



Longitudinal Surveillance Registry of the AUCITY™ Spiral Lead
LSR of AUCITY Spiral

CLINICAL PROTOCOL
Version 5.0 (90906796 Version AC)
December 6, 2012

Sponsored By
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1. INTRODUCTION

1.1. Background

Boston Scientific CRM (BSC) continuously strives to improve the performance of its products. To do so, a complete understanding of device performance is necessary through bench testing and real-world monitoring. While bench testing provides predictions to performance, real-world monitoring aids in understanding failure mechanisms that require monitoring of large sample sizes over extended periods of time. The Longitudinal Surveillance Registry of the ACUIITY™ Spiral Lead (LSR of ACUIITY Spiral) will monitor chronic performance of the ACUIITY Spiral Lead to assess time-dependent failure modes.

1.2. Registry Purpose

The primary purpose of the LSR of ACUIITY Spiral is to evaluate and report on the long-term reliability and clinical performance of BSC's ACUIITY Spiral Lead. Additionally system related information will be collected in this registry.

1.3. Registry Objective

The objective of the LSR of ACUIITY Spiral is to prospectively evaluate the complication-free rate of the ACUIITY Spiral Lead to verify long-term performance.

2. METHODS

2.1. Patient Population

Investigators are expected to approach all potentially eligible patients receiving the ACUIITY Spiral Lead at the investigational center for enrollment into this registry until the enrollment is complete. All patients will meet specific inclusion criteria and will not meet any exclusion criteria (listed in sections 2.3.1 and 2.3.2). Patients choosing to participate in the registry must be enrolled in the LSR of ACUIITY Spiral within 29 days of implant of the ACUIITY Spiral Lead, as long as required data are available from/since implant. Patients will have an in-clinic follow-up one month (15 to 29 days) post implant and then subsequently be followed according to the

center's standard follow-up schedule, with complete in-clinic system interrogation recommended to be at least once every six months.

2.2. Devices Under Surveillance

ACUITY Spiral Leads (Models 4591, 4592, 4593) as well as other components of the implanted system are included in this registry.

2.3. Investigator / Center Selection Criteria

In order to protect patients participating in the registry and ensure proper conduct of the registry the sponsor will consider many factors when selecting investigators and centers for participation. Diverse centers will be selected with respect to geography and clinical setting (i.e., university, private practice, etc.).

The current BSC process for evaluating and selecting clinical centers will be utilized. The evaluation and selection criteria include but are not limited to the following:

- Centers that have the personnel with knowledge to run a clinical study and enroll patients according to FDA and good clinical practice guidelines. This usually includes having a dedicated Research Coordinator.
- Centers that have a Principal Investigator (physician) who has a commitment to conducting research and is in good standing with the FDA.
- Centers that have the necessary knowledge and experience to implant CRM products and also have the potential patient volume to meet enrollment expectations.
- Center personnel that have a commitment to protocol compliance along with gathering and submitting timely and accurate data using an electronic data entry system.
- Centers that will support on-site clinical monitoring during the registry.

2.4. Registry Inclusion/Exclusion Criteria

2.4.1. Registry Inclusion Criteria

Participation in another study/registry is generally permitted for patients enrolled in LSR of ACUITY Spiral unless its requirements conflict with the conduct of LSR of ACUITY Spiral or the sponsor provides exclusions to co-enrollment. Patients who meet all of the following criteria may be considered for inclusion in the registry:

- Has been or will be implanted with the ACUITY Spiral Lead within 29 days

- Plans to remain in the long-term care of his/her enrolling physician
- Is willing and capable (or appropriate legal representative) of authorizing access to and use of health information as required by an institution's IRB
- Is willing and capable (or appropriate legal representative) of providing authorization for participation in the registry

2.4.2. Registry Exclusion Criteria

Patients who meet the following criteria will be excluded from the registry:

