ST. JUDE MEDICAL

STUDY PROTOCOL
FOR THE

ST. JUDE MEDICAL CARDIAC LEAD ASSESSMENT STUDY

September 18, 2015

60039775/K-CLINICAL
NCT01507987

Table of Contents

1.0 Introduction

Lead durability and integrity depend on several factors, such as lead design, lead material, and mechanical stress. More than half of all lead complications are insulation defects, most frequently due to subclavian crush syndrome, abrasion of the lead by direct contact to the pulse generator (i.e. pacemaker, ICD, or CRT-D), or abrasion of the lead against adjacent leads. Often these present clinically with evidence of impedance changes or inappropriate ventricular sensing and defibrillation[1].

St. Jude Medical Riata® and Riata® ST family of leads are high voltage implantable cardioverter defibrillator (ICD) endocardial leads with Silicone insulation. QuickSite® and QuickFlex® left ventricular leads also utilize silicone rubber for insulation. Silicone rubber, while representing the industry's most commonly used defibrillation lead insulation material over the past 20 years, has been observed to be vulnerable to abrasion[2,3,4]. Abrasion of silicone defibrillation leads is acknowledged within the clinical community as a well known clinical risk and is well documented in the literature as the number one cause of lead failure across the industry with reported failure rates ranging from 3 to 10 %[5,6,7].

A more recently reported manifestation of Riata lead insulation and QuickSite/QuickFlex lead abrasion involves conductors that are outside the lead body as detected by x-ray, fluoroscopy, or post-explant physical examination. This phenomenon, known as inside-out abrasion with externalized conductors, occurs when internal abrasion processes produce an outer insulation breach significant enough to allow the conductor to separate from the lead body in isolated regions. Such a separation does not guarantee an electrical abnormality because the conductors themselves are insulated with a robust layer of ethylenetetrafluoroethylene (ETFE) polymer.

The prevalence of externalized conductors proximal to the RV coil in Riata/Riata ST leads has been reported to vary from 0.5% to 33.3% depending on the lead model[8-11]. Some of these cases of externalized conductors have been accompanied with inappropriate shocks, oversensing, increased pacing impedance/ threshold and lead noise. It remains unclear whether externalized conductors caused these electrical problems, as approximately 85% of the returned leads with externalized conductors do not have their ETFE insulation compromised and therefore should not be the cause of any reported electrical problem.

The Durata® family of ICD leads utilizes a silicone polyurethane co-polymer insulation known as Optim which has been associated with a significant reduction in abrasion when compared to Riata and Riata ST silicone insulated leads. Although the incidence of these insulation abrasion issues is extremely low in Durata leads, the Durata leads are being included in this study for comprehensive

analysis across all St. Jude Medical ICD lead types. This study aims to prospectively determine the prevalence and incidence of lead compromise evidenced by imaging (includes externalized conductors and other visual lead anomalies, by each subcategory, as listed in Appendix A) and electrical dysfunction in patients with Riata, Riata ST silicone ICD, QuickSite/QuickFlex CRT and Durata ICD leads. Prevalence as well as incidence of externalized conductors and other visual lead anomalies will be separately analyzed and reported. In addition, this study will provide information to the physicians regarding the possibility that an observation of externalized conductors with normal electrical function may progress to an electrical malfunction. The SJM Cardiac Lead Assessment Study is sponsored by St. Jude Medical (SJM) and constitutes the modification of the "Riata Lead Evaluation Study".

2.0 Purpose

The objectives of the study are:

1. To determine the prevalence of externalized conductors at enrollment in Riata®, Riata® ST Silicone, QuickSite®/QuickFlex® and Durata® leads
2. To determine the prevalence of other visual lead anomalies by each subcategory per Appendix A at enrollment in Riata®, Riata® ST Silicone, QuickSite®/QuickFlex® and Durata® leads
3. To determine the prevalence of electrical dysfunction[§] at enrollment in Riata®, Riata® ST Silicone, QuickSite®/QuickFlex® and Durata® leads
4. To determine the incidence of externalized conductors after enrollment in Riata®, Riata® ST Silicone, QuickSite®/QuickFlex® and Durata® leads
5. To determine the incidence of other visual lead anomalies by each subcategory per Appendix A after enrollment in Riata®, Riata® ST Silicone, QuickSite®/QuickFlex® and Durata® leads
6. To determine the incidence of electrical dysfunction[§] after enrollment in Riata®, Riata® ST Silicone, QuickSite®/QuickFlex® and Durata® leads.
7. To evaluate the 30-day adverse event rate associated with lead revision procedures (include lead extractions or abandonments with or without lead replacement) in Riata®, Riata® ST Silicone, QuickSite®/QuickFlex®, and Durata® families of leads
8. To determine the prevalence of "other insulation anomalies" in "returned leads" for Riata®, Riata® ST Silicone, QuickSite®/QuickFlex®, and Durata® families of leads. "Other insulation anomalies" include any of the following:
    - Internal abrasion short under RV shock coil
    - Internal abrasion short under SVC shock coil
    - Exposed conductors defined as a breach of the outer insulation
    - Breach of the internal silicone lumen tubing, but the conductor cable is contained within the lead body diameter.

[§]"Electrical dysfunction" is determined to be present after adjudication of the following cases of potential electrical failures that led to the lead being either

surgically capped/extracted or electrically abandoned. Potential electrical failures include the following:

- Presence of non-physiologic noise not due to external interference
- Rise in pace/sense (p/s) conductor impedance to > 2000 Ω or increase of more than 200 Ω over previous 6 months or increase of 400 Ω over any period of time
- Decrease of more than 200 Ω over previous 6 months or to impedance < 200 Ω from baseline impedance > 300 Ω or decrease of 400 Ω over any period of time
- Change in any high voltage coil impedance of > 25 Ω or to > 125 Ω or < 20 Ω
- Capture threshold > 5 V or an increase of ≥ 2 V from baseline (all measurements) of < 1 V

NOTE: In all cases, external sources of "noise" and other header-connector causes would be excluded. Functional abnormalities, including exit block and physiologic oversensing in the presence of an electrically intact lead are not electrical failures.

3.0 Clinical Protocol

3.1 Study Design and Scope

This study is a prospective, non-randomized, multi-center, international post market study that will determine the prevalence and incidence of externalized conductors and other visual lead anomalies (as evidenced by imaging) and the risk of progression to electrical dysfunction in a large series of ICD/ CRT-D/CRT-P devices containing one or more of the following SJM leads: Riata leads, Riata ST silicone leads, Durata leads, QuickSite/QuickFlex CRT leads. A patient that has at least one market released lead implanted in time period indicated in Table 1 is eligible for enrollment in the study. Each lead group will be considered separately for independent analysis.

