S-ICD® System Post Approval Study (S-ICD PAS)

CLINICAL PROTOCOL

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1. PROTOCOL SYNOPSIS

Study Name	S-ICD Post Approval Study
Objective:	The primary purpose of the S-ICD Post Approval Study is to document long term safety and effectiveness outcomes associated with the implantation of the SQ-RX pulse generator and Q-TRAK electrode in a commercial clinical setting.
Indications for Use	The S-ICD System is intended to provide defibrillation therapy for the treatment of life-threatening ventricular tachyarrhythmias in subjects who do not have symptomatic bradycardia, incessant ventricular tachycardia, or spontaneous, frequently recurring ventricular tachycardia that is reliably terminated with anti-tachycardia pacing.
Test Device	The S-ICD System consists of four devices: • SQ-RX subcutaneous implantable defibrillator pulse generator; • Q-TRAK subcutaneous electrode; • Q-GUIDE electrode insertion tool (EIT); • Q-TECH programmer.
Study Design	The S-ICD Post Approval Study is a non-randomized registry that will retrospectively enroll subjects who participated in the S-ICD Clinical Investigation (IDE G090013) and prospectively enroll new candidates for the S-ICD System.
Planned Number of Subjects	The target enrollment sample size is 1,616 subjects [redacted] in the analysis cohort at 60 months.
Planned Number of Centers	Up to 150 centers in the US.
Primary Endpoints	• The primary safety endpoint of the study is the Type I (caused by the S-ICD System) Complication Free Rate at 60 months compared to a performance goal of 85%. • The primary effectiveness endpoint is the Overall Shock Effectiveness in Converting Spontaneous Discrete Episodes of VT/VF through 60 months compared to a performance goal of 94%.
Secondary Endpoints	• The secondary safety endpoint of the study is the Electrode-Related Complication Free Rate at 60 months compared to a performance goal of 92.5%. • The secondary effectiveness endpoint is First Shock Effectiveness in Converting Induced (Acute) and Spontaneous Discrete Episodes of VT/VF through 60 months compared to a performance goal of 84.0%.

Protocol Synopsis, Cont.

Additional Pre-Specified Analyses	• Freedom from complications requiring surgical revisions of the pulse generator or electrode, including pocket revisions, surgical repositioning or removal of the device in response to product performance issues • All cause mortality • Premature battery depletion and other device malfunctions • Mechanical electrode failures • Electrical performance data recorded by the device (e.g., electrode impedance status, total number of treated and untreated episodes since implant and since the last follow-up session, total number of shocks delivered since implant and since the last follow-up session, stored ECGs for all treated and untreated episodes, changes to programmed parameters) • Explants and causes (e.g., infection, need for pacing therapy, inappropriate shocks) • TV-ICD implantation following S-ICD explant • Surgical revisions in response to suboptimal placement or system movement • Chronic pain/discomfort requiring surgical intervention • Clinical Indications for implant • Demographics and baseline characteristics of the implant population • Programmed SQ-RX pulse generator settings – System performance in key subgroups, including, but not limited to: gender, race, body habitus, NYHA class, indication • Individual rates of each adverse event category contributing to the primary and secondary safety endpoints • Whether subject was also a candidate for a TV-ICD and reason for S-ICD System implantation • Type of anesthesia/analgesia • Implant test analysis (induced episode VT/VF conversion , VT/VF detection sensitivity and time to therapy) • Management of antiplatelet and anticoagulation medications during implant • Removal of S-ICD system in response to implant testing • Use of medical imaging during implant • Syncope associated with VT/VF episodes • Use of dual zone programming and rate cutoffs • Spontaneous episodes of VT/VF – Incidence – Shock effectiveness (treated episodes only) – Time to therapy (treated episodes only) • Inappropriate shock incidence – SVT with high ventricular rate – Discrimination errors for AF/SVT in the conditional shock zone – Oversensing
Follow Up Schedule	• Screening • Enrollment • Implant • Pre-Discharge • Annual Follow-Up Visits through 60 months
Study Duration	The duration is expected to be approximately 78 months from 1st enrollment to study closure.
Inclusion Criteria	Subjects must meet the following criteria to be eligible for inclusion in the study: 1. Eligible for implantation with an S-ICD System, OR previously implanted with an S-ICD System in the S-ICD System Clinical Investigation (IDE G090013) 2. Willing and able to provide written informed consent or have informed consent provided by a legal representative
Exclusion Criteria	Subjects who meet the following criteria must be excluded from the study: 1. Remaining life expectancy of less than 360 days

Protocol Synopsis, Cont.

Statistical Methods	
Primary Statistical Hypothesis	• The lower confidence bound of the Type I (caused by the S-ICD System) Complication Free Rate at 60 months is greater than 85%. • The lower confidence bound of the Overall Shock Effectiveness in Converting Spontaneous Discrete Episodes of VT/VF through 60 months is greater than 94%.
Statistical Test Methods	• The primary safety endpoint will be evaluated as the proportion of subjects free from Type I Complication at 60 months based on the Kaplan-Meier method including the one-sided lower 95% confidence interval • The primary effectiveness endpoint of overall shock effectiveness for spontaneous discrete episodes of VT/VF will be examined using the binomial estimate including the one-sided 95% lower exact confidence bound.
Sample Size Parameters	[redacted]

2. TABLE OF CONTENTS

TABLES

3. INTRODUCTION

Results from large, prospective, randomized clinical trials have previously demonstrated the mortality benefit of transvenous ICD (TV-ICD) usage in primary[1,2] and secondary[3] prevention subjects. In spite of the overall success of TV-ICD therapy, the complications associated with the therapy have come under increased scrutiny in light of several highly publicized device recalls in recent years.

A large proportion of the complications associated with TV-ICD therapy are related to leads that are implanted intravascularly. The implantation of such leads runs the risk of specific clinical complications such as pericardial tamponade, perforation and pneumothorax. In addition, repositioning of leads in the event of dislodgement, fracture or other mechanical failure has an associated risk. In a report on approximately 31,000 Medicare beneficiaries who underwent ICD implantation between October 2002 and September 2003, 11% experienced one or more early complications.[4] In smaller studies, overall complication rates have been reported to be as high as 30% after approximately 4 years of follow-up with lead-related complication rates accounting for 15% of events.[5] More recently, data published by Borleffs et al[6] and Kleeman et al[7] indicate that lead failure rates can be as high as 20-40% over 8-10 years of follow-up.

The S-ICD System was designed to minimize or eliminate many of the complications associated with traditional TV-ICD leads. The S-ICD System does not require an electrode to be placed either in (endocardially) or on (epicardially) the heart, which may be advantageous in reducing:

- Implant-associated risks related to central venous access or endocardial lead positioning and fixation.
- Exposure of the lead to stresses induced by repeated cardiac pulsations

1 Moss AJ et al., Multicenter Automatic Defibrillator Implantation Trial II Investigators. Prophylactic implantation of a defibrillator in subjects with myocardial infarction and reduced ejection fraction. (2002). N. Engl. J. Med. 346: 877-883
2 Bardy GH et al., Amiodarone or an Implantable Cardioverter-Defibrillator for Congestive Heart Failure (2005). N. Engl. J. Med. 352: 225-237
3 The Antiarrhythmics versus Implantable Defibrillators (AVID) Investigators. A comparison of antiarrhythmic-drug therapy with implantable defibrillators in subjects resuscitated from near-fatal ventricular arrhythmias. (1997) N. Engl. J. Med. 337: 1576-1583
4 Reynolds MR et al.The Frequency and Incremental Cost of Major Complications Among Medicare Beneficiaries Receiving Implantable Cardioverter Defibrillators (2006). J. Am. Coll. Cardiol. 47: 2493-2497
5 Alter P., et al., Complications of Implantable Cardioverter Defibrillator Therapy in 440 Consecutive Subjects (2005). Pacing Clin Electrophysiol. 28: 926-932
6 Borleffs CJW et al., Risk of Failure of Transvenous Implantable Cardioverter Defibrillator Leads (2009) Circ Arrhythmia Electrophysiol. 2:411-416
7 Kleeman T et al., Annual Rate of Transvenous Lead defects in implantable cardioverter-defibrilators over a period of > 10 yrs. (2007) Circulation 115: 2474-2480

- Infections with a direct pathway to the blood stream and endocardium
- Complications related to lead extraction
- Exposure to radiation and contrast dye during implant

The safety and effectiveness of the S-ICD System was demonstrated in a series of trials that culminated in the S-ICD Clinical Investigation conducted under IDE G090013. The initial human studies of the S-ICD System include two acute and two long-term studies conducted in New Zealand and Europe.[8] These studies provided the rationale for the S-ICD System Clinical Investigation, which was a 330 subject, single-arm, prospective, non-randomized, multicenter clinical study in the United States, New Zealand, the Netherlands and the United Kingdom. The co-primary endpoints for safety and efficacy were met in the S-ICD System Clinical Investigation:

- The 180-day system related complication-free rate of 99% [$LBCI_{95}$=97.3%] passed the pre-specified primary safety endpoint criteria of 79%
- The acute VF conversion rate of 96.5% [$LBCI_{95}$=93.8%] passed the pre-specified primary effectiveness endpoint criteria of 88%.

4. DEVICE DESCRIPTION

The S-ICD System is an implantable defibrillator that treats ventricular tachyarrhythmias using a subcutaneous pulse generator and a subcutaneous electrode rather than a transvenous lead. The S-ICD System received CE mark in 2009, PMA Approval in 2012 (anticipated) and is approved for distribution in the countries in which the study will be conducted. Current and future models of each device will be included in the study.

The S-ICD System consists of four devices:

- SQ-RX subcutaneous implantable defibrillator pulse generator; Model 1010 and future models.
- Q-TRAK subcutaneous electrode; Model [redacted] and future models
- Q-GUIDE electrode insertion tool (EIT); Model [redacted] and future models
- Q-TECH programmer; model [redacted] and future models.

8 Bardy GH, Smith WM, Hood MA, et al. An entirely subcutaneous implantable cardioverter-defibrillator. N Engl J Med. 2010;363(1):36-44.

The S-ICD System is designed to work with the following accessories:

- Programmer telemetry wand;
- Magnet;
- Suture sleeve, included in the electrode package;
- Torque wrench, included in the pulse generator package;
- SD memory card.

The S-ICD system also requires the use of a surface ECG based "screening tool" which is used to determine the adequacy of sensing.

5. OBJECTIVES

The primary objective of the S-ICD Post Approval Study is to document long-term safety and effectiveness outcomes associated with the implantation of the SQ-RX pulse generator and Q-TRAK electrode in commercial clinical subjects. Additional objectives include characterization of long term safety and effectiveness in subjects of varied body habitus and in traditionally underrepresented subject populations, such as women and African Americans.