- Is unable or unwilling to comply with the protocol requirements

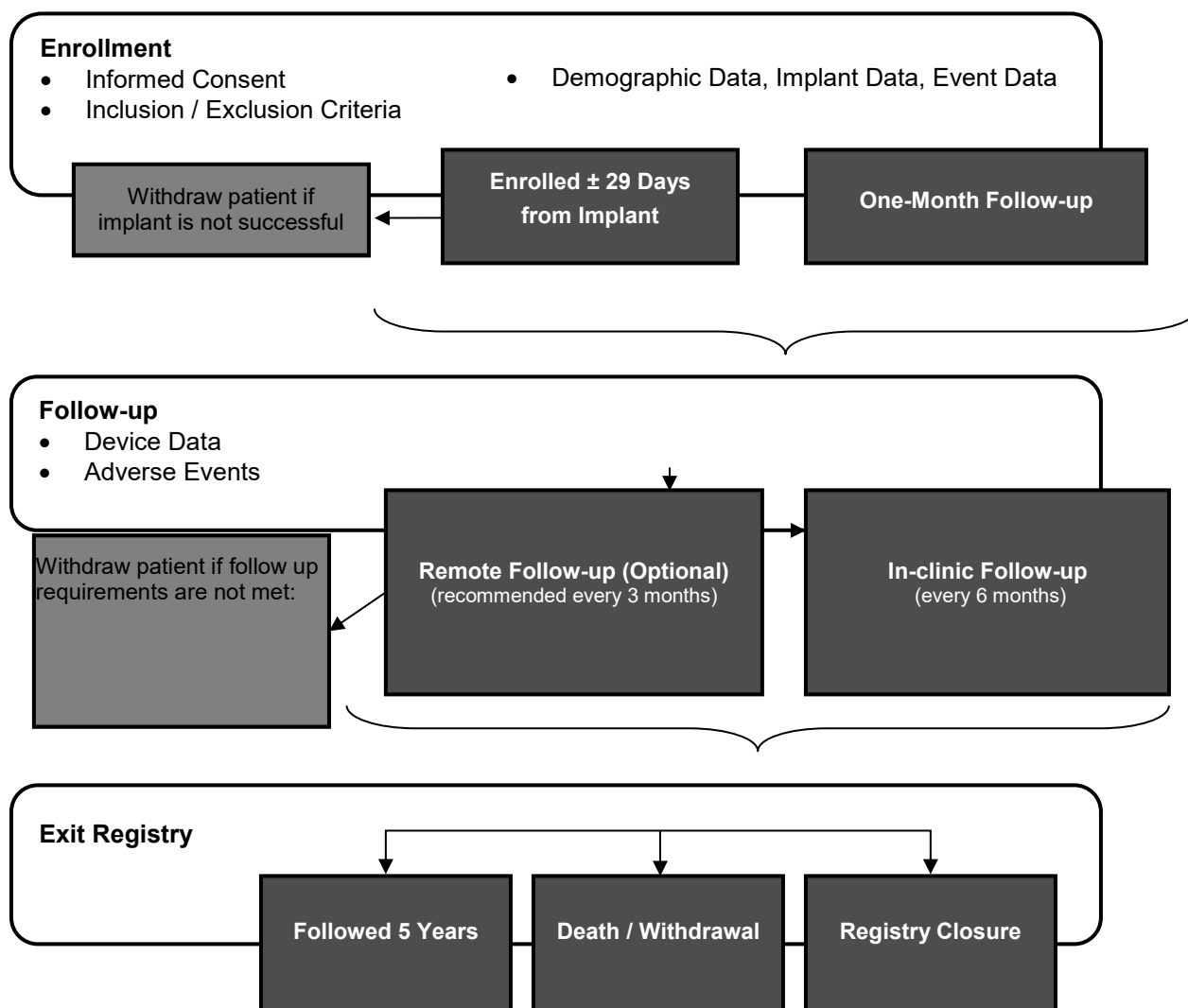
2.4.3. Enrollment Completion

Centers will be notified to cease enrolling patients for this registry when the enrollment target is reached or at the sponsor's discretion. This is expected to be when at least 1700 patients have been enrolled and successfully implanted with the ACUIITY Spiral Lead.

3. REGISTRY DESIGN

3.1. Registry Design

The LSR of ACUIITY Spiral is a prospective, non-randomized, multi-center registry of patients implanted with ACUIITY Spiral Lead. The LSR of ACUIITY Spiral is designed to collect product status information, any related adverse events and withdrawal data. Patient and device data from the enrollment/implant will be collected on the enrollment form. Patients will have an in-clinic full device evaluation done one month (15 to 29 days) post implant. Thereafter, it is recommended that the patient is seen for a full device evaluation at least once every six months and required at least once every 9 months. Patients may be optionally followed via the LATITUDE[®] remote monitoring system to facilitate ease of data collection. Upon activation in LATITUDE, data stored in the device including the latest in-clinic lead measurements will be collected via remote interrogation using the LATITUDE Patient Management system. Patients will be followed until they have completed five years of follow-up from implant or until death, withdrawal, or closure of the registry. The registry design is presented below in Figure 1.

Figure 1: Registry Design

3.2. Registry Type

This registry will follow 21 CFR Part 822 – Postmarket Surveillance.

3.3. Scale

The registry will be conducted by a maximum of 150 centers. At least 1700 patients will be enrolled and successfully implanted with the ACUITY Spiral Lead. Centers may continue to enroll patients until notified of enrollment completion.

3.4. Duration

The registry will last approximately five years after the last patient is enrolled. All patients enrolled in this registry must be followed according to the investigational plan unless BSC notifies the Investigator to the contrary or BSC has officially closed the registry. Patients should expect data collection to last five years from implant. After the patient has completed five years of follow-up their participation in the registry is complete. For additional information regarding the registry timeline, please consult Appendix B.

3.5. Visit Summary

The following sections describe the patient flow during patient visits. Patients will be followed by their respective center in accordance with the center's established practices for routine follow-up. For purposes of this registry, follow-up will include in-clinic visits that may be optionally documented by LATITUDE remote monitoring, thereby eliminating the need to complete an in-clinic follow up form in the electronic data capture system. In-clinic visits should be at least once every six months. A deviation is required if an in-clinic visit has not been recorded for a period of nine months.