Table 1: Leads Eligible for Enrollment

Lead Group	Model Numbers	Lead Implant Date
Riata	1560, 1561, 1562, 1570, 1571, 1572, 1580, 1581, 1582, 1590, 1591, 1592	2002-2009
Riata ST Silicone	7000, 7001, 7002, 7010, 7011, 7040, 7041, 7042	2006-2009
QuickSite/QuickFlex	1056T, 1058T, 1156T, 1158T	2006-2010
Durata	7120, 7121, 7122, 7130, 7131, 7120Q, 7121Q, 7122Q, 7170Q, 7171Q, 7172Q	2008-2010

In order to determine the prevalence and incidence of externalized conductors, other visual lead anomalies as well as electrical dysfunction in the population of leads being evaluated, a minimum of 1500 leads listed above will be enrolled at up to 60 sites. This will comprise a minimum of 300 leads in the Riata lead group and a minimum of 200 leads in the Riata ST lead group to make a combined total of at least 500 Riata and Riata ST silicone leads. The study will also include at least 500 leads in the QuickSite/QuickFlex and Durata lead groups. All patients will be followed every six months for three years.

Adequate representation across the different ages of the leads is also needed to understand the lead population being studied. Therefore, the leads from each group of leads will be compromised of subgroups based on the age of lead (at enrollment) being studied. The required minimum enrollment for each subgroup per lead group is indicated in Table 2. Even if the minimum enrollments indicated in Table 2 are met, extra enrollments may be required to ensure a minimum of 500 leads in each lead group.

Expected Attrition in patients with high voltage leads

Withdrawals due to death

Assuming an annual mortality of 7% in the ICD patient population, the mortality at 3 years is 20% [1 – (1-0.07)^3] In the recent RHYTHM ICD/QuickSite 1056K left heart lead study, the annual mortality was 12.8%, which would result in a mortality of 33.7 % [1 – (1-0.128)^3] at 3 years. If the ICD:CRT-D device mix is 60%:40% then the expected overall mortality in this study at 3 years is 25.5% (=0.6×0.20+0.4×0.337).

Withdrawals due to reasons other than death

In an ongoing St. Jude Medical post-approval study (SJ4 PAS), the attrition rate due to reasons other than death at 22 months of follow-up is 9%. Thus, it is anticipated that the attrition rate at 3 years for reasons other than death will be 15%.

Assuming that deaths and withdrawals are independent events, the total attrition is expected to be approximately 37% (= 1-(1-0.255)×(1-0.15)) over 3 years.

Since the Riata/Riata ST leads are recalled, it is more likely that some physicians will explant them, even when electrical function is normal. For this reason, an additional 10% of the patients are expected to be prematurely withdrawn. This leads to a total attrition of approximately 43% (= 1-(1-0.255)×(1-0.15)×(1-0.10)) over 3 years.

Expected Attrition in patients with left ventricular leads
Withdrawals due to deaths

In the RHYTHM ICD/QuickSite 1056K left heart lead study, the annual mortality was 12.8%, providing an estimated mortality rate of 33.7 % [1 – (1-0.128)^3] at 3 years.

Withdrawals for reasons other than death

In the ongoing St. Jude Medical post-approval study, the attrition rate due to reasons other than death at 22 months of follow-up is 9%. Thus, it is anticipated that the attrition rate at 3 years for reasons other than death will be 15%.

Assuming that deaths and withdrawals are independent events, the total attrition is expected to be approximately 43.6% (= 1-(1-0.337)×(1-0.15)) over 3 years.

Table 2: Enrollment in Lead Subgroups

Lead Group	Age of Lead at Enrollment (Years)	Min Enrollm-ent	Expected Attrition at 3 years*	Target Enrollment
Riata Silicone	≥ 7	100	47%	195
	≥ 6 and < 7	100	45%	185
	< 6	100	43%	180
Riata ST	≥ 5.5	100	45%	185
	< 5.5	100	43%	180
QuickSite 1056T/1058 and QuickFlex 1156T/1158T	≥ 6	115	46%	225
	≥ 5 and < 6	115	46%	225
	< 5	170	44%	300
Durata	≥ 5	167	37%	275
	≥ 4 and < 5	167	37%	275
	< 4	167	37%	275

*Expected attrition in each of the lead groups is based on the rationale provided above the table as well as larger attrition expected in older leads.

At enrollment, medical history, demographic data and lead measurement data will be collected. Additionally, cinefluoroscopy (AP, LAO 45° or the best possible LAO view, RAO 45° or the best possible RAO view) will be performed to determine the prevalence of lead compromise. A copy of

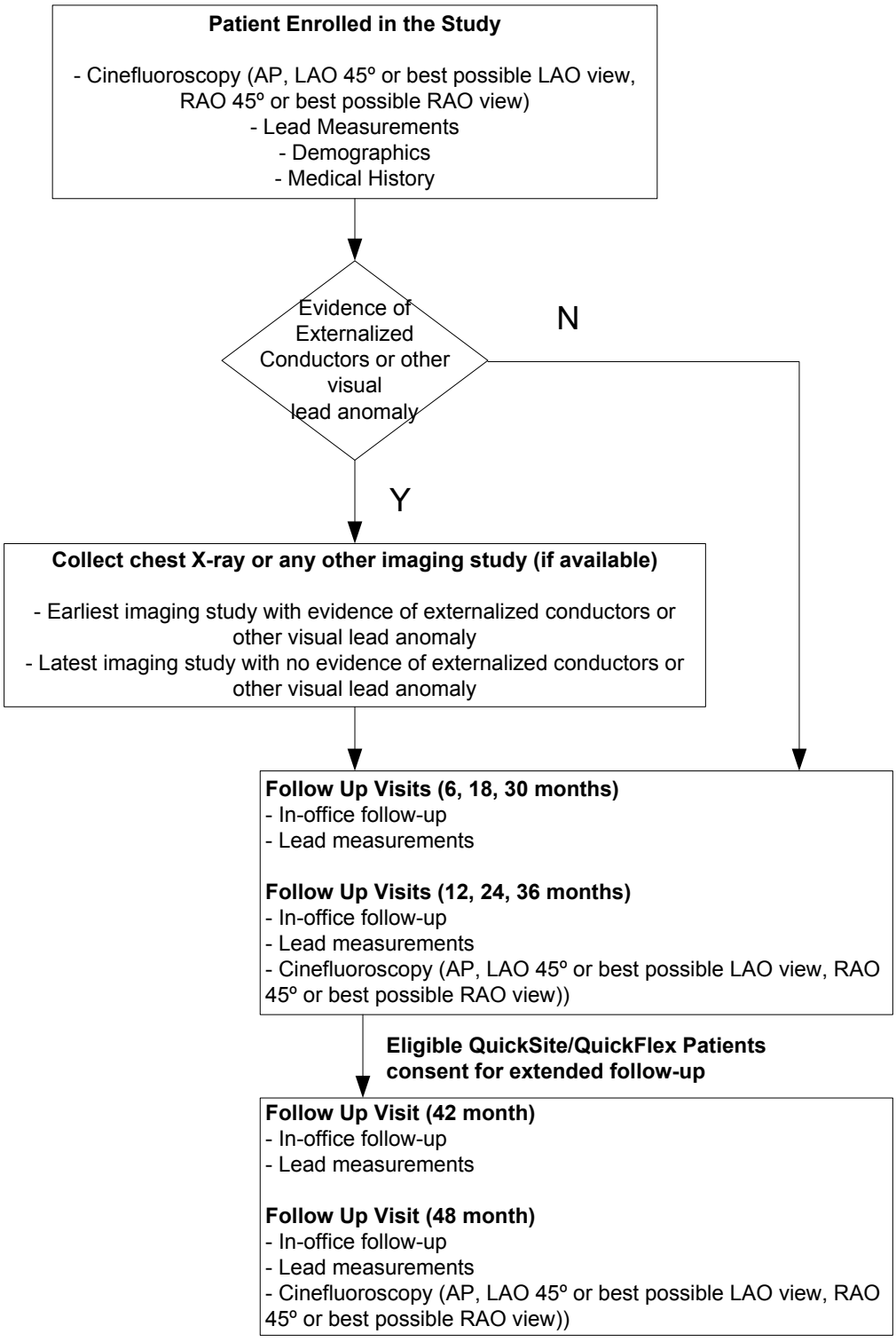
cinefluoroscopy performed as part of separate screening can be used to determine the prevalence of lead compromise as long as all three views (AP, LAO 45° or the best possible LAO view, RAO 45° or the best possible RAO view) are available. In patients with evidence of externalized conductors or other visual lead anomalies (fracture, subclavian crush, kink, broken filars on a shocking coil and other irregularities) the following chest x-rays or other available imaging studies will be collected (if available): a) earliest imaging study showing evidence of externalized conductors or other visual lead anomaly and b) latest imaging study that does not show any evidence of externalized conductors or other visual lead anomaly