6. ENDPOINTS

6.1 Primary Safety Endpoint

The primary safety endpoint of the study is defined as the Type I Complication Free Rate at 60 months (1800 days). Type I complications are adverse events caused by a component (i.e. pulse generator, electrode, EIT or programmer) of the S-ICD System that results in permanent loss of device function,[9] invasive intervention or death.

6.2 Secondary Safety Endpoint

The secondary safety endpoint of the study is defined as the Electrode-Related Complication Free Rate at 60 months. A complication is an adverse event that results in permanent loss of device function,[10] invasive intervention or death. Electrode relatedness is defined in section 10.2.1.

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[9] *Permanent loss of device function* refers to: 1) the permanent loss of shock therapy and/or post shock pacing; 2) permanent loss of appropriate sensing in all available sensing configurations (oversensing that results in persistent inappropriate shocks or undersensing that could lead to undetected arrhythmias). Loss of device function includes programming the PG permanently off or temporarily off in advance of an explant/revision.

[10] *Permanent loss of device function* refers to: 1) the permanent loss of shock therapy and/or post shock pacing; 2) permanent loss of appropriate sensing in all available sensing configurations (oversensing that results in

6.3 Individual Estimates for Secondary Safety Endpoint Related Events

In addition to the composite rate of electrode related complications, individual rates of each adverse event category contributing to the primary safety endpoint will be examined including two-sided 95% exact confidence intervals.

6.4 Primary Effectiveness Endpoint

The primary effectiveness endpoint of the study is defined as the Overall Shock Effectiveness in Converting Spontaneous Discrete Episodes of VT/VF through 60 months. Overall shock effectiveness refers to conversion of an episode following any of the 5 shocks (maximum) that may be delivered during a single episode. Discrete episodes of VT/VF are those that are temporally independent (<3 within a 24 hour period), unlike storm episodes, which occur in clusters (≥3 episodes within a 24 hour period). Episodes that spontaneously terminate will be excluded from this endpoint since the effectiveness of the shock cannot be evaluated in such circumstances.

6.5 Secondary Effectiveness Endpoint

The secondary effectiveness endpoint of the study is defined as First Shock Effectiveness in Converting Induced (Acute) and Spontaneous Discrete Episodes of VT/VF through 60 months. Induced episodes following the initial implant procedure after enrollment (i.e., acute) will be counted towards the endpoint using the first shock delivered in the final position and final polarity. Because VT/VF induction test shocks are expected to be delivered at an energy below 80 J (e.g., 65 J), poolability with spontaneous episode shocks (all delivered at 80 J, non-programmable) will be assessed for the primary analysis. If the two data sets differ, separate analyses will be presented for first shock efficacy of induced episodes and first shock efficacy of spontaneous episodes.

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persistent inappropriate shocks or undersensing that could lead to undetected arrhythmias). Loss of device function includes programming the PG permanently off or temporarily off in advance of an explant/revision.

6.6 Additional Pre-Specified Safety Analyses

Additional pre-specified safety analyses include:

- Freedom from complications requiring surgical revisions of the pulse generator or electrode, including pocket revisions, surgical repositioning or removal of the device in response to product performance issues (the 95.0% one-sided lower confidence interval should exceed 75.0%.)
- Individual rates of each adverse event category contributing to the primary and secondary safety endpoints will be examined including two-sided 95% exact confidence intervals
- All cause mortality
- Premature battery depletions and other device malfunctions
- Electrical performance data recorded by the device (e.g., electrode impedance status, total number of treated and untreated episodes since implant and since the last follow-up session, total number of shocks delivered since implant and since the last follow-up session, stored ECGs for all treated and untreated episodes, changes to programmed parameters)
- Mechanical electrode failures
- Explants and causes (e.g., infection, need for pacing therapy, inappropriate shocks)
- TV-ICD implantation following S-ICD explant
- Surgical revisions in response to suboptimal placement or system movement
- Chronic pain/discomfort requiring surgical intervention
- Removal of S-ICD System in response to implant testing
- Syncope associated with VT/VF episodes
- Inappropriate shock incidence
  - SVT with high ventricular rate
  - Discrimination errors for AF/SVT in the conditional shock zone
  - Oversensing

7. DESIGN

The S-ICD Post Approval Study is a multi-site, non-randomized registry that will retrospectively enroll subjects who participated in the S-ICD Clinical Investigation (IDE G090013) and prospectively enroll subjects eligible for de novo implantation with the S-ICD System. Subjects will be followed annually according to standard of care through 60 months post implant or study exit. This study will follow 21 CFR 814.82(a)(2) Post-Approval Requirements.

7.1 Scale and Duration

The study will be conducted by approximately 100 (up to 150) US sites. At least 1,616 subjects will be enrolled. Sites may continue to enroll subjects until notified of enrollment completion. Sites may not enroll more than 15% of the enrollment target (242 subjects) without written permission from the sponsor. The duration of the study, from first enrollment to study closure, is expected to be approximately 78 months.

- Study initiation will begin approximately 3 months post PMA approval
- The number of sites with IRB approvals per month is estimated to be approximately 10 per month.
- Estimated first enrollment is 4 months post PMA approval.
- The number of enrollments per month is estimated at 80-100, once all sites are approved to enroll.
- The estimated date to complete enrollment is 18 months after the first enrollment.
- The estimated date to complete follow-up is 60 months after enrollment is complete.
- The final study report will be submitted no later than 3 months after the last participant completes follow-up.

7.2 Visit Schedule

Subjects will be followed according to the standard of care at the implanting/following institution. Data will be collected from each subject at enrollment, implant, pre-discharge, annual follow-up visits and from additional follow up visits associated with a Type I-II clinical event, device episode, suspected device malfunction or device programming change. Data will be collected through at least 60 months (1800 days) post implant or through study exit.

Figure 1. Subject Flow

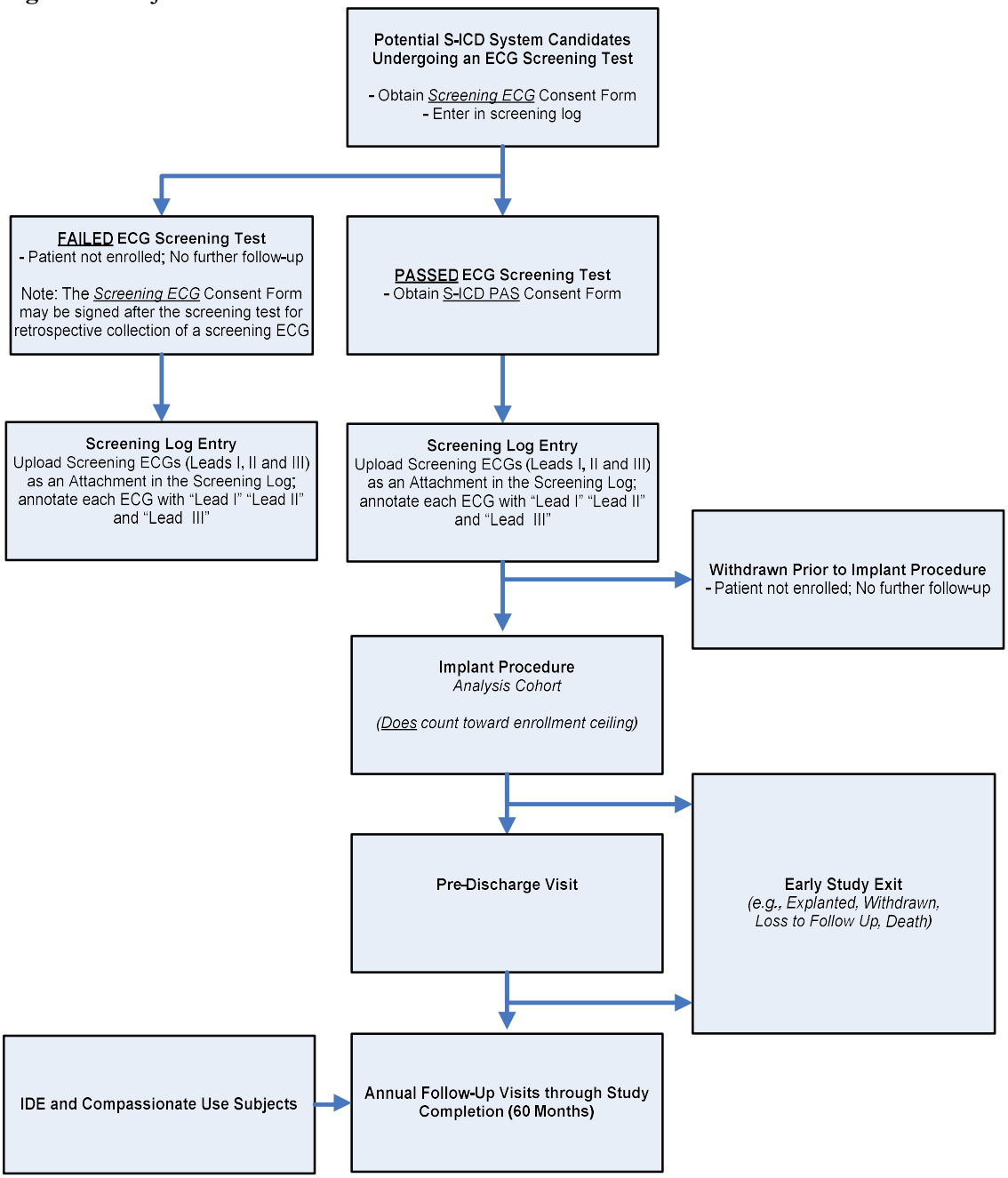


Table 2: Summary of Information Required Each Visit

	Failed ECG Screen	Passed Screening ECG								
	Screening log	Screening log	Enrollment Visit	Implant	Pre-Discharge	Annual Follow-up Visit	Additional Follow-up Visit	System Revision	Additional implant	Study Completion
"Screening ECG" Consent Date	X	X								
Screening ECG	X	X								
"S-ICD PAS" Consent Date		X								
Baseline Characteristics			X							
Cardiovascular Medications			X							
Implant Details				X					X	
S-ICD System Parameters				X	X	X	X	X	X	X
Conversion Testing (w/ external ECG strips[11])				Y	Y	Y	Y	Y	Y	Y
Adverse events				Y	Y	Y	Y	Y	Y	Y
Spontaneous Episodes				Y	Y	Y	Y	Y	Y	Y
Chest X-Ray				Y	Y	Y	Y	Y	Y	Y

X: Data Collected.
Y: Must assess whether the event occurred; additional data entered only if the event occurred.

[11] External ECGs are only required for sustained inductions that are shocked by the S-ICD System or external defibrillator.