3.5.1. Patient Enrollment Visit

At enrollment, the Patient Informed Consent process (Section 7) must be completed by the patient (with a legal representative if necessary). Patients who meet the inclusion/exclusion criteria and have a signed Patient Informed Consent are considered enrolled in the registry. The following information must be collected at enrollment/implant:

- Patient demographics, cardiac assessment and medical history
- System information (data required from implant may be collected from a retrospective chart review)

- PG model and serial number
- PG and Pocket location (right/left side as well as sub-pectoral or sub-cutaneous)
- Lead model and serial numbers for all implanted leads
- PG/Lead electrical measurements (can be recorded at time of enrollment if implant measurements are unavailable)
- Visual record of the ACUIITY Spiral Lead location on record (required in case of suspected lead dislodgment, and can be recorded at time of enrollment if unavailable from implant, prefer multi-planar cine but x-ray acceptable)
- Adverse Events (see Section 5)

The following information should be collected if available:

- Guide wire and catheters used for implanting the LV lead
- Implant technique (subclavian stick, axillary stick or cutdown)
- Attempted devices (PG or lead)
- LV lead location

Final patient status is defined as: *implant*, *attempt* or *intent*. The *implant* status definition refers to a patient who is successfully implanted with the ACUIITY Spiral Lead per the protocol. The *attempt* status definition refers to a patient who underwent anesthesia but was not implanted with the ACUIITY Spiral Lead. *Attempt* patients are to be withdrawn from the registry. The *intent* status definition refers to a patient who has been enrolled, but does not undergo an implant procedure. The original informed consent form and screening documentation for *intent* patients should be maintained in the center's administrative files.

3.5.2. One-Month Follow-up

A One-Month Follow-up (defined as 15 to 29 days post-implant) must be performed to provide a full device evaluation. If enrollment occurs during the One-Month Follow-up timeframe, this follow-up may be performed in conjunction with the Enrollment Visit.

- Measurements for all active leads
 - Amplitude (Sensing)
 - Impedance (Shock and Pacing)
 - Pacing Threshold including pulse width

- Adverse Events (see Section 5)

Data collected at the One-Month Follow-up needs to be entered into the electronic data capture system. Appropriate source documentation must be maintained by the center Section 10.1

3.5.3. In-Clinic Follow-up Visits

A standard device follow-up (including lead thresholds) needs to be performed during in-clinic visits and the following information must be collected.

- Measurements for all active leads
 - Amplitude (Sensing)
 - Impedance (Shock and Pacing)
 - Pacing Threshold including pulse width
- Adverse Events (see Section 5)

For patients enrolled in LSR of Acuity Spiral and also monitored via the LATITUDE remote monitoring system, lead measurement data will automatically be transferred via LATITUDE to the study database at the next LATITUDE transmission. Center personnel are required to report any adverse events that are identified.

In-clinic follow-up visits can be scheduled per standard of care at the participating center. It is recommended that they be scheduled at least every six months. If a period of nine months or greater passes between in-clinic follow-ups a deviation will be required. Centers are expected to make every effort to contact the patient (e.g., certified mail, phone calls, emails, etc.) and determine patient status in terms of verifying the last in-clinic follow-up and whether the patient intends to remain in the registry. Patients are considered lost-to-follow-up if the center has not had any contact for a year and cannot determine patient status.

To assist in follow-up tracking, a Patient Follow-up Log is available in the electronic data capture system. This log contains dates for in-clinic follow-up visits (as recorded by CRF or LATITUDE). This log will also assist in tracking when upcoming visits need to take place.

3.5.4. LATITUDE Remote Patient Monitoring

LATITUDE use is optional to facilitate ease of data collection.

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The LATITUDE Communicator (wireless option only) is a monitoring device that is located in the patient's home and enables collection of the same type of information remotely that normally would be collected during a routine office visit. With the LATITUDE Patient Management system, the data are collected wirelessly and sent over a phone line through the LATITUDE Communicator to the LATITUDE Patient Secure Server. Patient data will then be displayed on the LATITUDE website for physician review.

The results of in-office threshold tests will be uploaded to the LATITUDE system at the next scheduled remote transmission. Scheduled Remote Follow-ups are recommended to be programmed for at least once every three months and Weekly Device Checks should be turned on. All other follow-up LATITUDE settings are at physician discretion.

BSC is available for assistance in troubleshooting problems the patient may be encountering setting up their LATITUDE Communicator at 1.800.CARDIAC (1.800.227.3422).

LATITUDE alerts are categorized as red or yellow. Urgent red alerts are declared when conditions are detected that could potentially leave the patient without available life-saving therapy. The LATITUDE Patient Management system does not permit red alerts to be programmed off. Yellow alerts are declared when an out of range device measurement or patient heart-health issue is detected that may warrant physician review or investigation. Yellow alerts may be configured per physician discretion with the exception of the following Yellow alerts that are recommended to be active:

LV Lead Alerts:

- Low left ventricular intrinsic amplitude
- Low left ventricular pacing lead impedance
- High left ventricular pacing lead impedance

Other Lead System Alerts:

- Low atrial pacing lead impedance
- High atrial pacing lead impedance

Please Note: Entire system data are collected to insure related system integrity

For the purpose of the LSR of ACUIITY Spiral, the preceding alerts will trigger center notification. Lead-related alerts must be acknowledged on the LATITUDE Alert Log located on the electronic data capture system. Alerts that identify reportable adverse events meeting the definition in Section 5 and result in the patients being brought in to the office/hospital/center must be further explained by completing an Adverse Event Form. Repetitive alerts that are determined not to be lead-related can be responded to one time and programmed off at that time.

3.5.4.1. System Programming

For the purpose of the LSR of ACUIITY Spiral, implanted PGs may be programmed per physician discretion unless otherwise specified.