Data will be collected at 6, 12, 18, 24, 30, and 36 months post enrollment and during any unscheduled follow-up visits due to patient symptoms suggestive of or with evidence of lead electrical problems. Additionally, cinefluoroscopy (AP, LAO 45° or the best possible LAO view, RAO 45° or the best possible RAO view) will be performed in all patients to determine the incidence and mechanical progression of externalized conductors at the 12, 24, and 36 month visits.

During any follow-up visits, device data and stored electrograms will be collected. All clinical events such as hospitalizations, emergency room visits, and adverse events will also be collected. All study data, including device data and stored electrograms will be sent to SJM electronically. If any lead being followed in this study develops a significant electrical abnormality suggestive of lead malfunction and x-ray or cinefluoroscopy would be performed as per the site standard of care then copies of x-ray or cinefluoroscopy should be submitted to SJM.

During the course of the study, any explanted leads should be returned to Returned Goods, St Jude Medical, Sylmar, CA, for analysis.

Study Flow Diagram



3.1.1 Projected Study Timeline

A projected timeline for the SJM Cardiac Lead Assessment Study is provided below. Since patients implanted with Riata and Riata ST silicone leads enrolled in the Riata Lead Evaluation Study will be rolled over to this protocol, the timeline takes into the account the initiation of the Riata Lead Evaluation Study done in the 4th quarter of 2011; dates will change based on the date enrollment begins again, and/or the actual enrollment rate.

Time = 0; month 1 **September 2011**	**Time = month 2**	**Time = month 3**	**Time = month 4** **December 2011**	**Time = month 5**	**Time = month 6** **February 2012**	**Time = month 7**	**Time = month 8**	**Time = month 9**	**Time = month 10** **June 2012**	**Time = month 11**	**Time = month 12** **August 2012**
Study Initiation			4 site with IRB approval	9 sites with IRB approval	11 sites with IRB approval	17 sites with IRB approval	22 sites with IRB approval	24 sites with IRB approval	24 sites with IRB approval	Enrollment Closed for Riata Silicone Leads	Received FDA 522 Order
			Enrollment = 5	Enrollment = 36	Enrollment = 72	Enrollment = 216	Enrollment = 329	Enrollment = 77	Enrollment = 47		
		Cumulative enrollment	5	41	113	329	658	735	782	Patient follow-up	----------

Time = month 13 **September 2012**					**Time =** **FDA approval of Initial Protocol Rev F February 2013**	**Time = FDA approval + 1 month**	**Time = FDA approval + 2 months**	**Time = FDA approval + 3 months**	**Time = FDA approval + 4 months**	**Time = FDA approval + 5 months**	**Time = FDA approval + 6 months**
Protocol Submitted to FDA based on 522 order	//	//	//	//			Enrollments for 522 Order Eligible Leads				29 sites with IRB approval
	//	//	//	//	522 Order eligible enrollments= 720	Enrollment = 4	Enrollment = 56	Enrollment = 66	Enrollment = 77	Enrollment = 126	Enrollment = 128
Patient follow-up	----------	----------	----------	----------	----------	Cumulative enrollment= 724	780	846	923	1049	1177

Time = FDA approval + 7 months	**Time = FDA approval + 8 months**	**Time = FDA approval + 9 months**	**Time = FDA approval + 10 months**	**Time = FDA approval + 11 months**	**Time = FDA approval + 12 months** **Feb. 2014**	----------	**Time = FDA approval + 18 months**	----------	**Time = FDA approval + 24 months** **Feb. 2015**	----------	----------
Enrollment = 168	Enrollment = 80	Enrollment = 58	Enrollment = 36	Enrollment = 16	35 sites with IRB approval Enrollment = 77		43 sites with IRB approval Enrollment = 217		44 sites with IRB approval Enrollment = 135		
Cumulative enrollment = 1345	1425	1483	1519	1535	1612		1829		1964		

Time = Orig. FDA approval + 32 months **October 2015** Anticipate FDA approval of protocol revision K	----------	**Time = Orig. FDA approval + 37 months** Durata and Riata enrollment completed	----------	**Time = Orig. FDA approval + 42 months** QuickSite/ QuickFlex enrollment completed	----------	----------	**Time = Orig. FDA approval + 78 months**	**Time = Orig. FDA approval + 79 months**	**Time = Orig. FDA approval + 80 months**	**Time = Orig. FDA approval + 81 months**	**Time = Orig. FDA approval + 82 months**
		55 sites with IRB approval		Patient follow-up	//	//	Follow-up completed		Complete Monitoring	Data Analysis	Final report submission
Projected Cumulative enrollment = 2025		2060		2110							

3.2 Study Outcome Measures

3.2.1 Primary Outcome Measures

3.2.1.1 The prevalence of electrical dysfunction in the Riata, Riata ST, QuickSite/QuickFlex (1056T, 1058T, 1156T, 1158) and Durata leads.