7.2.1 Screening Log and Consent

All subjects who undergo a screening ECG to determine eligibility for implantation with the S-ICD System will sign a 'Screening ECG" Informed Consent Form (ICF) and be entered into the screening log. All screening ECGs (in all leads and postures evaluated) are to be uploaded as attachments to the screening log. Both passed and failed Screening ECGs are to be collected in the screening log. The Screening ECG ICF applies only to the screening ECG and does not enroll the subject in the study. For subjects who fail the screening ECG, no further data are to be collected. For subjects who pass the screening ECG, study participation must be systematically offered to all subjects in order to avoid bias in subject selection. Subjects who choose to participate must sign the "S-ICD PAS" ICF. A subject who signs the "S-ICD PAS" ICF and does not proceed to the implant procedure will not count toward the enrollment ceiling.

Table 3: Screening Log Data

Data Collection	Retention of Original Source Documentation
"Screening ECG" for all subjects screened[12] "S-ICD PAS Consent" Form if subject to undergo an implant procedure	Investigational Center
Pre-operative screening ECG	Investigational Center; upload copy to BSC

7.2.2 Enrollment

Participants in the S-ICD Clinical Investigation (G090013), including subjects enrolled under an approved compassionate use application, are considered enrolled after providing written informed consent. All other subjects are considered enrolled after providing written informed consent and undergoing an implant procedure for the S-ICD System. For the purpose of this protocol, any subject receiving anesthesia for an S-ICD System implant will be considered to have undergone an implant procedure. Subjects who do not receive anesthesia in preparation for an S-ICD System implant procedure will not be considered to be enrolled in the study.

[12] The Screening ECG consent form may be used to collect screening ECGs from any subject who is screened. This includes subjects who pass the ECG screening criteria, but do not sign the S-ICD PAS consent.

7.2.3 Enrollment Data

Subject demographics, medical history and indications will be collected for all enrolled subjects. Table 4 lists the data collected at the enrollment visit.

Table 4: Enrollment Data Collection

Data Collection	Retention of Original Source Documentation
Demographics Physical and Medical History Cardiovascular Medications	Investigational Center

7.2.4 Implant Procedure

Implant, testing, and programming the S-ICD System should be performed using the standard of care methods established by the investigational center. Refer to the S-ICD System User's Manual for detailed instructions regarding the implantation and use of the S-ICD System.

7.2.5 Conversion Testing

As part of the S-ICD System implant procedure, conversion testing should be performed according to the standard practices of the investigator. Conversion testing may also be performed at other times during the course of the study at the discretion of the investigator. Only sustained ventricular arrhythmias that result in a shock, either from the S-ICD System or from an external defibrillator, require documentation by capturing and annotating an ECG strip.

7.2.6 Implant Data

S-ICD System procedural data such as peri-operative medication management, use of medical imaging, product information, VT/VF conversion testing, programming parameters and adverse events are collected at implant. The initial implant and any additional implant procedures have the same data requirements, as described in this section. **Table 5** lists the data collected at the implant visit.

Table 5: Implant Data Collection

Data Collection	Retention of Original Source Documentation
Peri-operative medication worksheet (anticoagulation; antiplatelets; antibiotics; type of anesthesia) Implanted product and accessories utilized for S-ICD System (model/serial/lot/batch/etc.) Medical notes/worksheets documenting use of medical imaging (e.g., fluoroscopy) Adverse events, if applicable	Investigational Center
Q-TECH Programmer Printouts: - Final Summary Report - Captured S-ECG in each sensing vector - Device episodes, if applicable Shocked induced VT/VF episodes (external ECG strips),[13] if performed Post implant chest x-ray(s) if applicable[14]	Investigational Center; upload copy to Cameron Health/BSC
SD Card Data	Cameron Health/BSC (e.g. via CAMELION)

[13] Any time induction testing is performed in the study, external ECG strips are only required for sustained ventricular arrhythmias that result in a shock, either from the S-ICD System or from an external defibrillator.
[14] An X-ray is not required per protocol; upload only if a chest x-ray of the S-ICD System was taken to assess the position of the S-ICD System, an S-ICD System-related adverse event, or suspected product issue.

7.2.7 Pre-Discharge: Initial Device Set-Up and Programming

All device programming is at the discretion of the investigator. Investigators are encouraged to use two zones when appropriate, based on results from the S-ICD Clinical Investigation showing that dual zone programming significantly reduces adverse events for inappropriate shocks. In that study, dual zone programming was associated with a 70% relative reduction in the incidence of inappropriate shocks due to SVT and a 56% relative reduction in the incidence of inappropriate shocks due to oversensing, when compared to single zone programming.

7.2.8 Pre-Discharge Data

Captured ECGs in each sensing vector may be obtained any time prior to pre-discharge. Additionally, programming parameters and any VT/VF conversion testing, adverse events or x-rays are collected at pre-discharge. **Table 6** summarizes the data required at the pre-discharge visit.

Table 6: Pre-Discharge Data Collection

Data Collection	**Retention of Original Source Documentation**
Adverse events, if applicable	Investigational Center
Q-TECH Programmer Printouts: - Initial and Final Summary Reports - Captured S-ECG in each sensing vector, if sensing vector changed - Device episodes, if applicable Shocked induced VT/VF episodes (external ECG strips),[15] if performed Chest x-ray(s) if applicable[16]	Investigational Center; upload copy to Cameron Health/BSC
SD Card Data	Cameron Health/BSC (e.g. via CAMELION)

[15] Any time induction testing is performed in the study, external ECG strips are only required for sustained ventricular arrhythmias that result in a shock, either from the S-ICD System or from an external defibrillator.
[16] An X-ray is not required per protocol; upload only if a chest x-ray of the S-ICD System was taken to assess the position of the S-ICD System, an S-ICD System-related adverse event, or suspected product issue.

7.2.9 Annual Follow-up Visit

After implant, scheduled follow-up visits are to be performed annually (±60 days) from the implant date in order to capture:

- Spontaneous episodes that have not been previously reported;
- Adverse events that have not been previously reported;
- Programming changes that have not been previously reported;
- Product experience reports that have not been previously reported.

For participants in the S-ICD Clinical Investigation (IDE G090013), annual follow-up visit windows are calculated from the original S-ICD System implant date (day 0) and take into account the last follow-up visit conducted in the S-ICD Clinical Investigation (e.g., if the last follow-up conducted in the S-ICD Clinical Investigation (IDE G090013) was the 540 day follow-up visit, then the first S-ICD PAS annual follow-up visit should occur at 720 days post implant).

Aside from the annual follow-up visit, other scheduled and unscheduled visits throughout the year (e.g., standard of care device checks) should not be submitted unless they are associated with a Type I-II clinical event, device episode, suspected device malfunction or device programming change[17], in which case they should be submitted as additional follow-up visits as described in Section 7.2.10, below.

The final annual follow-up visit must occur more than 1800 days after the initial implant procedure. The first standard of care visit within the annual follow-up visit window that occurs after the 1800 day mark should be submitted as an annual follow-up visit; if that is not possible, then the next standard of care visit may be submitted as an additional follow-up visit to allow for timely study completion. **Table 7** lists all the data required at annual follow-up visits.

[17] A programming change refers to any difference between *Initial Device Settings* and *Current Device Settings* under the *Programmable Parameters* section of an S-ICD Summary Report.

Table 7: Annual Follow-Up Visit Data Collection

Data Collection	Retention of Original Source Documentation
Adverse events, if applicable	Investigational Center
Q-TECH Programmer Printouts: - Initial and Final Summary Reports - Captured S-ECG in each sensing vector - Device episodes, if applicable Shocked induced VT/VF episodes (external ECG strips),[18] if performed Chest x-ray(s) if applicable[19]	Investigational Center; upload copy to Cameron Health/BSC
SD Card Data	Cameron Health/BSC (e.g. via CAMELION)

7.2.10 Additional Follow-up Visits

Physician office visits, emergency room visits, out-patient hospital visits, and hospitalizations related to the S-ICD System (associated with a Type I-II adverse event, treated episode, suspected device malfunction or device programming changes[20]) should be recorded as an additional follow-up visit. A subject status check may also be performed by telephone and recorded as an additional follow-up visit under special circumstances defined by the sponsor or in order for the subject to complete the study after 1800 days post implant; otherwise, additional follow-up visits should not be reported unless they are associated with a Type I-II adverse event, treated episode, suspected device malfunction or device programming changes. **Table 8** lists all the data required from additional follow-up visits.

[18] Induction testing is not required per protocol; upload only if performed. Any time induction testing is performed in the study, external ECG strips are only required for sustained ventricular arrhythmias that result in a shock, either from the S-ICD System or from an external defibrillator.
[19] An X-ray is not required per protocol; upload only if a chest x-ray of the S-ICD System was taken to assess the position of the S-ICD System, an S-ICD System-related adverse event, or suspected product issue.
[20] A programming change refers to any difference between *Initial Device Settings* and *Current Device Settings* under the *Programmable Parameters* section of an S-ICD Summary Report.

Table 8. Additional Follow-Up Visit Data Collection

Data Collection	Retention of Original Source Documentation
Adverse events, if applicable	Investigational Center
Q-TECH Programmer Printouts: - Initial and Final Summary Reports - Captured S-ECG in each sensing vector, if sensing vector changed - Device episodes, if applicable Shocked induced VT/VF episodes (external ECG strips),[21] if performed Chest x-ray(s) if applicable[22]	Investigational Center; upload copy to Cameron Health/BSC
SD Card Data (if new spontaneous episodes were recorded)	Cameron Health/BSC (e.g. via CAMELION)

[21] Induction testing is not required per protocol; upload only if performed. Any time induction testing is performed in the study, external ECG strips are only required for sustained ventricular arrhythmias that result in a shock, either from the S-ICD System or from an external defibrillator.

[22] An X-ray is not required per protocol; upload only if a chest x-ray of the S-ICD System was taken to assess the position of the S-ICD System, an S-ICD System-related adverse event, or suspected product issue.

7.3 Revisions, Replacements and Explants

In the event that the electrode or PG is surgically revised after the initial implant procedure, the system revision form is used to record changes to the system. If either the PG or electrode is removed from service, a device status form must be completed for the out-of-service device(s). If the system is revised without replacing any system components, a system revision form is completed. If the PG or electrode is replaced, the new device(s) will be recorded on an additional implant form. **Table 9** lists all the data required for system revisions.

Table 9. System Revision Data Collection

Data Collection	Retention of Original Source Documentation
Adverse events, if applicable Newly implanted product and accessories utilized for S-ICD System (model/serial/lot/batch/etc.), if applicable	Investigational Center
Q-TECH Programmer Printouts: - Initial and Final Summary Reports - Captured S-ECG in each sensing vector, if sensing vector changed - Device episodes, if applicable Shocked induced VT/VF episodes (external ECG strips),[23] if performed Chest x-ray(s) if applicable[24]	Investigational Center; upload copy to Cameron Health/BSC
SD Card Data (if new spontaneous episodes were recorded)	Cameron Health/BSC (e.g. via CAMELION)

[23] Induction testing is not required per protocol; upload only if performed. Any time induction testing is performed in the study, external ECG strips are only required for sustained ventricular arrhythmias that result in a shock, either from the S-ICD System or from an external defibrillator.
[24] An X-ray is not required per protocol; upload only if a chest x-ray of the S-ICD System was taken to assess the position of the S-ICD System, an S-ICD System-related adverse event, or suspected product issue.