3.5.5. Chart Review

The presence/absence of adverse events identified during patient chart review must be reported. Chart review should be completed and documented twice yearly in conjunction with in-clinic visits to confirm all known adverse events are reported.

4. ENDPOINTS AND DATA ANALYSIS

4.1. Endpoints

4.1.1. Primary Endpoint: Chronic LV Lead-Related Complication-Free Rate

4.1.1.1. Description and Rationale for Endpoint Selection

The ACUIITY Spiral Lead will be evaluated by a chronic LV lead-related complication-free rate over a five year follow-up period.

The primary endpoint analysis will include confirmed chronic LV lead related complications that result in permanent loss of therapy, invasive intervention, injury or death.

LV lead-related adverse events within 45 days* following invasive cardiac surgery (device implant, PG change-out, cardiac catheterization, etc.) need to be reported, but will be omitted from the endpoint analysis. In addition, the following events will be collected, but will be excluded from the endpoint analysis unless determined by the Clinical Events Committee (See Section 4.2.2) to be attributed to a structural lead failure.

- Inability to place the LV lead
- Implant procedure related complications such as CS dissection, CS perforation, pneumothorax, arrhythmias, cardiac tamponade, hematoma
- LV Lead-related thrombosis
- In-patient damage to LV lead (e.g., accidental cut to lead body during pocket revision, device replacement, etc.)
- LV Lead dislodgments up to 180 days post implant procedure
- Twiddler's syndrome leading to LV lead dislodgment
- High LV pacing threshold, intermittent LV capture, no capture of LV lead
- Diaphragmatic/pectoral stimulation
- Infection
- Atrial lead, ICD lead, or generator adverse events requiring additional interventions
- Non-LV lead-related hospitalizations
- Non-LV lead-related death
- Lead revisions to optimize therapy
- Exit block
- Physiologic oversensing or undersensing

* Based on review of previous clinical studies, using a maximum of 45 days post implant gives centers an opportunity to enroll patients while allowing for a consistent time period for enrollment post implant and assessing acute adverse events without excluding adverse events that characterize long-term lead performance.

4.1.1.2.Hypotheses

H₀: The five year chronic lead-related complication-free rate $\leq 92.5\%$

H_A: The five year chronic lead-related complication-free rate $> 92.5\%$

The null hypothesis will be rejected if the lower one-sided 95% confidence bound for the chronic lead-related complication-free rate is greater than 92.5%.

4.1.1.3.Sample Size

Based on the calculations below, the sample size for this registry is approximately 1700 patients implanted with the ACUIITY Spiral Lead.

A binomial exact calculation with the parameters in Table 4 was used to determine the approximate sample size necessary to detect a clinically meaningful change with 80% power and a one-sided α -level of 0.05.

Table 2: Sample Size Parameters and Justification

Primary Endpoint	N	P	Δ	95% Confidence Boundary	Justification
Chronic LV lead-related complications	1000	94.5%	2.0	92.5%	Prospectively defined based on predicate data from EASYTRAK lead [†] . 95% confidence boundary is clinically acceptable.

Attrition is expected due to death, withdrawal, and loss-to-follow-up. Assuming an annual attrition rate of 10%, a minimum of 1700 patients implanted with the ACUIITY Spiral Lead is necessary to obtain 5-year follow-up data on approximately 1000 patients.

4.2. Data Analysis

4.2.1. Endpoint Analysis

For the ACUIITY Spiral Lead, the primary endpoint for this registry will evaluate the proportion of patients without a chronic ACUIITY Spiral Lead-related complication within five years post-implant. When the final patient reaches five years of follow-up, the primary analysis will be based on the Kaplan-Meier method for the estimation of the five-year chronic lead-related complication-free rate, including the lower one-sided 95% confidence interval. The censoring mechanism of the Kaplan-Meier analysis incorporates all available data on patients, including those that withdraw or are lost to follow-up.

The Kaplan-Meier analysis will begin at 45 days post-implant for each patient. All patients that are successfully implanted with the ACUIITY Spiral Lead and still actively followed in the study at 45 days post implant will be included in the analysis. The endpoint adverse events are defined as confirmed lead-related complications meeting the criteria in section 4.1.1.1. The

[†] The EASYTRAK lead was studied as part of the CONTAK CD/EASYTRAK Post Approval Study (PMA P010012). Mean implant duration was 26±13 months, with a cumulative implant duration of over 25,000 patient-months. The 3 year chronic lead-related complication free rate was 97.9% using Kaplan-Meier methods. Assuming a continued 1.7% annual rate (consistent with observed year to year changes in rates from previous pre-market LV lead studies) from years 3 to 5 would result in an estimated 94.5% chronic complication free-rate at 5 years for the EASYTRAK LV lead.

determination for inclusion of adverse events in the endpoint analysis will be made by an independent Clinical Events Committee. Additionally, since this registry is focused on chronic LV-lead performance, acute adverse events associated with attempted leads will not be included in this analysis as they would fall within the 45 days of an invasive cardiac surgery, therefore not meeting the criteria outlined in Section 4.1.1.1.

4.2.2. Clinical Events Committee (CEC)

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. The CEC will review a safety event dossier, which may include copies of subject source documents provided by study sites, for all reported cases of LV lead-related adverse events and LV lead-related death.