Lead Population
All enrolled leads within the Riata, Riata ST, QuickSite/QuickFlex (1056T, 1058T, 1156T, 1158) and Durata lead groups.

Analysis:
The prevalence of electrical dysfunction will be calculated as the number of leads that have electrical dysfunction at the time of enrollment in each of the 4 lead groups divided by total number of leads in enrolled patients in each of the 4 lead groups. The one-sided 95% UCB for prevalence will be calculated using Clopper-Pearson exact method.

3.2.1.2 The prevalence of externalized conductors in the Riata, Riata ST, QuickSite/QuickFlex (1056T, 1058T, 1156T, 1158) and Durata leads.

Lead Population
All enrolled leads within the Riata, Riata ST, QuickSite/QuickFlex (1056T, 1058T, 1156T, 1158) and Durata lead groups.

Analysis:
The prevalence of externalized conductors will be calculated as the number of leads that have been shown to have externalized conductors by imaging at the time of enrollment in each of the 4 lead groups divided by total number of leads in enrolled patients in each of the 4 lead groups. The one-sided 95% UCB for prevalence will be calculated using Clopper-Pearson exact method.

3.2.1.3 The prevalence of other visual lead anomalies by each subcategory (fracture, kink, subclavian crush, other irregularities) in the Riata, Riata ST, QuickSite/QuickFlex (1056T, 1058T, 1156T, 1158) and Durata leads.

Lead Population
All enrolled leads within the Riata, Riata ST, QuickSite/QuickFlex (1056T, 1058T, 1156T, 1158) and Durata lead groups.

Analysis:
The prevalence of other visual lead anomalies (by each subcategory) will be calculated as the number of leads that have been shown to have other visual anomaly (by each subcategory) at the time of enrollment in each of the 4 lead groups divided by total number of leads in enrolled patients in each of the 4 lead groups. The one-sided 95% UCB for prevalence will be calculated using Clopper-Pearson exact method.

3.2.1.4 The annual hazard rate of lead electrical dysfunction (from enrollment) by lead subgroups in the Riata, Riata ST, QuickSite/QuickFlex (1056T, 1058T, 1156T, 1158) and Durata leads.

Lead Population
All enrolled leads being followed in this study within the Riata, Riata ST, QuickSite/QuickFlex (1056T, 1058T, 1156T, 1158) and Durata lead groups.

Analysis:
The annual hazard rate will be assessed separately in each of the 4 lead groups along with the subgroups listed in Table 2.

For QuickSite/QuickFlex leads only, data from patients with an additional 1 year of follow-up will contribute to 2 separate lead subgroups (See Section 3.4.5).

3.2.1.5 The annual hazard rate of new cases of externalized conductors (from enrollment), by lead subgroups in the Riata, Riata ST, QuickSite/QuickFlex (1056T, 1058T, 1156T, 1158) and Durata leads.

Lead Population
All enrolled leads being followed in this study within the Riata, Riata ST, QuickSite/QuickFlex (1056T, 1058T, 1156T, 1158) and Durata lead groups.

Analysis:
The annual hazard rate will be assessed separately in each of the 4 lead groups along with the subgroups listed in Table 2.

For QuickSite/QuickFlex leads only, data from patients with an additional 1 year of follow-up will contribute to 2 separate lead subgroups (See Section 3.4.5).

3.2.1.6 The annual hazard rate of new cases of other visual lead anomalies by each subcategory (from enrollment), by lead subgroups in the Riata, Riata ST, QuickSite/QuickFlex (1056T, 1058T, 1156T, 1158) and Durata leads.

Lead Population
All enrolled leads being followed in this study within the Riata, Riata ST, QuickSite/QuickFlex (1056T, 1058T, 1156T, 1158) and Durata lead groups.

Analysis:
The annual hazard rate will be assessed separately in each of the 4 lead groups along with the subgroups listed in Table 2.

For QuickSite/QuickFlex leads only, data from patients with an additional 1 year of follow-up will contribute to 2 separate lead subgroups (See Section 3.4.5).

3.2.1.7 Prevalence of "other insulation anomalies" in "returned leads" (as defined in section 2.0), by lead subgroups in the Riata, Riata ST, QuickSite/QuickFlex (1056T, 1058T, 1156T, 1158) and Durata leads.

Lead Population
Any enrolled lead in the study that gets returned to St. Jude Medical for analysis.

Analysis:
The prevalence of "other insulation anomalies" will be calculated as the number of returned leads that have "other insulation anomalies" in each of the 4 lead groups divided by the total number of returned leads in enrolled patients in each of the 4 lead groups. The one-sided 95% UCB for prevalence will be calculated using Clopper-Pearson exact method.

3.2.2 Secondary Outcome Measures

3.2.2.1 Time from enrollment to externalized conductors by lead subgroups

Lead Population
All the leads without externalized conductors at enrollment within the Riata, Riata ST silicone, QuickSite/QuickFlex (1056T, 1058T, 1156T, 1158) and Durata lead groups

Analysis:
Time to externalized conductors will be analyzed using the Kaplan-Meier method. Those patients who do not experience externalized conductors will be censored 3 years after enrollment in this trial. A separate Kaplan-Meier curve will be calculated for each of the lead subgroups outlined in Table 2.

For QuickSite/QuickFlex leads only, data from patients with an additional 1 year of follow-up will contribute to 2 separate lead subgroups (See Section 3.4.5).

3.2.2.2 Time from enrollment to other visual lead anomalies (evidenced by imaging) by lead subgroups and each subcategory

Lead Population
All the leads without other visual lead anomalies at enrollment (by each subcategory) within the Riata, Riata ST silicone, QuickSite/QuickFlex (1056T, 1058T, 1156T, 1158) and Durata lead groups

Analysis:
Time to other visual lead anomalies (by each subcategory) will be analyzed using the Kaplan-Meier method. Those patients who do not experience other visual lead anomalies (by each subcategory) will be censored 3 years after enrollment in this trial. A separate Kaplan-Meier curve will be calculated for each of the lead subgroups outlined in Table 2.

For QuickSite/QuickFlex leads only, data from patients with an additional 1 year of follow-up will contribute to 2 separate lead subgroups (See Section 3.4.5).

3.2.2.3 Time from enrollment to electrical dysfunction, by lead subgroups

Lead Population
All the leads without electrical dysfunction at enrollment within the Riata, Riata ST silicone, QuickSite/QuickFlex (1056T, 1058T, 1156T, 1158) and Durata lead groups

Analysis:
Time to electrical dysfunction will be analyzed using the Kaplan-Meier method. Those patients who do not experience an electrical dysfunction will be censored 3 years after enrollment in this trial. A separate Kaplan-Meier curve will be calculated for each of the lead subgroups outlined in Table 2.