7.4 Study Completion

Subjects may be withdrawn from the study for a variety of reasons including:

- Subject withdraws consent for any reason;
- Subject is lost to follow-up despite best efforts to locate the subject;
- The S-ICD System is permanently explanted;
- The subject has been followed >60 months from the original implant date.

Subjects who undergo a permanent explant or who commence, but do not complete, an implant procedure should be contacted, either in person or by telephone, at least 30 days after the permanent explant or implant attempt in order to record any adverse events before being withdrawn from the study. The study completion form documents withdrawal of any subject from the study.

There are no additional follow-up requirements once a subject has been withdrawn from the study. **Table 10** lists all the data that are required for study completion.

Table 10. Study Completion Data Collection

Data Collection	Retention of Original Source Documentation
Adverse events, if applicable	Investigational Center
Q-TECH Programmer Printouts: - Initial and Final Summary Reports - Captured S-ECG in each sensing vector, if sensing vector changed - Device episodes, if applicable Shocked induced VT/VF episodes (external ECG strips),[25] if performed Death letter, if applicable Chest x-ray(s) if applicable[26]	Investigational Center; upload copy to Cameron Health/BSC
SD Card Data (if new spontaneous episodes were recorded)	Cameron Health/BSC (e.g. via CAMELION)

[25] Induction testing is not required per protocol; upload only if performed. Any time induction testing is performed in the study, external ECG strips are only required for sustained ventricular arrhythmias that result in a shock, either from the S-ICD System or from an external defibrillator.
[26] An X-ray is not required per protocol; upload only if a chest x-ray of the S-ICD System was taken to assess the position of the S-ICD System, an S-ICD System-related adverse event, or suspected product issue.

7.5 Adverse events and Spontaneous Episode Classification

Complications and treated spontaneous episodes will be preliminarily classified by investigational sites and reviewed for final adjudication by a Clinical Events Committee (CEC).

8. SUBJECT SELECTION

Subjects with a remaining life expectancy of at least 360 days who are eligible for implantation with an S-ICD System, OR who were previously implanted with an S-ICD System in the S-ICD System Clinical Investigation (IDE G090013) study, are eligible for participation. Approximately 1,616 subjects will be enrolled at a maximum of 150 investigational sites.

8.1 Subject Population

Any subject who meets the inclusion criteria, does not meet the exclusion criterion, and provides informed consent will be enrolled in the study upon undergoing an implant procedure for the S-ICD System. Subjects who do not undergo an implant procedure will not count toward the enrollment ceiling.

8.2 Devices Under Surveillance

The following information is a brief summary of the S-ICD System and its principle of operation. Refer to the S-ICD System User's Manuals for additional information.

8.2.1 SQ-RX Pulse Generator

The SQ-RX pulse generator comprises an inner structure of discrete electrical components, [redacted] The header contains a single port for connection of the Q-TRAK subcutaneous electrode to accommodate sensing, pacing, and defibrillation. [redacted] The SQ-RX pulse generator is capable of delivering high energy defibrillation shocks as well as bradycardia demand mode cardiac pacing for a period up to thirty seconds following defibrillation therapy. Future generations of the SQ-RX pulse generator may be included in the study.

8.2.2 Q-TRAK Subcutaneous Electrode

[redacted] Future generations of the Q-TRAK subcutaneous electrode may be included in the study.

8.2.3 Q-GUIDE Electrode Insertion Tool

[redacted] Future generations of the Q-GUIDE EIT may be included in the study.

8.2.4 Q-TECH Programmer Description

The Q-TECH programmer is a completely self-contained, non-sterile, non-implantable, lightweight, easily portable computer that does not allow general purpose computing.

Future generations of the Q-TECH programmer may be included in the study.

8.3 Study Inclusion/Exclusion Criteria

8.3.1 Inclusion Criteria

Subjects must meet the following criteria to be eligible for inclusion in the study:

- Eligible for implantation with an S-ICD System, OR previously implanted with an S-ICD System in the S-ICD System Clinical Investigation (IDE G090013)
- Willing and able to provide written informed consent or have informed consent as provided by a legal representative

8.3.2 Exclusion Criterion

Subjects who meet the following criterion must be excluded from the study:

- Remaining life expectancy of less than 360 days

8.3.3 Enrollment Completion

Investigational sites will be notified to cease enrolling subjects for this study when the enrollment target is reached or at the sponsor's discretion in consultation with FDA. This notification is expected to happen when at least 1,616 subjects have been enrolled.

8.4 Investigator/Site Selection Criteria

The sponsor will consider many factors to ensure selection of sites and investigators that are qualified through their training and experience to properly conduct the study. Diverse sites will be selected with respect to geography and clinical setting (e.g., university, private practice, etc.). The current BSC process for evaluating and selecting clinical sites will be utilized. The evaluation and selection criteria include but are not limited to the following:

- Participation in the S-ICD Clinical Investigation (G090013)
- Sites that have the personnel with knowledge to run a clinical study and enroll subjects according to FDA and good clinical practice guidelines. It is recommended that sites have a dedicated Research Coordinator and exceptions will be evaluated on a case-by-case basis
- Sites that have a Principal Investigator (physician) who has a commitment to conducting research and is in good standing with the FDA

- Sites that have the necessary knowledge and experience to implant CRM products and also have the potential subject volume to meet enrollment expectations
- Site personnel that have a commitment to protocol compliance along with gathering and submitting timely and accurate data using an electronic data entry system
- Sites that will support on-site clinical data monitoring during the study

8.5 Justification for the Study Design

The S-ICD Post Approval Study is designed to assess long term safety and effectiveness outcomes associated with the implantation of the SQ-RX pulse generator and Q-TRAK subcutaneous electrode in a commercial clinical setting. As such, it is designed as a standard of care registry that will compare observed measures of safety and effectiveness at 5 years to performance goals that were derived from the same endpoints observed at shorter time periods (e.g., 1 year) in the S-ICD Clinical Investigation (IDE G090013). The S-ICD Post Approval Study will also provide an active reporting mechanism for close monitoring of device performance during the initial US commercialization, permitting characterization of low-frequency adverse events.

9. SUBJECT ACCOUNTABILITY

9.1 Point of Enrollment

A participant in the S-ICD Clinical Investigation (IDE G090013) who is implanted with the S-ICD System is considered enrolled upon signing the informed consent form (ICF). Subjects who did not participate in the S-ICD Clinical Investigation (IDE G090013) will be considered enrolled after both signing an informed consent and undergoing an implant procedure. A subject who signs an informed consent, but does not undergo an implant procedure does not count toward the enrollment ceiling and has no follow-up requirements.

9.2 Withdrawal

All subjects enrolled in the clinical study (including those withdrawn from the clinical study or lost to follow-up) shall be accounted for and documented. If a subject withdraws from the clinical investigation, the reason(s) shall be reported.

10. STATISTICAL CONSIDERATIONS

The S-ICD Post Approval Study is designed to examine the long-term safety and effectiveness of the S-ICD System. The study design includes two co-primary endpoints maintaining a family-wise significance level of 0.05 by defining a hierarchical testing procedure. The safety endpoint will be tested first. If the test is successful then the effectiveness endpoint will be tested at the same significance level. Primary endpoints will be tested prior to testing the secondary endpoints. Individual rates of each adverse event contributing to the primary safety endpoint will be examined including two-sided 95% exact confidence intervals. Other pre-specified observational analyses are defined to further investigate the long-term safety and effectiveness of the S-ICD System.

Subjects from the IDE study who provide informed consent for this study will be followed through 60 months post implant. All subjects enrolled in the S-ICD System Clinical Investigation (IDE G090013) who underwent an implant attempt will contribute to the analyses of the safety and effectiveness endpoints and additional analyses. Data from IDE subjects who do not provide consent for the study or subjects who previously exited the IDE will be censored at the time of IDE study exit in the endpoint analyses, but will not count toward the target enrollment sample size. All non-IDE subjects who undergo an implant procedure for the S-ICD System will be included in the endpoint analyses and will count toward the enrollment ceiling. All analyses may be done separately on IDE study subjects vs de novo implants. The statistical analyses related to this study will be executed by the sponsor and/or business partners working on behalf of the sponsor.

10.1 Primary Safety Endpoint

The primary safety endpoint of the study is defined as the Type I Complication Free Rate at 60 months (1800 days). Type I complications are adverse events caused by a component (i.e. pulse generator, electrode, EIT or programmer) of the S-ICD System that results in permanent loss of device function,[27] invasive intervention or death.

10.1.1 Primary Safety Endpoint Performance Goal

[redacted], the primary safety endpoint performance goal is 85.0%.

10.1.2 Primary Safety Endpoint Hypothesis

The primary safety endpoint null and alternative hypotheses are as follows:

Ho: The Type I Complication Free Rate at 60 months (p1) does not exceed the performance goal of 85.0%.

$$Ho: p1 \leq 85.0\%$$

Ha: The Type I Complication Free Rate at 60 months (p1) does exceed the performance goal of 85.0%.

$$Ha: p1 > 85.0\%$$

[27] *Permanent loss of device function* refers to: 1) the permanent loss of shock therapy and/or post shock pacing; 2) permanent loss of appropriate sensing in all available sensing configurations (oversensing that results in persistent inappropriate shocks or undersensing that could lead to undetected arrhythmias). Loss of device function includes programming the PG permanently off or temporarily off in advance of an explant/revision.

The null hypothesis will be rejected if the lower one-sided 95% confidence bound[28] of the Kaplan-Meier estimate, using the Peto method for standard error, exceeds the performance goal of 85.0%.

10.2 Secondary Safety Endpoint

The secondary safety endpoint of the study is defined as the Electrode-Related Complication Free Rate at 60 months. A complication is an adverse event that results in permanent loss of device function, invasive intervention or death. Electrode relatedness is defined in section 10.2.1.

10.2.1 Secondary Safety Endpoint Related Adverse events

The following complications occurring ≤ 30 days after initial implant will be included in the secondary safety endpoint analysis if determined to be attributable to structural electrode failure OR occurring > 30 days after implant regardless of cause:

- Electrode movement (>5 cm)
- Electrode impedance out of range
- Electrode conductor fracture
- Electrode deformation and/or breakage
- Electrode insulation failure

The following complications occurring > 30 days after initial implant will be included in the secondary safety endpoint analysis if determined to be attributable to a structural electrode failure:

- Incomplete/improper electrode-header connection
- In-subject damage to electrode (e.g., accidental cut to electrode body during pocket revision, PG replacement, etc.)
- Electrode revisions to optimize therapy
- Electrode movement
- Infection
- Oversensing
- Undersensing

[28] Using the Peto estimate for the standard error.

10.2.2 Secondary Safety Endpoint Performance Goal

[redacted], the primary safety endpoint performance goal is 92.5%.

