

Performance requirements are not pre-specified for this objective. The endpoint, defibrillation testing success, is defined as:

- Single SSVA conversion at 20J, or
- Conversion of two consecutive episodes of SSVA at 30J in final system configuration.

Notes:

- In one of the two consecutive SSVA episodes, up to two 30J shocks are permitted.
- To achieve final system configuration, changing the position of the ICD generator and/or the lead or changing shock polarity is permitted.
- Subjects can return for testing on another day if testing is not fully completed on the day of implant.

7.7.2.3 Rationale for Performance Criteria

This objective is for the purpose of gathering data pertaining to defibrillation efficacy at implant. There are no pre-specified performance criteria.

7.7.2.4 Analysis Methods

Results will be summarized in aggregate using descriptive statistics. Subjects will be partitioned by the results of their defibrillation testing (e.g., no rescue shocks required, one rescue shock required), with counts and percentage falling into each subgroup reported. Each subject who completes the defibrillation protocol will be determined to either have successfully met the defibrillation endpoint or not met the endpoint. The proportion of subjects having EV ICD defibrillation success at implant will be calculated: the denominator is the number of subjects who complete the defibrillation protocol, and the numerator is the number of subjects who have defibrillation success at implant. Subjects who do not complete the defibrillation protocol will not be included in this primary analysis.

7.7.2.5 Determination of Subjects/Data for Analysis

All subjects who complete the defibrillation protocol will be included in the analysis.

7.7.3 Ancillary Objective #1: Appropriate and Inappropriate Shocks

Characterize appropriate and inappropriate shocks.

7.7.3.1 Hypothesis

There are no hypotheses for this objective. Spontaneous episodes receiving shocks will be summarized.

7.7.3.2 Performance Requirements and Endpoint Definition

Performance requirements are not pre-specified for this objective. The endpoint is defined as a shock delivered by the EV ICD. Spontaneous arrhythmic episodes resulting in a shock will be adjudicated to determine the underlying rhythm.

7.7.3.3 Rationale for Performance Criteria

Due to the minimal number of appropriate and inappropriate shocks expected for spontaneous arrhythmias, this objective is intended to only characterize device performance with regard to sensing ventricular arrhythmias and delivering shocks when the episode either does not self-terminate or is not terminated by ATP. There are no pre-specified performance criteria.

7.7.3.4 Analysis Methods

Results will be summarized in aggregate using descriptive statistics. All shocks delivered by the device for spontaneous arrhythmias will be partitioned by whether the treated rhythm was a VT/VF episode, and by the specific rhythm of the episode. Both the number of episodes and the number of subjects experiencing such episodes will be reported, as well as the energy delivered. Kaplan-Meier curves for time to first appropriate shock and time to first inappropriate shock may be provided to demonstrate shock incidence. Any instances of VT/VF terminated by ATP but also receiving a shock following ATP delivery will be reported.

7.7.3.5 Determination of Subjects/Data for Analysis

All subjects successfully implanted with an EV ICD having at least one device interrogation post-implant will be included in the analysis. At minimum, all episodes occurring by the date at which all implanted subjects have had the opportunity to be followed for 2 weeks post-implant will be included.

7.7.4 Ancillary Objective #2: Electrical Performance

Characterize electrical performance (pacing capture thresholds, pacing impedance, sensing amplitudes) over time.

7.7.4.1 Hypothesis

There are no hypotheses for this objective. Pacing capture performance, as well as pacing impedance and sensing amplitudes, will be summarized.

7.7.4.2 Performance Requirements and Endpoint Definition

Performance requirements are not pre-specified for this objective. The endpoints are defined as pacing capture threshold, pacing impedance, and sensing amplitude. The pacing testing will be performed at pre-hospital discharge, as well as visits at 2 weeks, 3- and 6-months post-implant and every 6 months thereafter.

7.7.4.3 Rationale for Performance Criteria

This objective is for the purpose of characterizing device performance with regard to achieving pacing capture and determining sensing performance over time. There are no pre-specified performance criteria.

7.7.4.4 Analysis Methods

Results will be summarized in aggregate using descriptive statistics. For each follow-up visit, the proportion of subjects undergoing pacing testing will be reported, as well as the proportion for whom capture is obtained. Mean impedance and R-wave amplitudes will also be reported at each follow-up for which the testing occurs (pre-hospital discharge, 2 weeks, 3- and 6-months post-implant, and every 6 months thereafter).