For QuickSite/QuickFlex leads only, data from patients with an additional 1 year of follow-up will contribute to 2 separate lead subgroups (See Section 3.4.5).

3.2.2.4 Time from externalized conductors to electrical dysfunction, by lead subgroups

Lead Population
All the leads with externalized conductors but without electrical dysfunction within the Riata, Riata ST silicone, QuickSite/QuickFlex (1056T, 1058T, 1156T, 1158) and Durata lead groups

Analysis:
Time to electrical dysfunction will be analyzed using the Kaplan-Meier method. The zero time will be the date at which externalized conductor was detected. Those patients who experience an externalized conductor after enrollment, but do not experience an electrical dysfunction will be censored 3 years after enrollment in this trial. A separate Kaplan-Meier curve will be calculated for each of the lead subgroups outlined in Table 2.

For QuickSite/QuickFlex leads only, data from patients with an additional 1 year of follow-up will contribute to 2 separate lead subgroups (See Section 3.4.5).

3.2.2.5 Time from other visual lead anomalies by each lead subcategory to electrical dysfunction, by lead subgroups

Lead Population
All the leads with other visual lead anomalies (by each subcategory) but without electrical dysfunction within the Riata, Riata ST silicone, QuickSite/QuickFlex (1056T, 1058T, 1156T, 1158) and Durata lead groups

Analysis:
Time to electrical dysfunction will be analyzed using the Kaplan-Meier method. The zero time will be the date at which other visual lead anomaly (by each subcategory) was detected. Those patients who experience other visual lead anomaly (by each subcategory) after enrollment, but do not experience an electrical dysfunction will be censored 3 years after enrollment in this trial. A separate Kaplan-Meier curve will be calculated for each of the lead subgroups outlined in Table 2.

For QuickSite/QuickFlex leads only, data from patients with an additional 1 year of follow-up will contribute to 2 separate lead subgroups (See Section 3.4.5).

3.2.2.6 Adverse Event rate through 30 days post-intervention for lead (e.g. extraction, abandonment, revision, other)

Lead Population
All the leads within the Riata, Riata ST silicone, QuickSite/QuickFlex (1056T, 1058T, 1156T, 1158) and

Durata lead subgroups that require an intervention/revision (e.g. extraction, abandonment, other)

Analysis
The 30-day adverse event rate will be calculated as the number of adverse events within 30 days associated with study lead related interventions in each of the 4 lead groups divided by total study lead related interventions in each of the 4 lead groups.

3.2.2.7 Time from externalized conductors to clinical intervention

Lead Population
All the leads with externalized conductors within the Riata, Riata ST silicone, QuickSite/QuickFlex (1056T, 1058T, 1156T, 1158), and Durata lead groups

Analysis:
Time to clinical intervention will be analyzed using the Kaplan-Meier method. The zero time will be the date at which externalized conductor was detected. Those patients who experience externalized conductor after enrollment but do not experience clinical intervention will be censored 3 years after enrollment in this trial. A separate Kaplan-Meier curve will be calculated for each of the lead subgroups outlined in Table 2.

For QuickSite/QuickFlex leads only, data from patients with an additional 1 year of follow-up will contribute to 2 separate lead subgroups (See Section 3.4.5).

3.2.2.8 Time from other visual lead anomalies by each subcategory to clinical intervention

Lead Population
All the leads with other visual lead anomalies (by each sub category) within the Riata, Riata ST silicone, QuickSite/QuickFlex (1056T, 1058T, 1156T, 1158), and Durata lead groups

Analysis:
Time to clinical intervention will be analyzed using the Kaplan-Meier method. The zero time will be the date at

which other visual lead anomaly (by each subcategory) was detected. Those patients who experience other visual lead anomaly (by each subcategory) after enrollment but do not experience clinical intervention will be censored 3 years after enrollment in this trial. A separate Kaplan-Meier curve will be calculated for each of the lead subgroups outlined in Table 2.

For QuickSite/QuickFlex leads only, data from patients with an additional 1 year of follow-up will contribute to 2 separate lead subgroups (See Section 3.4.5).

3.2.2.9 Comparison of patients with lead compromise as evidenced by imaging (includes externalized conductors and other visual lead anomalies by each subcategory) to those without lead compromise

Patient Population
All the patients within the Riata, Riata ST silicone, QuickSite/QuickFlex (1056T, 1058T, 1156T, 1158) and Durata lead subgroups.

Analysis
Demographic and clinical parameters will be compared between patients who experience a lead compromise as evidenced by imaging and those who do not experience a lead compromise. Specifically, the variables age, gender, body mass index, lead size, lead model, and implant factors such as venous access site, number of other leads in the vasculature, fixation location in the right ventricle, level of activity (based on functional NYHA class scale I, II, III, IV), level of therapy that patient received (no ATP/shock, ATP or shock) and slack (grades 0, 1, 2, 3, 4 based on the scale described by Ha et al., 2010[12]) in the lead will be used for the comparison. Continuous variables such as age or body mass index will be compared using Student's T-tests while categorical variables such as gender or lead models will be compared using Pearson's Chi-square statistic. Point estimates and p-values will be provided from these analyses.

3.2.2.10 Comparison of patients with electrical dysfunction to those without electrical dysfunction.

Patient Population
All the patients within the Riata, Riata ST silicone, QuickSite/QuickFlex (1056T, 1058T, 1156T, 1158) and Durata lead subgroups.

Analysis
Demographic and clinical parameters will be compared between patients who experience electrical dysfunction and those who do not experience electrical dysfunction. Specifically, the variables age, gender body mass index, lead size, lead model, and implant factors such as venous access site, number of other leads in the vasculature, fixation location in the right ventricle, level of activity (based on functional NYHA class scale I, II, III, IV), level of therapy that patient received (no ATP/shock, ATP or shock) and slack in the lead (grades 0, 1, 2, 3, 4 based on the scale described by Ha et al, 2010[12]) will be used for the comparison. Continuous variables such as age or body mass index will be compared using Student's T-tests while categorical variables such as gender or lead models will be compared using Pearson's Chi-square statistic. Point estimates and p-values will be provided from these analyses.

In addition, the two patient groups will be compared for the following endpoints:

1. Frequency of externalized conductors. This will be done using a Pearson's Chi-square analysis.
2. Frequency of other visual lead anomalies. This will be done using a Pearson's Chi-square analysis.
3. Time to detection of externalized conductors. A Kaplan-Meier analysis will be used for this comparison.
4. Time to detection of other visual lead anomalies. A Kaplan-Meier analysis will be used for this comparison.
5. The extent of externalization will be compared using Pearson's Chi-square analysis.
6. Number of zones with externalization within one lead will be compared using a Student's T-test.
7. Location of externalization will be compared using Pearson's Chi-square analysis.
8. Amount of slack in the lead (based on the scale described by Ha et al, 2010)[12] will be compared using Pearson's Chi-square analysis.