10.2.3 Secondary Safety Endpoint Hypothesis

The primary safety endpoint null and alternative hypotheses are as follows:

Ho: The Electrode-Related Complication Free Rate at 60 months (p1) does not exceed the performance goal of 92.5%.

$$Ho: p1 \leq 92.5\%$$

Ha: The Electrode-Related Complication Free Rate at 60 months (p1) does exceed the performance goal of 92.5%.

$$Ha: p1 > 92.5\%$$

The null hypothesis will be rejected if the lower one-sided 95% confidence bound[29] of the Kaplan-Meier estimate using the Peto method for standard error exceeds the performance goal of 92.5%.

10.2.4 Individual Estimates for Secondary Safety Endpoint Related Events

In addition to the composite estimate of electrode related complications, individual rates of each adverse event category contributing to the primary safety endpoint will be examined including two-sided 95% exact confidence intervals.

[29] Using the Peto estimate for the standard error.

10.3 Primary Effectiveness Endpoint

The primary effectiveness endpoint of the study is defined as the Overall Shock Effectiveness in Converting Spontaneous Discrete Episodes of VT/VF through 60 months. Overall shock effectiveness refers to conversion of an episode following on any of the 5 shocks (maximum) that may be delivered during a single episode. Discrete episodes of VT/VF are those that are temporally independent (<3 within a 24 hour period), unlike storm episodes, which occur in clusters (≥3 episodes within a 24 hour period). Episodes that spontaneously terminate will be excluded from this endpoint since the effectiveness of the shock cannot be evaluated in such circumstances.

10.3.1 Primary Effectiveness Endpoint Performance Goal

[redacted]

10.3.2 Primary Effectiveness Endpoint Hypothesis

The primary effectiveness endpoint null and alternative hypotheses are as follows:

Ho: Overall Shock Effectiveness in Converting Spontaneous Discrete Episodes of VT/VF through 60 months (p1) does not exceed the performance goal of 94.0%.

$$Ho: p1 \leq 94.0\%$$

Ha: Overall Shock Effectiveness in Converting Spontaneous Discrete Episodes of VT/VF through 60 months (p1) does exceed the performance goal of 94.0%.

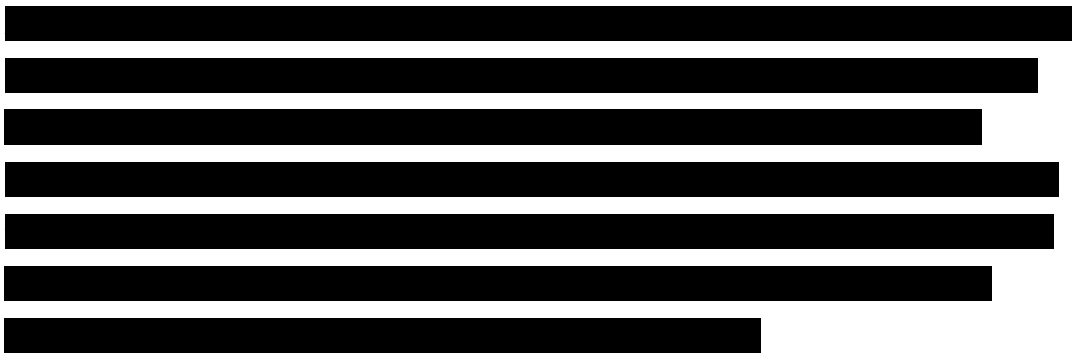
$$Ha: p1 > 94.0\%$$

The null hypothesis will be rejected if the lower one-sided 95% exact confidence bound of the estimate exceeds the performance goal of 94.0%.

10.4 Secondary Effectiveness Endpoint

The secondary effectiveness endpoint of the study is defined as First Shock Effectiveness in Converting Induced (Acute) and Spontaneous Discrete Episodes of VT/VF through 60 months. Induced episodes following the initial implant procedure after enrollment (i.e., acute) will be counted towards the endpoint using the first shock delivered in the final position and final polarity. Because VT/VF induction test shocks are expected to be delivered at an energy below 80 J (e.g., 65 J), poolability with spontaneous episode shocks (all delivered at 80 J, non-programmable) will be assessed for the primary analysis. If the two data sets differ, separate analyses will be presented for first shock efficacy of induced episodes and first shock efficacy of spontaneous episodes.

10.4.1 Secondary Effectiveness Endpoint Performance Goal



10.4.2 Secondary Effectiveness Endpoint Hypothesis

The secondary effectiveness endpoint null and alternative hypotheses are as follows:

Ho: The First Shock Effectiveness in Converting Induced (Acute) and Spontaneous Discrete Episodes of VT/VF through 60 months (p1) does not exceed the performance goal of 84.0%.

$$Ho: p1 \leq 84.0\%$$

Ha: The First Shock Effectiveness in Converting Induced (Acute) and Spontaneous Discrete Episodes of VT/VF through 60 months (p1) does exceed the performance goal of 84.0%.

$$Ha: p1 > 84.0\%$$

The null hypothesis will be rejected if lower one-sided 95% exact confidence bound of the estimate exceeds the performance goal of 84.0%.

10.5 Additional Pre-Specified Effectiveness Analyses

Other effectiveness objectives that will be collected and analyzed are as follows:

- Implant test analysis (induced episode VT/VF conversion, VT/VF detection sensitivity and time to therapy)
- Spontaneous episodes of VT/VF
  - Incidence
  - Rhythm and rate
  - Time to therapy (treated episodes only)
  - Conversion rate for spontaneous VT/VF storms

10.6 Sample Size Determination

The MINITAB software, version 14.0 was used to calculate the sample size in this study.

[redacted]

10.6.1 Target Sample Size

[redacted]

10.7 Data Analysis

10.7.1 Safety Endpoint Analyses

The primary safety endpoint will be evaluated as the proportion of subjects free from Type I Complication at 60 months based on the Kaplan-Meier method including the one-sided lower 95% confidence interval.[30]

The secondary safety endpoint will be evaluated as the proportion of subjects free from Electrode Related Complication at 60 months based on the Kaplan-Meier method including the one-sided lower 95% confidence interval.[30]

The Kaplan-Meier analysis will take into account the time from implant until the occurrence of the complication and data from any subjects who are complication-free will be right censored at the last known follow-up including subjects who exited the study.

10.7.2 Individual Adverse events Analyses

Individual rates of each adverse event category contributing to the primary and secondary safety endpoints will be examined using the binomial estimate including the two-sided 95% exact confidence intervals.

10.7.3 Additional Pre-Specified Safety Analyses

The appropriate statistical methods will be utilized to evaluate the additional pre-specified analyses listed in section 6.6 including:

- Kaplan-Meier method for time to event analyses
- Binomial estimates and exact confidence intervals for rates
- Descriptive statistics such as mean, standard deviation, median, interquartile range, minimum and maximum for continuous data and frequency and percentage for discrete data.

10.7.4 Effectiveness Endpoint Analyses

The primary effectiveness endpoint of overall shock effectiveness for spontaneous discrete episodes of VT/VF will be examined using the binomial estimate including the one-sided 95% lower exact confidence bound.

[30] Peto method for standard error estimate

The secondary endpoint of first shock effectiveness for acute and spontaneous discrete episodes of VT/VF will be examined using the binomial estimate including the one-sided 95% lower exact confidence bound. If the difference in first shock effectiveness rate for the acute and spontaneous episodes is statistically significant at a 0.05 significant level using a chi-square test then separate analyses will be presented for first shock efficacy of induced and spontaneous episodes.

10.7.5 Additional Pre-Specified Effectiveness Analyses

Descriptive statistics such as mean, standard deviation, median, and ranges for continuous data and frequency and percentage for discrete data will be utilized to analyze the additional pre-specified effectiveness data listed in section 10.5.

10.7.6 Baseline and Procedural Experience Analyses

Demographics and baseline clinical variables, including but not limited to relevant descriptors from the medical history, risk factors, co-morbidities, NYHA functional class for heart failure and medications will be summarized for the cohort of subjects enrolled in this study. Continuous variables will be summarized as means, standard deviations, medians and ranges. Categorical variables will be summarized as frequencies or percentages. A summary of the eligibility status of enrolled subjects will be performed.

Also outcomes related to the S-ICD System procedure such as, but not limited to, type of anaesthesia, implant duration, use of fluoroscopy or X-ray for system positioning, length of hospital stay and use of dual zone programming and rate cut-offs will be summarized.

10.7.7 Poolability Analysis

Poolability analysis for both primary safety and effectiveness endpoint will be analyzed.

[redacted] The log-rank test will be utilized to determine any relevant difference in Kaplan-Meier curves with the primary safety endpoint. A chi-square test will be used to analyze the difference in overall shock effectiveness rate for the primary effectiveness endpoint.

10.7.8 Sensitivity Analysis

Every effort will be utilized to minimize missing data. The denominator for each variable and all analyses will be presented in each report. The number of subjects withdrawing from the study will be presented with the corresponding time of discontinuation. [redacted]

10.7.9 Subgroup Analysis

[redacted]

[redacted]

[redacted]	[redacted]							
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	■	■	■	■	■	■	■	■
[redacted]	■	■	■					
[redacted]	■	■	■	■	■	■	■	■
[redacted]	■	■	■	■	■	■	■	■
[redacted]	■	■	■	■	■	■	■	■
[redacted]	■	■	■	■	■	■	■	■
[redacted]	■	■	■	■	■	■		
[redacted]	■	■	■	■	■	■		
[redacted]	■	■	■	■	■	■		■
[redacted]				■	■	■		
[redacted]		■	■				■	■
[redacted]	■	■	■	■	■	■	■	
[redacted]	■	■	■				■	■
[redacted]		■	■				■	

10.8 Reports

At a minimum, an annual report to the FDA will be provided by the sponsor summarizing the following: enrollment and implant status, device usage including out of service devices, protocol deviations, baseline characteristics, procedural data, reported adverse events, unanticipated adverse device effects, deaths, number of spontaneous episodes of VT/VF and corresponding conversion results.

10.9 Additional Pre-specified Analyses

Descriptive statistics will be used to further characterize the performance of the S-ICD System. Additional pre-specified analyses will include, but are not limited to, the

additional safety analyses listed in section 6.6, additional effectiveness analyses listed in section 10.5 and the following:

- Clinical Indications for implant
- Demographics and baseline characteristics of the implant population
- Whether subject was a candidate for a TV-ICD and reason for S-ICD System implantation
- Type of anesthesia/analgesia
- Management of antiplatelet and anticoagulation medications during implant
- Use of medical imaging during implant
- Programmed settings
- Use of dual zone programming and rate cutoffs

10.10 Other Statistical Considerations

[redacted]

11. ADVERSE EVENTS

11.1 Adverse event Reporting

All adverse events related to the S-ICD System must be reported to the sponsor. An adverse event should not be reported if it was considered a pre-existing medical condition or a non-cardiovascular related event clearly unrelated to the S-ICD System or procedure. In addition, events in which there is no untoward clinical occurrence in the subject should not be reported.