Committee membership will include practitioners with clinical expertise in electrophysiology who are familiar with ventricular lead performance, as well as other experts with the necessary therapeutic and subject matter expertise to adjudicate the event categories outlined above. CEC responsibilities, qualifications, membership, and committee procedures are outlined in the CEC charter.

All PG- or Lead-related adverse events occurring at or after implant events will be sent to the CEC for review and adjudication. If death is considered Acuity Spiral Lead-related, the associated Adverse Event will be sent for adjudication.

4.2.3. Trend Analysis

BSC trend management procedures provide criteria for initiating trend analysis and will be utilized in conjunction with data collected in this registry. Device performance information is received from many sources through various channels including clinical studies and registries. BSC monitors product performance information from many sources including suppliers, testing, manufacturing, clinicians, physicians, patients and field based personnel to identify opportunities for improvement. When a device is returned to BSC, laboratory technicians and engineers assess overall device function and perform analysis using specific tests related to the clinical

observation(s). Test results are compared to original manufacturing records and design intent. Clinical observations are added to laboratory findings to help determine root cause of the clinical observation(s). Each discrete event is then compared to other similar-appearing events. If a pattern is detected, actions are taken to identify a common root cause, and improvements focused on improving product reliability may be implemented. Improvements, when made, may include design changes in existing or subsequent generations, manufacturing and supplier process modifications, software updates, educational communications, and/or labeling changes as examples.

4.2.4. Progress Report Analysis

Progress reports to the FDA will be provided by the sponsor every six months. These reports will include:

- A summary of enrollment and lead status
- A Kaplan-Meier plot of time to first endpoint defined chronic ACUITY Spiral Lead-related complication
- A summary of trend analysis
- A summary of LV lead-related adverse events

4.2.5. Product Performance Reporting

In order to share information learned from this registry with practitioners on an on-going basis, data will be published in the BSC Product Performance Report (no sooner than one year post registry initiation, at least 200 patients participating in the registry and implanted with the ACUITY Spiral Lead, and at least 50 patients having entered a reporting interval).

5. Adverse Events

5.1. Adverse Event Reporting

The investigator must report all PG- or lead-related adverse events occurring **at or after implant** to BSC in a timely manner following the occurrence or discovery of an adverse event. Adverse events must be reviewed and classified by the investigator for the registry using the definitions outlined below.

5.2. Adverse Event Definitions

Reportable adverse events are defined as inappropriate performance of the PG or lead that result in an undesirable or unanticipated procedure or clinical occurrence. Investigators are responsible for providing an event narrative, classifying each reported adverse event, corrective action taken, method used to confirm the adverse event, clinical outcome, and root cause of the adverse event based on the information available. All adverse events must be reported on the Adverse Event Form and reported in accordance with Medical Device Regulations.

The list of adverse events in Table 3 and the supporting information in Table 4 are intended to be complete, but additional adverse events may be identified as more is learned about device performance.

Table 3: Reportable Adverse Events

<u>PG-related:</u>	<u>RA Lead-, RV Lead-, or LV Lead-related:</u>
<ul style="list-style-type: none"> • Accelerated arrhythmia episode (ventricular) • Inability to deliver shock or pace therapy • Inappropriate therapy (e.g., shocks, ATP, pacing) • Incomplete lead connection with pulse generator • Migration of pulse generator • Pectoral muscle stimulation • Possible malfunction • Post-shock rhythm disturbances • Pulse generator fault detected • Skin erosion • Other 	<ul style="list-style-type: none"> • Cardiac Perforation • Conductor fracture • Elevated thresholds • Extracardiac stimulation (e.g., phrenic, diaphragm) • High pacing lead impedance • High shock lead impedance • High shock lead impedance when attempting to deliver a shock • Inappropriate shock due to oversensing • Intermittent sensing • Lead migration/dislodgment • Lead insulation break or abrasion • Loss of capture • Low pacing lead impedance • Low shock lead impedance • Low shock lead impedance when attempting to deliver a shock • Oversensing/Multiple Counting • Undersensing • Other

Table 4: Supporting Adverse Event Information

<u>Corrective Action:</u>	<u>Method Used to Confirm Event:</u>	<u>Root Cause of Event (Physician Assessment):</u>
<p>Any of the following corrective actions will be collected to aid in determination of a device malfunction.</p> <ul style="list-style-type: none"> • Lead surgically repositioned • Lead surgically abandoned/capped • Lead electrically abandoned (e.g., PG pacing mode change) • Lead/generator explanted • Lead/generator replaced • Lead polarity changed (e.g., unipolar to bipolar, bipolar to unipolar) • Lead pace/sense configuration changed • Device output programming adjusted (e.g., change pulse width) • Generator pacing mode changed • No action taken based on medical judgment 	<p>Appropriate methods for confirmation of specific event types are included in the specific event definition in Appendix A.</p> <ul style="list-style-type: none"> • Device-based (programmer) • Device-based (LATITUDE) • Direct visual observation • Egram-based • Imaging (e.g., x-ray, cine, fluoroscopy, etc.) • Isometric testing (e.g., Valsalva maneuver, patient position, etc.) • Pocket manipulation • Pacing System Analyzer (PSA) test • Other, specify 	<p>ACUIITY Spiral Lead-related complications must be reported as possibly lead-related unless confirmed.</p> <ul style="list-style-type: none"> • PG related • Lead-related* (assign lead – RA, RV, LV) <ul style="list-style-type: none"> ○ Confirmed lead-related ○ Possibly lead-related • Patient condition

* Additional information will be required if the adverse event is suspected to be ACUIITY Spiral Lead-related in order to determine if the adverse event is a chronic lead-related complication

6. Electronic Case Report Form Data Collection

In the LSR of ACUITY Spiral, case report forms take the form of electronic web pages on the electronic data capture website.