7.7.4.5 Determination of Subjects/Data for Analysis

All subjects successfully implanted with an EV ICD having relevant data (pacing tests, impedance, sensing amplitudes) will be included in the analysis of that endpoint at that timepoint.

7.7.5 Ancillary Objective #3: Extracardiac Pacing Sensation

Characterize extracardiac pacing sensation.

7.7.5.1 Hypothesis

There are no hypotheses for this objective.

7.7.5.2 Performance Requirements and Endpoint Definition

Performance requirements are not pre-specified for this objective. The endpoint will be defined as whether pacing therapies were programmed OFF due to pacing sensation.

7.7.5.3 Rationale for Performance Criteria

There are no pre-specified performance criteria; pacing sensation at follow-up will be summarized and reported.

7.7.5.4 Analysis Methods

Results will be summarized in aggregate using descriptive statistics. Descriptive statistics will be used to summarize distribution among the subjects who completed each follow-up visit, and whether pacing therapies, specifically ATP, were programmed OFF due to the subject reporting pacing sensation. This objective will be analyzed using data from the pre-hospital discharge, 2 weeks, 3- and 6-month, and long-term visits.

7.7.5.5 Determination of Subjects/Data for Analysis

For each visit (e.g., PHD, 2 weeks), all subjects successfully implanted with an EV ICD who complete that visit will be included in the analysis.

7.7.6 Ancillary Objective #4: Asystole Pacing

Characterize asystole pacing.

7.7.6.1 Hypothesis

There are no hypotheses for this objective, as the purpose of this objective is simply to characterize prevalence of asystole pacing in this population.

7.7.6.2 Performance Requirements and Endpoint Definition

Performance requirements are not pre-specified for this objective. The endpoint is the amount of pacing for asystole the subject received.

7.7.6.3 Rationale for Performance Criteria

This objective is for the purpose of characterizing prevalence of need for asystole pacing in this population. There are no pre-specified performance criteria.

7.7.6.4 Analysis Methods

The CIP Section 8.6 specifies the programming requirements and recommendation at the pre-hospital discharge visit, where the requirements on pause prevention is for asystole pacing. Descriptive statistics will be used to summarize the number of subjects and amount of asystole pacing experienced during follow-up.

7.7.6.5 Determination of Subjects/Data for Analysis

All subjects successfully implanted with an EV ICD with at least one device interrogation post-implant will be eligible for the analysis. At minimum, all instances occurring on or before the date at which all implanted subjects have had the opportunity to be followed for 2 weeks post-implant will be included.

7.7.7 Ancillary Objective #5: ATP Performance

Summarize ATP performance with spontaneous arrhythmias.

7.7.7.1 Hypothesis

There are no hypotheses for this objective, as the purpose is to characterize defibrillation performance through use of ATP.

7.7.7.2 Performance Requirements and Endpoint Definition

Performance requirements are not pre-specified for this objective. The endpoint is defined as whether a spontaneous ventricular tachycardia episode for which ATP was delivered by the EV ICD was terminated by ATP. Spontaneous arrhythmias will be adjudicated to determine the underlying rhythm and whether they were terminated by ATP.

7.7.7.3 Rationale for Performance Criteria

It is projected that only a small subset of implanted subjects may experience one or more ventricular arrhythmias during follow-up. Therefore, device performance regarding such episodes will be characterized only. There are no pre-specified performance criteria.

7.7.7.4 Analysis Methods

Results will be summarized in aggregate using descriptive statistics. All monomorphic and polymorphic ventricular arrhythmias with EGM will be partitioned by whether the treated rhythm received ATP and/or shock, whether it successfully terminated as a result, and by the specific rhythm of the episode (monomorphic vs. polymorphic VT/VF). Both the number of episodes and the number of subjects experiencing such episodes will be reported, as well as the percentage of monomorphic VT episodes successfully terminated by ATP.

7.7.7.5 Determination of Subjects/Data for Analysis

All subjects successfully implanted with an EV ICD having at least one device interrogation post-implant will be included in the analysis. At minimum, all VT/VF episodes occurring on or prior to the date by which all implanted subjects have had the opportunity to be followed for 2 weeks post-implant will be included in the analysis.