Investigators must report clinical events to the sponsor as described in **Table 12**.

Table 12: Investigator Reporting Timelines for Deaths and Clinical Events

Event Type	Reporting Time
Death and all SA(D)Es	As soon as possible, but no later than 2 working days after becoming aware
Reportable Adverse Device Effect	As soon as possible, but no later than 10 working days after becoming aware
Device Deficiencies	As soon as possible, but no later than 1 working day after becoming aware

Examples of events that do not require reporting include:

- Follow-up or exacerbation/worsening of pre-existing conditions including: diabetes, cancer, allergies, osteoporosis, arthritis, heart failure, etc.
- New medical conditions unrelated to the S-ICD System including: diabetes, cancer, allergies, osteoporosis, arthritis, etc.
- Physical trauma or injury unrelated to the S-ICD System including: musculoskeletal injuries, joint aches and pains, tendonitis, bursitis or burns from external causes.
- Rotation of the pulse generator in which the subject experiences no discomfort or other untoward clinical occurrence.
- Device explant or replacement in the absence of any untoward medical occurrence, including normal battery depletions
- Adverse events or sequelae related to a different procedure or separate medical device, such as a concomitant pacemaker or abandoned/extracted lead
- Normal battery depletion
- Inability to implant the device (e.g., due to high DFTs)

If it is unclear whether or not an event should be reported, investigators should conservatively report the event.

11.2 Adverse event Definitions

Adverse event – Any untoward medical occurrence in a subject. This definition does not imply that there is a relationship between the event and the system under investigation.

Adverse Device Effect - Any untoward or unintended response to a medical device. This definition includes any event resulting from insufficiencies or inadequacies in the instructions for use or deployment of the device. It also includes any event that is a result of user error.

Serious Adverse Event – An adverse event that:

- Led to a death;

- Led to a serious deterioration in the health of the subject that:
    - resulted in a life-threatening illness or injury,
    - resulted in a permanent impairment of a body structure or a body function,
    - required in-subject hospitalization or prolongation of existing hospitalization,
    - resulted in medical or surgical intervention to prevent permanent impairment to body structure or a body function;
- Led to fetal distress, fetal death or a congenital abnormality or birth defect.

Serious Adverse Device Effect- An adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event or that might have led to any of these consequences if suitable action had not been taken or intervention had not been made or if circumstances had been less opportune.

Observation – An adverse event that does not result in invasive intervention. Examples of such non-invasive intervention include, system reprogramming, antibiotic treatment of pocket infection, or change in medications.

Complication – An adverse event that results in permanent loss of device function,[31] invasive intervention or death.

11.3 Classification of Adverse events

All adverse events will be categorized as observations or complications based on the intervention required to resolve the adverse event. A complication is an adverse event that results in permanent loss of device function, invasive intervention or death.

All adverse events will also be classified by type based on the cause of the adverse event. The following definitions for adverse event types will be used:

- Type I: Caused by a component of the S-ICD System, including the pulse generator, electrode, electrode insertion tool or programmer

[31] *Permanent loss of device function* refers to: 1) the permanent loss of shock therapy and/or post shock pacing; 2) permanent loss of appropriate sensing in all available sensing configurations (oversensing that results in persistent inappropriate shocks or undersensing that could lead to undetected arrhythmias). Loss of device function includes programming the PG permanently off or temporarily off in advance of an explant/revision.

- Type II: Other adverse events not specifically caused by a component of the S-ICD System, but would not have occurred in the absence of the implanted S-ICD System
- Type III: Caused by a change in the subject's condition
- Type IV: Pre-existing medical condition or occurred while the subject was not enrolled

Adverse events will typically be labelled and categorized according to the clinical presentation, including device malfunctions.

In the event of a subject death, the S-ICD System should be interrogated, removed from the subject, and returned to BSC for analysis. The data related to the death should be recorded in the database in a timely fashion. A detailed death letter should also be provided to the sponsor.

In the event that the SQ-RX pulse generator or Q-TRAK subcutaneous electrode cannot be removed, the SQ-RX pulse generator should be interrogated prior to interment. Note that failure to remove the S-ICD System from a deceased subject prior to cremation may cause the battery to explode when the device is exposed to extreme temperatures.

All subject deaths will be reported by the sponsor to the appropriate regulatory agencies.

11.4 Device Deficiencies

A device deficiency is defined as an inadequacy of a medical device related to its identity, quality, durability, reliability, safety or performance, such as malfunction, misuse or use error and inadequate labelling.

12. ELECTRONIC CASE REPORT FORM DATA COLLECTION

All study data will be entered into electronic case report forms (CRFs) that are located on the study's electronic data capture system (EDC). Data can be recorded on a worksheet and then entered electronically. Alternatively, CRF data can be directly entered electronically. Either worksheets or information from subjects' medical charts serve as source documentation for electronically entered data. Site personnel are required to conduct an active subject chart review (e.g., implant, pre-discharge and any subsequent follow-up) to ensure the capture of possible acute adverse events during and between visits. Upon thorough review of subject chart, center personnel are asked whether adverse

events are identified by answering a designated questionnaire on the corresponding case report form and to verify whether any of the reportable adverse events as described in section 11 have occurred.

12.1 Enrollment Form

An Enrollment Form is completed when a subject has completed their Enrollment visit and all required data collection is complete as outlined in section 7.2.3.

12.2 Implant Form

An Implant Form is completed when a subject has completed their Implant visit and all required data collection is complete as outlined in section 7.2.6.

12.3 Pre-Discharge Form

A Pre-Discharge Form is completed when pre-discharge data collection is complete as outlined in section 7.2.8.

12.4 Annual Follow-up Visit Form

An Annual Follow-up Visit Form is completed when a subject has completed their annual visit and all required data collection is complete as outlined in section 7.2.9.

12.5 Additional Follow-up Visit Form

An Additional Follow-up Form is completed when a subject completes an additional visit that meets the definition of an additional follow-up visit and all required data collection is complete as outlined in section 7.2.10

12.6 Revision, Replacement and Explant Forms

In the event that the electrode or PG are surgically revised after the initial implant procedure, the appropriate revision forms are used to record changes to the system and all data required as outlined in section 7.3.

12.7 Study Completion Form

A Study Completion Form is completed when a subject has exited the study for any reason and all required data collection is complete as outlined in section 7.4.

12.8 Protocol Deviations

This is a standard of care registry. Deviations will only be issued for the following events:

- Inappropriate or unavailable informed consent
- Inclusion/exclusion criteria violations
- Failure to obtain required data

13. SUBJECT INFORMED CONSENT

Subject participation in this clinical study is voluntary. Informed Consent is required from all subjects or their legally authorized representative. Informed consent is required from all subjects or their legal representative, prior to participation in this study. The sponsor will provide a template informed consent document in local language. For sites where IRB approval is required, the informed consent should also be approved. In the event no IRB approval is required, the final version of the informed consent will be agreed between the sponsor and the investigational center. Significant changes to the consent document provided by the sponsor may need to be reviewed and approved by the sponsor before a subject provides written informed consent. Boston Scientific will provide study-specific template of the Screening ECG ICF and S-ICD PAS ICF to investigators participating in this study. The ICF templates may be modified to meet the requirements of the investigative center's IRB/EC. Any modification requires approval from BSC prior to use of the form. The ICFs must be in a language understandable to the subject and if needed, BSC will assist the center in obtaining a written consent translation. Translated ICFs must also have IRB/EC approval prior to their use. Privacy language shall be included in the body of the form or as a separate form as applicable.

The Investigator is responsible for ensuring that Informed Consent is obtained prior to data collection.

The obtaining and documentation of Informed Consent must be in accordance with the principles of the Declaration of Helsinki, ISO 14155, any applicable national regulations, and local Ethics Committee and/or Regulatory authority body, as applicable. The ICF must be approved by the center's IRB/EC, or central IRB, if applicable.

A Screening/Enrollment Log will be maintained to document select information about candidates who fail to meet the entry criteria. For subjects with a failed ECG screening test, the ECG may be collected only if a separate "Screening ECG" ICF is signed by the subject. This Screening ECG ICF allows collection of the screening ECG only and does not enroll the subject in the study. A separate "S-ICD PAS" ICF will be used to enroll subjects in the study.

The process of obtaining Informed Consent shall:

- be conducted by the Principal Investigator or designee authorized to conduct the process,
- include a description of all aspects of the clinical study that are relevant to the subject's decision to participate throughout the clinical study,
- avoid any coercion of or undue influence of subjects to participate,
- not waive or appear to waive subject's legal rights,
- use native language that is non-technical and understandable to the subject or his/her legal representative,
- provide ample time for the subject to consider participation and ask questions if necessary,
- Ensure important new information is provided to new and existing subjects throughout the clinical study.

The ICFs shall always be signed and personally dated by the subject or legal representative and by the investigator or an authorized designee responsible for conducting the informed consent process. If a legal representative signs, the subject shall be asked to provide informed consent for continued participation as soon as his/her medical condition allows. The original signed ICFs will be retained by the center and a copy of the signed and dated document and any other written information must be given to the person signing the form.

Failure to obtain subject consent will be reported by BSC to the applicable regulatory body according to their requirements (e.g., FDA requirement is within 5 working days of learning of such an event). Any violations of the informed consent process must be

reported as deviations to the sponsor and local regulatory authorities (e.g. IRB/EC), as appropriate.

If new information becomes available that can significantly affect a subject's future health and medical care, that information shall be provided to the affected subject(s) in written form via a revised ICF or, in some situations, enrolled subjects may be requested to sign and date an addendum to the ICF. In addition to new significant information during the course of a study, other situations may necessitate revision of the ICF, such as if there are amendments to the protocol, a change in Principal Investigator, administrative changes, or following annual review by the IRB/EC. The new version of the ICF must be approved by the IRB/EC. Boston Scientific approval is required if changes to the revised ICF are requested by the center's IRB/EC. The IRB/EC will determine the subject population to be re-consented.

14. INSTITUTIONAL REVIEW BOARD

Prior to gaining Approval-to-Enroll status, the investigational center will provide to the sponsor documentation verifying that their IRB is registered or that registration has been submitted to the appropriate agency, as applicable according to national/regulatory requirements.

A copy of the written IRB of the protocol and Informed Consent Form must be received by the sponsor before recruitment of subjects into the study and shipment of investigational product/equipment. Prior approval must also be obtained for other materials related to subject recruitment or which will be provided to the subject.

Annual IRB approval and renewals will be obtained throughout the duration of the study as required by IRB requirements. Copies of the Investigator's reports and the IRB continuance of approval must be provided to the sponsor.