6.1. Enrollment / Implant Form

An Enrollment / Implant Form is completed when a patient has completed their Enrollment visit and all required data collection is complete as outlined in Section 3.5.1.

6.2. One-Month Follow-up Form

A One-Month Follow-up Form will be completed to record all lead measurements collected during the visit.

6.3. Patient / Device Status Form

A Patient / Device Status Form will be completed when a patient or device is no longer active in the registry. Reasons for change in patient status include but are not limited to the following:

- Withdrawn
 - patient did not maintain eligibility criteria,
 - patient refused testing/follow-up
 - patient withdrawn by physician
 - patient lost to follow-up
 - out-of-service (OOS) Acuity Spiral lead (including permanent electrical abandonment)
- Patient deceased
- Patient completed five years of follow-up
- Study completed

Lead status must be reported at the time of withdrawal from the registry.

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6.3.1. Additional Information Collected at System Revision

In the event of a system revision, a detailed assessment of proximal end of lead and header at device change-outs will be required. Any newly implanted devices and system measurements will be collected similar to implant.

6.3.2. Additional Information Collected at Lead Failure

If the reason for withdrawal is lead failure, objective evidence supporting the allegation is required. Objective evidence includes but is not limited to PSA measurements demonstrating lead performance, cine recordings, x-rays; please refer to Appendix A for suggested confirmation depending on the lead failure mode. A detailed assessment of proximal end of lead and header at device change-outs will be required. Explantation data will also be requested including extraction method and tools used.

Please make every attempt to return explanted product to the manufacturer. BSC provides a Returned Products Kit (Model 6499) that can be ordered through BSC's Customer Service Department at 1.800.CARDIAC (1.800.227.3422) or 1.651.582.2698 or online at www.bostonscientific.com/ppr.

6.3.3. Additional Information Collected at Patient Death

Additional data will be collected upon a patient's death:

- Was the PG explanted (Yes, No, Unknown)? Please attempt to return PG to BSC upon death.
- Was an autopsy performed (Yes, No, Unknown)?
- Was the PG interrogated "in situ" after death (Yes, No, Unknown)?
- PG status at time of death (Monitor + Therapy, Monitor Only, Off, Not Functioning, Unknown)?
- Primary organ cause (Cardiac: arrhythmic, pump function, ischemic, other cardiac, unknown; Noncardiac; Unknown).
- If ischemic (Acute, MI, Non acute MI, MI unknown).

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- Temporal course (Sudden, Nonsudden, Unknown – Presumed Sudden, Unknown).
- Antecedent worsening HF (Yes, No, Unknown).
- Operative relationship (Pre-operative, Peri-operative, Post-operative).
- Death witnessed (Yes, No, Unknown).
- Death monitored (Yes, No, Unknown).
- If death monitored (VT, Bradyarrhythmia, Pulseless electrical activity, Other, Unknown).
- If bradyarrhythmia (Sinus bradyarrhythmia, High-degree AV block with slow ventricular response, Asystole).
- Cause of death (Procedure-related, Pulse-generator-related, Lead/Catheter-related, Unknown, Other).

6.3.4. Patient Follow-up Completion

Five years of follow-up are complete when the patient has been seen on or after the five year anniversary of the ACUIITY Spiral Lead implant. Centers will verify that all adverse events have been reported. Completing the Patient / Device Status Form signals the completion of the patient's participation in the LSR of ACUIITY Spiral.

6.4. Patient Follow-up Log

The Patient Follow-up Log is intended to aid centers in monitoring follow-ups. This log will display the last in-clinic follow-up that has been completed as well as the timing requirements for the next in-clinic follow-up. For patients using LATITUDE, both the in-clinic and remote follow-up data are transferred directly from the device to the sponsor through the LATITUDE Patient Management system.

6.5. LATITUDE Alert Log

As described in Section 3.5.4 the LATITUDE Alert Log needs to be completed in response to LATITUDE Alerts to determine if an Adverse Event is present. Centers are

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required to investigate the Alert and determine if it should be reported as an Adverse Event.

6.6. In-Clinic Follow-up Form

In the event that data from the last in-clinic follow-up are not received via LATITUDE, an In-Clinic Follow-up Form must be completed. Electrical lead measurements from the follow-up will be collected on this form. This form can be completed retrospectively from the patient's medical record.

6.7. Adverse Event Form

The Adverse Event Form needs to be completed when reportable adverse events occur.

6.8. Deviations

Deviations are defined as any divergence from the registry protocol. Reasons for a deviation include but are not limited to: patient consent not obtained, testing incomplete/not done, and no in-clinic follow-up in over nine months.