3.2.3 Additional Data

- Adverse events
- Lead Electrical Measurements: capture threshold, signal amplitude and impedance
- Types of clinical interventions following externalized conductors
- Types of clinical interventions following other visual lead anomalies
- Types of events leading to detection of externalized conductors
- Types of events leading to detection of other visual lead anomalies by each subcategory
- Types of events leading to detection of electrical dysfunction

3.3 Patient Selection

3.3.1 Inclusion Criteria

Eligible patients will meet **all** of the following:

1. Patient has a market released SJM ICD, CRT-D or CRT-P already implanted.
2. Patient has at least one market released Riata/ Riata ST/QuickSite/QuickFlex/Durata already implanted in which the lead model number and lead implant date is indicated in Table 1.*
3. Have the ability to provide informed consent for study participation and be willing to comply with the prescribed evaluations as detailed in this study plan.
4. Are 18 years or above.

*As different subgroups reach the minimum number of patients required for analysis, St. Jude Medical may notify the sites in writing that enrollment for a specific age of lead within a lead group are no longer eligible for enrollment. This will ensure a more even distribution of lead ages and lead types across the study population.

3.3.2 Exclusion Criteria

Patients will be excluded if they meet **any** of the following:

1. Patient is currently pregnant.
2. *Enrolled or intend to participate in a clinical drug and/or device study, which could confound the results of this trial as determined by SJM, during the course of this clinical study.

*NOTE: Patients enrolled in St. Jude Medical SJ4 post approval study, OPTIMUM and SCORE registries can be enrolled in this study.

3.4 Study Procedures

Study procedures are described in the sections below. Refer to Table 3 for an overview of the required study procedures. St. Jude Medical will provide supplemental step by step instructions for obtaining required study data.

Table 3: Study Procedures

	Enrollment	6, 18, and 30 month visit	12, 24, and 36 month visit	Unscheduled visit	*Extended 42 month visit* [c]	*Extended 48 month visit* [c]
Informed Consent	✓					
Demographics	✓					
Medical History	✓					
Electrical Malfunction History	✓					
Cinefluoroscopy (AP, LAO 45° or the best possible LAO view, RAO 45° or the best possible RAO view)	✓[a]		✓			✓[c]
Chest X-ray or Any Imaging Study	✓[b]					
Lead Measurements	✓	✓	✓	✓	✓[c]	✓[c]

a - Patients who underwent cinefluoroscopy at enrollment as part of the "Riata Lead Evaluation Study" will not be required to undergo another baseline cinefluoroscopy.
b - In patients with evidence of externalized conductors under cinefluoroscopy at enrollment, the following chest x-ray or imaging study will be collected, if available: a) earliest chest x-ray or imaging study with evidence of externalized conductors and b) latest chest x-ray or imaging study with no evidence of externalized conductors.
c – For only eligible patients with QuickSite/QuickFlex leads that consent for an additional year of follow-up (42 and 48 Month Visits).

3.4.1 Enrollment

Upon determination of study eligibility, informed consent will be obtained from eligible patients by the principal investigator or designee prior to initiation of any study related screening activities.

Patients with Riata, Riata ST, QuickSite (1056T or 1058T), QuickFlex (1156T or 1158T), and Durata leads with model numbers and lead implant dates indicated in Table 1 will be screened for evidence of externalized conductors or other visual lead anomalies through cinefluoroscopy that will include three videos/cines of the entire lead length as well as the pocket area (AP, LAO 45º or best possible LAO, RAO 45º or best possible RAO). A copy of Cinefluoroscopy performed as part of separate screening can be used to determine the incidence of externalization as long as all three views (AP, LAO 45° or the best possible LAO view, RAO 45° or the best possible RAO view) are available. Patients who underwent cinefluoroscopy at enrollment as part of the "Riata Lead Evaluation Study" will not be required undergo another baseline cinefluoroscopy. In patients with evidence of externalized conductors, the following chest x-rays will be collected, if available: a) earliest chest x-ray or imaging study showing an evidence of externalized conductors or other visual lead anomalies and b) latest chest x-ray or imaging study that does not show any evidence of externalized conductors or other visual lead anomalies.

Data will be collected on the patient demographics (gender, age, medical history, history of electrical dysfunctions in the past, etc). Lead electrical performance will also be evaluated.

For the purposes of this study, a patient is considered enrolled upon signing of the consent form and collection of data at enrollment visit. Data previously collected from patients enrolled in other ongoing SJM registries may be used for this study.

Data to be captured at enrollment includes:

- RV lead capture threshold, lead pacing impedance and signal amplitude (only required if RV lead model and implant date is listed in Table 1)*
- LV lead capture threshold, lead pacing impedance in a bipolar configuration (only required if LV lead model and implant date is listed in Table 1)
- High Voltage Lead impedance (HVLI) testing – mandatory for Current/ Promote or later ICD and CRT-D, optional for devices before Current/Promote ICD and CRT-D, and not applicable to CRT-P
- It is recommended that the Stored EGM Configuration be programmed to the following in patients with

Current/Promote or newer devices ICDs and CRT-Ds:

- RV Bipolar
- RV Unipolar Tip
- Custom: RV Coil to Can (optional)

* **Note:** If patient is pacer dependent or R-wave is not available then RV signal amplitude is not required.

Upon completion of the enrollment visit, complete the enrollment case report form (CRF) using the EDC system and submit the supportive data listed below to St. Jude Medical. Contact and address information are available on the last page of the CRF worksheet.

Enrollment CRF

Electronic device session records

Cinefluoroscopy (AP, LAO 45º or best possible LAO view, RAO 45º or best possible RAO view)

Earliest Chest X-ray or imaging study with evidence of externalized conductors or other visual lead anomalies, if available

Latest Chest X-ray or imaging study with no evidence of externalized conductors or other visual lead anomalies, if available

All eligible patients will be required to undergo the protocol specified follow-up visits. Patient participation in the study will be terminated once the 36 month visit is completed or after all leads being followed by the study are extracted and/or abandoned and the patient is monitored for 30 days.

3.4.2 Follow-up Requirements

The schedule of follow-up visits is based on the date of enrollment. Table 4 outlines the time window that is permitted for each of the study interval visits.

Table 4: Study Interval Time Windows

Visit Type	6*, 12, 18, 24, 30, and 36 months	42** and 48** Months
Window	± 60 days*	± 60 days**

*In order to accommodate many patients with Riata/Riata ST silicone leads who were previously enrolled in the "Riata Lead Evaluation Study" in last 10 months, the window for the 6 month visit will be -60 days to + 120 days.
**For only those eligible QuickSite/Quickflex patients that consent to extended follow-up.