15. CONFIDENTIALITY AND RISK ANALYSIS

15.1 Subject Confidentiality

Subject data will be treated as confidential information by the sponsor. The sponsor will limit access to confidential information to those individuals requiring access. Regulatory agencies maintain the right to review records pertinent to this clinical study. Unless

required by law, the sponsor will report de-identified data in an effort to secure subject confidentiality.

15.2 Health Insurance Portability and Accountability Act (HIPAA)

The HIPAA requirements affect clinical trials in three key areas as described below:
Accounting of Disclosures: Data collected during the conduction of pre-screening activities for this study are subject to the HIPAA accounting of disclosures' regulations. It is the responsibility of the investigative center to tell all subjects whose records were screened for eligibility in the study that their records were used in this manner if he or she requests an accounting of when his or her data were disclosed.

Consent: All subjects participating in the study will be made aware that their participation in the study will involve disclosure of certain protected health information to BSC and for what purpose. The ICF will contain a listing of the type of information that will be disclosed during the course of the clinical study.

Withdrawal of Consent: HIPAA specifically allows companies such as BSC that are subject to the jurisdiction of the FDA access to protected health information for activities related to the quality, safety or effectiveness of devices. This means that BSC can use data from this study even if the individual withdraws his or her authorization.

15.3 Analysis of Risks

A complete list of anticipated cautions, warnings and potential adverse events is included in the User Manual.

Potential adverse events related to implantation of the S-ICD System may include, but are not limited to, the following:

- Acceleration/induction of atrial or ventricular arrhythmia
- Adverse reaction to induction testing
- Allergic/adverse reaction to system or medication
- Bleeding
- Conductor fracture
- Cyst formation
- Death
- Delayed therapy delivery
- Discomfort or prolonged healing of incision
- Electrode deformation and/or breakage
- Electrode insulation failure
- Erosion/extrusion
- Failure to deliver therapy
- Fever
- Hematoma
- Hemothorax
- Improper electrode connection to the device
- Inability to communicate with the device
- Inability to defibrillate or pace
- Inappropriate post-shock pacing
- Inappropriate shock delivery
- Infection
- Keloid formation
- Migration or dislodgement
- Muscle stimulation
- Nerve damage
- Pneumothorax
- Post-shock/post-pace discomfort
- Premature battery depletion
- Random component failures
- Stroke
- Subcutaneous emphysema
- Surgical revision or replacement of the system
- Syncope
- Tissue redness, irritation, numbness or necrosis

If any adverse events occur, invasive corrective action and/or S-ICD System modification or removal may be required.

Subjects who receive an S-ICD System may develop psychological disorders that include, but are not limited to, the following:

- Depression
- Fear of shocks
- Phantom shocks

15.4 Risk Minimization

Risks associated with the S-ICD System can be minimized by following the detailed instructions in the User's Manual.

15.5 Potential Benefits

This clinical evaluation is intended to evaluate long term clinical outcome associated with the S-ICD System. The S-ICD System does not require any component of the system to be placed in the vasculature or the heart, and therefore, eliminates risks and complications associated with transvenous lead placement.

16. COMPLIANCE

16.1 Statement of Compliance

This study will be conducted in accordance with the relevant parts of the ICH Guidelines for Good Clinical Practices and ethical principles that have their origins in the Declaration of Helsinki, and pertinent laws and regulations. The study shall not begin until the required approval/favorable opinion from the IRB. Any additional requirements imposed by the IRB or regulatory authority shall be followed, if appropriate.

16.2 Monitoring

Monitoring will be performed during the study to assess continued compliance with the protocol and applicable regulations. In addition, the monitor verifies that study records are adequately maintained, that data are reported in a satisfactory manner with respect to timeliness, adequacy, and accuracy, and that the Investigator continues to have sufficient staff and facilities to conduct the study safely and effectively. The Investigator/institution guarantees direct access to original source documents by BSC personnel, their designees, and appropriate regulatory authorities.

The study may also be subject to a quality assurance audit by BSC or its designees, as well as inspection by appropriate regulatory authorities. It is important that the Investigator and relevant study personnel are available during on-site monitoring visits or audits and that sufficient time is devoted to the process. Monitoring activities may include:

- Review of Informed Consent documentation;
- Review/maintenance of medical records and source documents;

- Verification of subject eligibility requirements as stated in the clinical protocol;
- Review of case report forms and data clarifications/queries;
- Review of IRB or EC requirements, reports and correspondence;
- Review of study records and correspondence;
- Verification that personnel with trial related responsibilities have been trained prior to conducting study activities.
- Evaluation of facilities;

Should BSC determine that an investigator is not complying with the signed investigator agreement, this protocol, other applicable FDA regulations, or any conditions of approval imposed by the reviewing IRB or FDA, BSC shall promptly either secure compliance or, at its sole discretion, terminate the investigator's participation in the investigation.

16.3 Complaint Reporting and Return of S-ICD Systems

In the event that any product needs to be returned due, for example to explant or perceived malfunction, or to report a complaint or product experience, the contact information for Cameron Health/BSC Customer Service is as follows:

US Customer Service	
Telephone:	[redacted]
Free:	1 800 227 3422 1 800 CARDIAC
Fax:	[redacted]
Email:	[redacted]

16.4 Securing Compliance

The sponsor is responsible for ensuring investigator compliance with the clinical protocol, the investigator agreement and applicable regulatory requirements. The sponsor will attempt to secure compliance by discussing the non-compliance and the corrective action with investigators in person, on the telephone, or in writing. The sponsor reserves the right to terminate investigators' participation for continued non-compliance.

16.5 Insurance

Where required by local/country regulation, proof and type of insurance coverage, by BSC for subjects in the study will be obtained.

17. RESPONSIBILITIES

17.1 Sponsor Responsibilities and Contact Information

The sponsor is responsible for selecting qualified investigators and providing them with the information they need to conduct the investigation properly, ensuring appropriate monitoring of the investigation, ensuring that IRB review and approval are obtained as required and ensuring that any reviewing IRB or Regulatory Agency is promptly informed of significant new information about an investigation.

Questions regarding this study should be directed to the local sponsor representative or designee.

17.2 Role of Sponsor Field Clinical Engineers

BSC personnel can provide technical assistance to the investigator and other health care personnel as needed during enrollment, implant, conversion testing, and follow-up visits. Assistance may include training, assistance with data entry, addressing questions, or providing clarification concerning the operation of the S-ICD System, procedures or testing described in this protocol, or the case report forms.

At the request of the investigator and while under their supervision, BSC personnel may operate equipment during enrollment, implant, conversion testing or follow-up visits and interact with the subject to accomplish the requested activities.

BSC personnel will not:

- Practice Medicine
- Provide medical diagnosis or treatment to subjects
- Discuss a subject's condition or treatment with a subject without the approval and presence of the investigator or other health care personnel

17.3 Investigator Responsibilities

Investigators are responsible for the following:

- Ensuring that the study is conducted according to any signed agreements, the Protocol and applicable regulations for protecting the rights, safety, and welfare of subjects under the investigator's care
- Ensuring that the study is conducted with the express approval of the Institution's IRB or providing appropriate documentation that such approval is not required
- Ensuring that conducting the study will not give rise to conflicts of interest
- Informing the sponsor in writing of the reason(s) for any withdrawal of any IRB approval
- Ceasing the enrollment of subjects immediately in the event of the withdrawal of any IRB approval
- Ensuring that no subjects will be enrolled, without prior, written Approval to Enroll from the Sponsor
- Agreeing to use their best efforts to satisfactorily complete the planned work and to comply at all times with accepted good clinical practice.
- Informing the sponsor of any conditions under which prior research was terminated
- Ensuring that informed consent is obtained appropriately and that the conditions of informed consent are complied with
- Ensuring the appropriate completion of all case report forms with the understanding that certain records and reports may be submitted to regulatory agencies by the Sponsor to support regulatory submissions
- Maintaining all records as described in the Protocol
- Supporting a monitor/auditor (as applicable) in their activities

- Informing the Sponsor of all adverse events and adverse device effects in a timely manner and informing the IRB of any serious adverse device effects as applicable

17.4 Selection of Investigators

Investigators will be Board Certified Electrophysiologists and Cardiologists with transvenous ICD implant experience who have expressed willingness to adhere to the investigational plan and provide all required data on a timely basis.

17.5 Enrollment Commencement Requirements

Investigators will be required to submit the following documents to the Sponsor prior to the first subject enrollment:

- Current curriculum vitae of investigator and co-investigators;
- Signed Clinical Trial Agreement or equivalent
- Signed Financial Agreement (separate or incorporated with a clinical trial agreement)
- Documentation that the study has obtained appropriate IRB approval or that such approval is not required
- Approved Subject Informed Consent Form (ICF)
- Financial Disclosure; and
- IRB roster, Multiple Project Assurance (MPA) number or Federal Wide Assurance (FWA)

The principal investigator at each investigational center is responsible for the proper conduct of the trial at the center. Some responsibilities may be assigned to co-investigators or other appropriately trained personnel, at the clinical center; however, the principal investigator remains responsible for the proper conduct of the clinical investigation.

18. RECORDS AND REPORTING

Case Report Forms should be submitted within 10 business days after the corresponding visit. However, adverse events and deaths should be reported according to the timelines shown in Table 12. Investigators are responsible for notifying the sponsor of any changes to previously reported data.

Original source documentation must be maintained at the investigational center to substantiate data entered on case report forms. Source data must be made available by the investigator to facilitate monitoring, as described in section 16.1. Specific source document requirements are included throughout section 7.2.

Interim progress reports will be generated every 6 months for the first two years of the study and annually thereafter from the negotiated start date for the study. Reports will include sections outlined in the relevant FDA guidance documents pertaining to post approval studies.

18.1 Investigator Records

Investigators are required to maintain complete and accurate records pertaining to the study. Relevant records include:

- IRB approvals, renewals, and withdrawals;
- Records of systems used in the study, including traceability to the subject that received the system;
- Records of any systems returned to the sponsor;
- Signed informed consent form(s) for each enrolled subject;
- Completed case report forms;
- Records of all adverse events and supporting documentation;
- Records pertaining to the death of any subject participating in the study;
- Copies of the current approved version of the protocol.

Records should be maintained for at least 3 years following the completion or termination of the investigation or the time dictated by national guidelines if longer.

18.2 Amendments to the Protocol

In the event an amendment to the protocol is required, the sponsor will inform all Principal Investigators in writing including an explanation of any reason for change. Subjects may not be enrolled according to the requirements of any amendment until appropriate approval is obtained including the IRB approval as required.

19. COMMITTEES

19.1 Clinical Events Committee

A Clinical Events Committee (CEC) is an independent group of individuals with pertinent expertise that reviews and adjudicates important endpoints and relevant adverse events reported by study investigators.

Committee membership will include experts with the necessary therapeutic area and subject matter expertise to adjudicate adverse events. CEC responsibilities, qualifications, membership, and committee procedures will be outlined in a CEC charter.