7. PATIENT INFORMED CONSENT

Patient participation in the LSR of ACUITY Spiral is voluntary. A Patient Informed Consent form is required for all patients prior to their participation in this registry and **must be obtained** in accordance with FDA regulation 21CFR, Part 50. The Patient Informed Consent process must be followed prior to patient participation in this registry. With prior approval from BSC, the Patient Informed Consent may be modified to meet the requirements of the designated Institutional Review Board (IRB).

8. INSTITUTIONAL REVIEW BOARD

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Investigators must provide BSC with documentation of IRB approval of this registry protocol and the Patient Informed Consent form before patient enrollment in the registry begins at the center. Investigators must also provide IRB approval of revisions to the Patient Informed Consent form or amendments to the protocol.

9. CONFIDENTIALITY AND RISK ANALYSIS

9.1. Patient Data Confidentiality

All information sent to BSC (including LATITUDE data) or entered on the electronic data capture website concerning patients or their participation in the registry will be considered confidential. Authorized BSC and FDA personnel have the right to inspect and/or copy all records pertinent to the registry. Data from the registry that are used in reporting will be without identifiable reference to a specific patient.

9.2. Health Insurance Portability and Accountability Act (HIPAA)

The HIPAA requirements affect clinical trials¹ in three key areas as described below:

Accounting of Disclosures: Data collected during the conduction of prescreening activities for this registry are subject to the HIPAA accounting of disclosures' regulations. It is the responsibility of the investigative center to tell all patients whose records were screened for eligibility in the registry 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 patients participating in the registry will be made aware that their participation in the registry will involve disclosure of certain protected health information to BSC and for what purpose. The Patient Informed Consent form will contain a listing of the type of information that will be disclosed during the course of the clinical registry.

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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 registry even if the individual withdraws his or her authorization.

9.3. Risks and Minimization of Those Risks

This registry does not involve any additional risks as this registry is collecting additional data consistent with approved device labeling and physician standard of care. The risks associated with this registry are those of a standard device procedure. Please see the Physician's Manual for reference.

10. MONITORING PROCEDURE

10.1. Investigator Responsibilities

The investigator is responsible for conducting the registry in accordance with the signed agreement, protocol, applicable laws, FDA regulations and any conditions of approval imposed by the reviewing IRB. An investigator may require the presence of BSC personnel at device-related procedures.

A participating Investigator shall maintain accurate, complete and current records, including record of each patient's case history and exposure to the device. Source documentation is required during acute testing, post-implant and chronic device evaluation, and adverse events. Source documentation is per Investigator's discretion but should include patient medical records, worksheets, CRFs, parameter reports, and electrograms.

NOTE: for non-BSC PGs source documentation for verification purposes will be the technical source form provided. Centers should maintain source data for all PGs (i.e programmer printouts).

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10.2. Sponsor Responsibilities

Boston Scientific will serve as the sponsor of this clinical investigation. A sponsor is defined as a person or organization that initiates, but does not actually conduct the investigation (FDA regulation 21 CFR§ 812.3 (N)). It is the responsibility of BSC as the sponsor to ensure proper monitoring of the investigation and to see that all clinical requirements are met. In addition, BSC representatives may participate in the conduct of the trial to the extent described in the following section on the role of BSC representatives. BSC personnel may or may not be blinded to the registry results. Participation in the registry will be limited to BSC personnel who are appropriately qualified and trained such as those personnel with an engineering, technical or nursing degree or equivalent training, or significant experience in cardiology, electrophysiology, or the implantable cardiovascular device industry. All personnel will be trained on the appropriate clinical study regulations and guidelines for medical device trials.

Role of Boston Scientific Representatives

BSC personnel can provide technical support to the investigator and other health care personnel (collectively HCP) as needed during implant, testing required by the protocol, and follow-ups. Support may include HCP training, addressing HCP questions, or providing clarifications to HCPs concerning the operation of BSC equipment (including programmers, analyzers, and other support equipment) or the procedures and forms related to the protocol.

At the request of the investigator and while under their supervision, BSC personnel may operate equipment during implant or follow-up, assist with the conduct of testing specified in the protocol, and interact with the patient to accomplish requested activities.

Typical tasks may include:

- Interrogating the device or programming device parameters to physician requested settings

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- Performing lead diagnostic testing using a Pacing System Analyzer or programmer to obtain pacing and sensing thresholds and impedance measurements
- Clarifying device behavior, operation or diagnostic output as requested by the investigator or other health care personnel
- Assisting with the collection of study data from Pacing System Analyzers, programmers and other equipment
- Entering data on registry worksheets as long as the responsible HCP verifies and signs the completed worksheet

In addition, BSC personnel can perform certain activities to ensure registry quality. These activities may include:

- Observing testing or medical procedures to provide information relevant to protocol compliance
- Reviewing collected data and registry documentation for completeness and accuracy

Boston Scientific personnel will not:

- Practice medicine
- Provide medical diagnosis or treatment to patients
- Discuss a patient's condition or treatment with a patient without the approval and presence of the HCP
- Independently collect critical registry data (defined as primary or secondary endpoint data).
- Enter data in electronic data capture systems
- Administer and/or sign as a witness for the Informed Consent Form
- Be involved in the recruitment of patients

10.3. Registry Monitoring

A monitor and/or BSC representative may visit an investigator during the registry to assess the following criteria:

- Adherence to the protocol and applicable regulations regarding the obligations of the investigator
- Maintenance of adequate records
- Accurate registry data entry

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In the event of noncompliance (e.g. repeated failure to transfer data, multiple deviations), as determined by registry management, a monitor and/or BSC representative may attempt to secure compliance by one or more actions:

- Corresponding with the investigator
- Telephoning the investigator
- Visiting the investigator/center

If an investigator is found to be repeatedly noncompliant with the signed agreement, the protocol or any other conditions of the registry, BSC will either secure compliance or, at its sole discretion, terminate the investigator's participation in the registry.