Cinefluoroscopy (AP, LAO 45° or the best possible LAO view, RAO 45° or the best possible RAO view) will be taken to determine the incidence/ mechanical progression of externalized conductors at the 12, 24, and 36 month visits for all patients and at the 48 month visit for only those eligible QuickSite/QuickFlex patients that consent for extended follow-up.

If the Riata, Riata ST, QuickSite (1056T/1058T), QuickFlex (1156T/1158T), or Durata lead develops a significant electrical abnormality suggestive of lead malfunction and x-ray or cinefluoroscopy would be performed as per the site's standard of care. The x-ray or cinefluoroscopy should be submitted to SJM.

All patients will be required to attend the in-clinic follow-up visits at 6, 12, 18, 24, 30, and 36 months. Only those eligible QuickSite/QuickFlex patients that consent for extended follow-up will be required to attend the 42 month in-clinic follow-up visit. Data to be captured includes the following:

- RV lead capture threshold, lead pacing impedance and signal amplitude (only required if RV lead model and implant date is listed in Table 1) *
- LV lead capture threshold, lead pacing impedance in a bipolar configuration (only required if LV lead model and implant date is listed in Table 1)
- High Voltage Lead impedance (HVLI) testing – mandatory for Current/ Promote or later ICD and CRT-D, optional for devices before Current/Promote ICD and CRT-D, and not applicable to CRT-P

* **Note:** If patient is pacer dependent or R-wave is not available then RV signal amplitude is not required.

Upon completion of the follow-up above visits, complete the applicable CRFs using the EDC system and submit the supportive data listed below to St. Jude Medical.

- Follow-up CRF
- Product Out of service (if applicable)
- Electronic device session records
- Cinefluoroscopy (AP, LAO 45º or best possible LAO view, RAO 45º or best possible RAO view)

- System Revision (if applicable)

If an adverse event, hospitalization, death, or deviation occurs during the course of study testing and data collection, as applicable, also fill out and submit the following:

- Adverse Event CRF
- Hospitalization CRF
- Deviation CRF
- Death CRF
- Withdrawal CRF
- Supporting documentation of adverse events, deviation(s) from the protocol, and/or death

3.4.3 System Revision

All pulse generator and lead related system revisions should be reported. If a patient's existing Riata, Riata ST, QuickSite (1056T/1058T), QuickFlex (1156T/1158T), or Durata lead is extracted or capped, and no other of the above mentioned leads are still implanted then the patient will be followed for 30 days and withdrawn from the study. It is recommended to provide fluoroscopy data, RV (if applicable) and LV (if applicable) capture threshold, pacing impedance and signal amplitude measurements, and session records at system revision.

Upon completion of system revision, complete the following case report forms using the EDC system and submit the supportive data listed below:

- System Revision
- Product Out of service (if applicable)
- Device session records
- Fluoroscopy/ CXR images (if applicable)
- Adverse Event CRF
- Withdrawal CRF (if applicable)
- Supporting documentation of adverse events, deviation(s) from the protocol, and/or death

3.4.4 Unscheduled Follow-up

Unscheduled follow-up visit data will be captured if patients present in the clinic with any symptoms suggestive of or with evidence of lead related electrical problems for non protocol specified visits. It is recommended to do all the applicable RV and

LV (if applicable) lead measurements at that time. A follow-up CRF must be submitted for these unscheduled visits.

3.4.5 Extended Follow-up (Eligible QuickSite/QuickFlex patients only)

The purpose of extending follow-up for eligible patients with QuickSite/QuickFlex leads is to address challenges with fulfilling the minimum number of leads to enroll for the QuickSite/QuickFlex lead group/subgroups as shown in Table 2.

The extended follow-up will help address this issue since the data from patients with extended follow-up will contribute to 2 separate sub-group cohorts for the primary and secondary outcome measure analyses.

For example, a patient who was enrolled with a QuickSite/QuickFlex lead that was implanted for 5 years at the time of enrollment will contribute to the ≥ 5 to <6 year age of lead subgroup cohort (data from lead 5, 6, 7, and 8 years implanted). After this patient provides consent and completes the additional year of follow-up, this patient will also contribute to the ≥ 6 year age of lead subgroup cohort (data from lead 6, 7, 8, and 9 years implanted) as shown in Table 5 below.

Table 5: Extended Follow-Up Example

QS/QF Subgroup cohort Age of Lead @ Enrollment	Primary and Secondary Outcome Measure Data Analyses Timepoints				Extended Follow-up
	Enrollment /Baseline	12 Mo. Visit	24 Mo. Visit	36 Mo. Visit	48 Mo. Visit
≥ 5 and < 6 year	5 yr. lead data	6 yr. lead data	7 yr. lead data	8 yr.lead data	9 yr. lead data
≥ 6 year	6 yr. lead data	7 yr. lead data	8 yr. lead data	9 yr. lead data	

Patients eligible for extended follow-up are those already enrolled with QuickSite/QuickFlex leads that have not previously withdrawn and have a QuickSite/QuickFlex lead that will contribute to a second subgroup cohort with an additional year of follow-up.

In order to maintain an unbiased study design, all eligible patients will be approached to provide consent for extended follow-up. SJM will provide study sites with a list of all eligible patients upon approval of this protocol. After eligible patients have been approached to consent for extended follow-up, complete the Extended Follow-Up Consent CRF using the EDC system.

Eligible patients must provide consent for extended follow-up prior to completing the 42 and 48 month follow-up visits (See Section 14.0). Refer to Table 3 and Section 3.4.2 for the requirements for these additional follow-up visits.

4.0 Protocol Deviations

Investigators are required to adhere to the investigational plan, signed Investigator's Agreement, applicable federal (national) or state/local, laws and regulations, and any conditions required by the IRB/MEC or applicable regulatory authorities.

A protocol deviation is used to describe situations in which the study protocol was not followed. All deviations from the study protocol must be reported to St. Jude Medical as soon as possible but no later than 10 working days of notification of event. In addition, all deviations must be reported to the reviewing IRB per the IRB's reporting requirements.

5.0 Hospitalization

Hospitalization for any reason other than a system revision must be reported to St. Jude Medical via the Hospitalization Case Report Form using the EDC system within 10 working days of the center becoming aware of the patient's admission to the hospital.

6.0 Adverse Events

Adverse events are any unfavorable clinical event which impacts, or has the potential to impact the health or safety of a patient caused by or associated with a study device or intervention. Adverse events will be classified as complication or observations.

Complications: Adverse events that require invasive intervention (e.g. lead dislodgment requiring repositioning).

Observations: Adverse events that can be managed without invasive intervention (e.g., oversensing or loss of pacing capture, which is remedied by reprogramming of the pulse generator).

HV and CRT lead related adverse events along with other adverse events like cardiac tamponade, hematoma, high DFTs, infection and therapy for non-ventricular rhythm will be collected in the study

If the patients with no evidence of externalized conductors by imaging at enrollment show evidence of externalization later in the study, please submit an adverse event form for lead insulation damage (i.e. externalized conductors).