7.7.8 Ancillary Objective #6: Adverse Events

Summarize adverse events.

7.7.8.1 Hypothesis

There are no hypotheses for this objective, as safety of the EV ICD System is being evaluated by Primary Objective #1 (see section 7.7.1). This objective is to provide a comprehensive summary of adverse events experienced during follow-up.

7.7.8.2 Performance Requirements and Endpoint Definition

Performance requirements are not pre-specified for this objective. The endpoint is an adverse event (see CIP Table 10 for definition of adverse event) experienced by a subject post-enrollment and prior to exit. Adverse events will be adjudicated by a Clinical Events Committee for relatedness to the EV ICD System and procedure.

7.7.8.3 Rationale for Performance Criteria

This objective is for the purpose of gathering comprehensive data pertaining to subject health over at least the first two weeks post-implant. There are no pre-specified performance criteria.

7.7.8.4 Analysis Methods

Results will be summarized in aggregate using descriptive statistics. Counts and percentages of subjects experiencing system and/or procedure-related adverse events will be reported, as well as, in the case of system-related events, the specific component of the system to which the event was related. Adverse Events will be broken out by MedDRA key term, with both counts of events and counts of subjects experiencing each type of event reported. The seriousness of adverse events and adverse device effects will also be summarized. Details of individual adverse events including MedDRA key term, center diagnosis, description, actions, outcome, relatedness and seriousness will be listed. When deemed necessary, individual adverse events where center investigator classification on relatedness differs from the CEC adjudication and/or center investigator assessment on seriousness differs from the Medtronic Safety assessment will be identified for reporting.

7.7.8.5 Determination of Subjects/Data for Analysis

All subjects for whom an implant of the investigational product is attempted will be included in the analysis. At minimum, all adverse events recorded by the date by which all implanted subjects have been followed at least 2 weeks post-implant will be included.

7.7.9 Ancillary Objective #7: Chronic Defibrillation Testing

Characterize EV ICD defibrillation testing conducted per physician discretion.

7.7.9.1 Hypothesis

No statistical hypotheses will be tested for this objective.

7.7.9.2 Performance Requirements and Endpoint Definition

Chronic defibrillation testing per physician discretion as a part of device troubleshooting or after a system modification. According to CIP section 8.7.5, if device troubleshooting includes a chronic defibrillation test, it is recommended to follow the steps outline in CIP Appendix H: Chronic Defibrillation Testing Protocol. According to CIP section 8.13, if a system modification involves replacing or repositioning the lead, it is recommended to demonstrate at least a 10J safety margin.

Performance requirements are not pre-specified for this objective.

7.7.9.3 Rationale for Performance Criteria

Chronic defibrillation testing is rarely done as standard of care, and no single testing protocol is required for chronic testing. There are no performance criteria for this objective.

7.7.9.4 Analysis Methods

Results will be summarized in aggregate using descriptive statistics. Subjects will be partitioned by the results of their defibrillation testing (e.g., no rescue shocks required, one rescue shock required), with counts and percentage falling into each subgroup reported.

7.7.9.5 Determination of Subjects/Data for Analysis

All subjects for whom defibrillation testing is attempted per physician discretion will be included in the analysis.

7.7.10 Supplemental Analysis

Quality of Life/subject acceptance will also be measured through the SF-12 Questionnaire at baseline and 6 months. The tool will be administered so that subject response in this study may be compared to response to such tools in other ICD studies. Data collected through these questionnaires will be summarized using descriptive statistics. For the SF-12, the version 2 of the questionnaire (SF-12v2) will be used and the data handling will be based on the instructions provided by Ware et al.[1]

7.8 Safety Evaluation

Ancillary objective #6 is to summarize adverse events, see section 7.7.8 for details. In addition, the term and center description of individual device deficiencies and whether they could have led to a serious adverse device effect will be reported. Individual deaths including death classification per center investigator and per CEC adjudication will also be listed.

8. Validation Requirements

Level I validation will be performed on programs related to the primary objectives, while level II validation will be performed for programs related to all other objectives, as well as for programs summarizing non-objective related information such as baseline demographics, study deviations, follow-up compliance, and study exits.

1 Ware JE et al. How to Score Version 2 of the SF-12 Health Survey (With a Supplement Documenting Version 1). QualityMetric Incorporated, ISBN: 1-891810- 10- 3,