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11. REFERENCES

1. Muhlbaier LH. HIPAA A Training Handbook for Researchers. Marblehead, MA: Opus Communications, Inc.; 2002.

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APPENDIX A: Glossary

Definitions based on AdvaMed's March 2009 draft *Proposal for Uniform Reporting of Clinical Performance of Cardiac Rhythm Management Pulse Generators and Leads*

Cardiac Perforation - Penetration of the lead tip through the myocardium (including microperforation) or associated venous anatomy, either clinically suspected or confirmed by chest x-ray, fluoroscopy, echocardiogram, intracardiac electrogram, and/or visually.

Conductor fracture – A mechanical break within the lead conductor (includes connectors, coils and/or electrodes) observed visually, electrically, or radiographically. Preferred confirmation is a multi-planar cine of fracture site illustrating lead fracture. X-ray displaying lead fracture also is acceptable. If explanted, return explanted lead with Suture Sleeve ligatures to lead retained.

Elevated thresholds - Sudden and significant increase in the pacing threshold value (compared to the previous measured value) at which 2:1 safety margin can no longer be achieved. Preferred confirmation is a visual confirmation that the lead has not moved (If the lead has moved see Lead migration/dislodgment). If lead revision is required, electrical lead measurements collected with PSA.

Extracardiac stimulation (e.g., phrenic, diaphragm) – Clinical observation of inadvertent muscle/nerve stimulation other than cardiac muscle.

High pacing lead impedance – Pacing impedance is considered high if a measurement is $\geq 2000^{\#}$ ohms. If a conductor fracture is suspected to be the cause the preferred confirmation is a multi-planar cine of fracture site illustrating lead fracture. X-ray displaying lead fracture also is acceptable. If explanted, return explanted lead with Suture Sleeve ligatures to lead retained.

High shock lead impedance – Shock lead impedance is considered high if a measurement is $\geq 100^{\#}$ ohms.

High shock lead impedance when attempting to deliver a shock – High shock lead impedance ($\geq 100^{\#}$ ohms) when attempting to deliver a shock.

Inappropriate shock due to oversensing – Shock delivered due to oversensing.

[#] This value is different from AdvaMed's definition to align with Boston Scientific's system guides

Intermittent sensing - Intermittent loss of sensing or failure to detect intended intrinsic cardiac signals (atrial or ventricular) during non-refractory periods at programmed sensitivity settings

Lead insulation break or abrasion – A disruption or break in lead insulation observed visually, electrically, or radiographically.

Lead migration/dislodgment – Radiographic and electrical evidence of electrode displacement from the original implant site or electrode displacement that adversely affects pacing, and/or lead performance.

An ACUITY Spiral Lead-related adverse event will be classified as a dislodgment when the following conditions are met:

- Confirmed radiographic evidence of a lead shift
- Resulting electrical change (example: elevated thresholds, extracardiac stimulation, loss of capture)
- Requiring reprogramming or surgical intervention to correct the event

Loss of Capture - Intermittent or complete failure to stimulate cardiac depolarization at programmed settings delivered outside of the cardiac refractory period. If a conductor fracture is suspected to be the cause the preferred confirmation is a multi-planar cine of fracture site illustrating lead fracture. X-ray displaying lead fracture also is acceptable. If explanted, return explanted lead with Suture Sleeve ligatures to lead retained.

Low pacing lead impedance - Pacing impedance is considered low if a measurement is ≤ 200 ohms.

Low shock lead impedance – Shock lead impedance is considered low if a measurement is ≤ 20 ohms.

Low shock lead impedance when attempting to deliver a shock - Low shock lead impedance (≤ 20 ohms) when attempting to deliver a shock.

Oversensing / Multiple Counting – The occurrence of cardiac or non-cardiac events being misinterpreted as cardiac depolarization, (e.g., T waves, multiple counting, skeletal muscle potentials, and extracardiac electromagnetic interference).

Undersensing - Complete or intermittent loss of sensing or failure to detect the intended intrinsic cardiac signals (atrial or ventricular).

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APPENDIX B: Registry Timeline

The following is an expected schedule for conduct of the LSR of ACUITY Spiral.

Registry Initiation: BSC plans on approaching centers for participation in this registry upon FDA approval of the protocol.

Site Enrollment rate: BSC expects approximately 5 centers per month will agree to participate in the registry.

IRB approval rate: BSC expects approximately 5 centers per month will obtain IRB approval approximately within 90 days of agreement to participate.

Registry enrollment rate: Participating centers are expected to enroll 1 patient per month, with full enrollment in approximately 2 years.

Approximate enrollment completion date: Enrollment should be completed approximately 2 years following the first enrollment

Approximate last follow-up date: The last follow-up will be when the 1000th patient has his/her five year follow-up or five years post implant of the final implant, whichever occurs first.

Approximate final report submission: The final report submission will occur within 60 days following the final follow-up.

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