20. SUSPENSION OR TERMINATION

20.1 Premature Termination of the Study

Boston Scientific Corporation reserves the right to terminate the study at any stage but intends to exercise this right only for valid scientific or administrative reasons and reasons related to protection of subjects. Investigators, associated IRBs/ECs, and regulatory authorities, as applicable, will be notified in writing in the event of study termination.

20.2 Criteria for Premature Termination of the Study

Possible reasons for premature study termination include, but are not limited to, the following.

- The occurrence of unanticipated adverse device effects that present a significant or unreasonable risk to subjects enrolled in the study.
- An enrollment rate far below expectation that prejudices the conclusion of the study.
- A decision on the part of Boston Scientific to suspend or discontinue development of the device.

20.3 Termination of Study Participation by the Investigator or Withdrawal of IRB/ EC Approval

Any investigator, or IRB/ EC may discontinue participation in the study or withdrawal approval of the study, respectively, with suitable written notice to Boston Scientific. Investigators, associated IRBs/ECs, and regulatory authorities, as applicable, will be notified in writing in the event of these occurrences.

20.4 Requirements for Documentation and Subject Follow-up

In the event of premature study termination a written statement as to why the premature termination has occurred will be provided to all participating centers by Boston Scientific. The IRB/EC and regulatory authorities, as applicable, will be notified. Detailed information on how enrolled subjects will be managed thereafter will be provided.

In the event an IRB or EC terminates participation in the study, participating investigators, associated IRBs/ECs, and regulatory authorities, as applicable, will be notified in writing. Detailed information on how enrolled subjects will be managed thereafter will be provided by Boston Scientific.

In the event an investigator terminates participation in the study, study responsibility will be transferred to a co-investigator, if possible. In the event there are no opportunities to transfer investigator responsibility; detailed information on how enrolled subjects will be managed thereafter will be provided by Boston Scientific.

The investigator must return all documents and investigational product to Boston Scientific, unless this action would jeopardize the rights, safety, or welfare of the subjects.

20.5 Criteria for Suspending/Terminating a Study Center

Boston Scientific Corporation reserves the right to stop the inclusion of subjects at a study center at any time after the study initiation visit if no subjects have been enrolled for a period beyond 12 months after center initiation, or if the center has multiple or severe protocol violations/noncompliance without justification and/or fails to follow remedial actions.

In the event of termination of investigator participation, all study devices and testing equipment, as applicable, will be returned to BSC unless this action would jeopardize the rights, safety or well-being of the subjects. The IRB/EC and regulatory authorities, as applicable, should be notified. All subjects enrolled in the study at the center will continue to be followed according to the standard of care. The Principal Investigator at the center must make provision for these follow-up visits unless BSC notifies the investigational center otherwise.

21. PUBLICATIONS POLICY

In accordance with the Corporate Policy on the Conduct of Human Subject Research, BSC requires disclosure of its involvement as a sponsor or financial supporter in any publication or presentation relating to a BSC study or its results. In accordance with the Corporate Policy for the Conduct of Human Subject Research, BSC will submit study results for publication (regardless of study outcome) following the conclusion or termination of the study. Boston Scientific Corporation adheres to the Contributorship Criteria set forth in the Uniform Requirements of the International Committee of Medical Journal Editors (ICMJE; http://www.icmje.org). In order to ensure the public disclosure of study results in a timely manner, while maintaining an unbiased presentation of study outcomes, BSC personnel may assist authors and investigators in publication preparation provided the following guidelines are followed.

- All authorship and contributorship requirements as described above must be followed.
- BSC involvement in the publication preparation and the BSC Publication Policy should be discussed with the Coordinating Principal Investigator(s) and/or Executive/Steering Committee at the onset of the project.
- The First and Senior authors are the primary drivers of decisions regarding publication content, review, approval, and submission.

Appendix A Acronyms and Definitions

bpm	beats per minute
CEC	Clinical Events Committee
CFR	Code of Federal Regulations
Adverse event	Any untoward medical occurrence in a subject
CRF	Case Report Form
Complication	A complication is an adverse event that results in permanent loss of device function, invasive intervention or death.
ECG	Electrocardiogram
EIT	Electrode Insertion Tool
FCC	Federal Communications Commission
ERI	Elective Replacement Indicator
FCE	Field Clinical Engineer
FDA	US Food and Drug Administration
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
ICD	Implantable Defibrillator
ICF	Informed Consent Form
IRB	Institutional Review Board
J	Joules
LVEF	Left Ventricular Ejection Fraction
ms	Millisecond
N/A	Not Applicable
NNT	Number Needed to Treat
NR	Not Required
Normal Battery Depletion	A pulse generator that is not associated with a complaint and has reached its elective replacement indicator(s) with implant time that meets or exceeds the nominal (50th percentile) predicted longevity at default (labelled) programmable settings OR with implant time exceeding 75% of the expected longevity using the longevity calculation tool available at time of product introduction, calculated using the device's actual use conditions and programmable settings
NSR	Normal Sinus Rhythm
NYHA	New York Heart Association
Observation	Observations are adverse events that do not result in invasive interventions. Examples are reprogramming or medication change.
OUS	Outside the United States
PCMCIA	Personal Computer Memory Card International Association
PCr	Serum (Plasma) Creatinine Level
Permanent Loss of Device Function	Refers to: 1) the permanent loss of shock therapy and/or post shock pacing; 2) permanent loss of appropriate sensing in all available sensing configurations (oversensing that results in persistent inappropriate shocks or undersensing that could lead to undetected arrhythmias). Loss of device function includes programming the PG

	permanently off or temporarily off in advance of an explant/revision.
PMA	Premarket Approval
ppm	pulses per minute
RF	Radio Frequency
SAS	Statistical Analysis System
Spontaneous Episode	Any arrhythmia that is stored by the SQ-RX pulse generator
SVT	Supraventricular Tachycardia
Time to Therapy	Time to therapy is defined as the interval starting 2000ms after the last induction artifact (the time of the post induction refractory) and ending at the onset of the shock deflection on the ECG recording.
S-ICD System	The Cameron Health/BSC subcutaneous defibrillator, including the SQ-RX Pulse Generator, the Q-TRAK Subcutaneous Electrode, the Q-TECH Programmer, and the Q-GUIDE Electrode Insertion Tool (EIT)
TV-ICD	Transvenous ICD
US	United States
VF	Ventricular Fibrillation
VT	Ventricular Tachycardia
VT/VF Storm	3 or more treated VT/VF episodes occurring within 24 hours

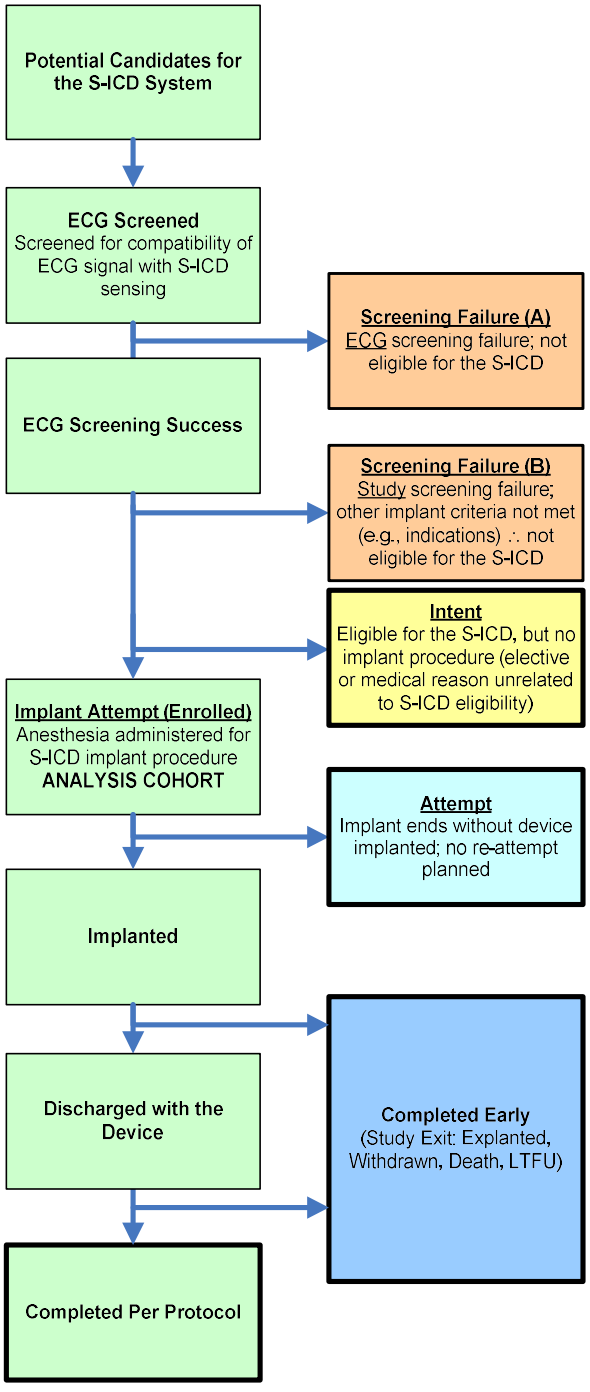
[redacted]

Appendix C Source Document Annotation Guidelines

Source Document	Annotation
Subject Informed Consent Form - "S-ICD PAS Consent" Form if subject to be enrolled in the study - "Screening ECG" Consent if subject not to be enrolled in the study	N/A
Pre-operative screening ECG	• Subject ID (passed ECG) or Screened Pt # (failed ECG) • ECG Lead (e.g., I, II, or III) • Position (e.g., supine, standing) • Pass or fail (each ECG)
Demographics, physical and medical history	N/A
Cardiovascular medication worksheet	N/A
Peri-operative medication worksheet	N/A
Implanted product and accessories utilized for S-ICD System (model/serial/lot/batch/etc.): medical notes or worksheet or labeling	N/A
Medical notes/worksheets documenting use of medical imaging (e.g., fluoroscopy)	N/A
VT/VF inductions (external ECG strips)	• Subject ID • Date • Page numbers (if >1 page) • Induction Test Shock # • Shock source (S-ICD or External) • Shock Energy (J) • Conversion (Y/N)
Device Reports - Summary Reports	• Redact subject name or replace with Subject ID • Study Visit
Device Reports - Captured ECG Report	• Redact subject name or replace with Subject ID • Study Visit • Posture
Device Reports - Episodes (treated and untreated)	• Redact subject name and replace with Subject ID • Study Visit • Rhythm / rate
Chest X-ray(s): an X-ray is not required per protocol; upload only if a Chest X-Ray of the S-ICD System was taken to assess the position of the S-ICD System, an S-ICD System-related adverse event, or product issue	• Subject ID. • Redact all identifying information • Date of X-ray
SD Card	N/A

Identifying information must be redacted from source documentation that is uploaded in the electronic case report form. Failure to annotate Device Reports uploaded from SD cards will not result in a deviation.

Appendix D Study Cohort Definitions



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