Should an adverse event occur, an Adverse Event Form must be completed and submitted to St. Jude Medical. Report the adverse event to the IRB/MEC per the IRB/MEC policy. Any explanted devices or leads should be returned to St. Jude Medical for analysis.

7.0 Other Reported Events

Other Reported Events is any other clinical event that is submitted by the investigator which is not caused by or associated with the study device and/or system component(s) and/or defined as an Adverse Event in section 6.0.

8.0 Deaths

All patient deaths that occur during this study must be reported to St. Jude Medical within 10 working days of the center being notified. Notification of death should include a detailed statement of the pertinent events and be signed by the investigator in addition to the appropriate case report forms (Patient Death form, Withdrawal form, and Product Out of Service form). It is the investigator's responsibility to notify the IRB/MEC per the IRB/MEC policy. The CEC will review and classify all patient deaths. Details of death and the following information, if available, should be provided in a letter to St. Jude Medical by the investigator summarizing the patient's course since enrollment in the study:

- Date of death
- Place death occurred (e.g. hospital, nursing home, patients home)
- If death was witnessed
- Identification of the rhythm at the time of death, if known
- Cause of death
- Any other circumstances surrounding the death
- Approximate time interval to death from the initiating event
- Autopsy report (if performed)
- Whether it was device and/or procedure related
- Whether it was related to the study
- Device configuration at the time of death

Provide clinical notes and witness statements. If possible, interrogate the pulse generator. Retrieve and print all episode diagnostics, IEGMs, and programmed parameters. If applicable, the pulse generator should then be programmed OFF.

Every attempt should be made to explant the pulse generator and/or leads intact. Any explanted devices or leads should be returned to St. Jude Medical for analysis promptly. In the event that the device is not explanted, the above procedure must be followed to retrieve the data. The reason the pulse generator and/or lead(s) are not being returned to St. Jude Medical must be stated clearly on the case report form.

9.0 Withdrawals

Withdrawal is defined as termination of participation of a patient from a clinical trial. All reasonable efforts should be made to retain the subject in the clinical trial until completion of the clinical trial. Reasons for withdrawal include, but are not limited to the following:

- Patient Lost to Follow-up - must be documented by two documented phone calls and one certified letter
- Death
- Patient had an explanted or abandoned Riata/ Riata ST RV lead and no other lead under investigation is currently implanted
- Patient had an explanted or abandoned Durata RV lead and no other lead under investigation is currently implanted
- Patient had an explanted or abandoned QuickSite/QuickFlex 1056T, 1058T, 1156T, or 1158T lead and no other lead under investigation is currently implanted
- Patient/Family request
- Participation terminated by Physician

Patient Relocation: If a patient moves from the geographic area of the investigator, then SJM will first attempt to place the patient with another St. Jude Medical Cardiac Lead Assessment Study investigator. If it is not possible to place the patient with another St. Jude Medical Cardiac Lead Assessment study investigator, SJM will request that the patient's new physician forward the patient's study information to the investigator.

Complete and submit a copy of the Withdrawal form to St. Jude Medical using the EDC system. Contact and address information is available on the Withdrawal form. **If there is a potential withdrawal in the study, please contact a member of the study team to see if there is anything that can be done to keep the patient in the study.**

10.0 Risks and Benefits

The risks involved with this study are similar to those associated with other commercially available ICD or CRT-D systems.

In addition, patients in this study will receive a minimum of 4 fluoroscopic procedures where each procedure is taken in 3 different views. Although these fluoroscopic procedures are short in duration (approximately 45 seconds) they do provide a minimum dose of radiation to the patient which may increase their risk of cancer.

Patients who enroll in this study may encounter an additional benefit if the incidence of externalized conductors is identified. All patients may also be more closely monitored by their physician.

11.0 Committees

11.1 Clinical Events Committee

The Clinical Events Committee (CEC) will be comprised of at least three Electrophysiologists or Cardiologists. The CEC will review and adjudicate all Adverse Events and Deaths. The CEC will base their final adjudication on the information provided on the case report forms, medical records, and their clinical knowledge and experience.

11.2 Cinefluoroscopy Adjudication Committee

Cinefluoroscopy Adjudication Committee (CAC) will be comprised of at least three Electrophysiologists or Cardiologists specially trained in using Cinefluoroscopy in this patient population. The role of the CAC is to adjudicate the cinefluoroscopy videos/images to determine the presence of lead compromise in the SJM Cardiac Lead Assessment study patient population. Committee members will be reviewing the cinefluoroscopy videos/images for the enrollment, 12, 24, and 36 month follow-up visits and any additional cinefluoroscopy videos/images received during the course of the study. Data will be sent either electronically or on a disk to the committee members. Once the adjudication is complete, a cinefluoroscopy adjudication form will be collected per patient per study visit. If the presence of externalized conductors is deemed to be 'indeterminate' then the cinefluoroscopy will be further reviewed by two other CAC members. Sample pictures/fluoros/x-rays and other examples of "other visual lead anomalies" will be provided to the adjudication committee to aid the committee members in identifying these "other visual lead anomalies" on the cinefluoroscopy videos/images received from the site.

Only the adjudicated imaging data will be included in the post market surveillance reports. Percentage of leads with compromise, evidenced by imaging, will be presented in the report. The type, extent and location of

lead compromise, as described in Appendix A, will also be included. As detailed in Appendix A, each region of the HV as well as CRT leads is divided into different regions. Both the proximal as well as distal ends of externalization will be recorded by the cinefluoroscopy adjudication committee. The distribution of externalization (both absolute number and percentage) by each region of the lead will be presented for both proximal and distal ends of externalization. The distribution of "other visual lead anomalies" (both absolute number and percentage) by each region of the lead and each individual subcategory of "other visual lead anomalies" will be presented. The frequency (both absolute number as well as percentage) of individual subcategories will be reported for "other visual lead anomalies".

11.3 Electrical Data Adjudication Committee

Electrical Data Adjudication Committee (EDAC) will be comprised of at least three Electrophysiologists or Cardiologists experienced in analyzing and interpreting device data. The role of the EDAC is to adjudicate the device session records to determine the presence of electrical dysfunction in the SJM Cardiac Lead Assessment study patient population. Committee members will be reviewing device session records for all leads taken out of service during the course of the study. Data will be sent either electronically or in a paper binder to the committee members. Once the adjudication is complete, an electrical data adjudication form will be collected per patient.

Only the adjudicated cases of electrical dysfunction will be included in the post market surveillance reports. Percentage of leads with electrical dysfunction (based on the definition in section 2.0) will be part of the reports.

12.0 Investigator Information

This clinical investigation will be conducted by investigators with experience and/or willingness to be trained in the use of the device therapy for the treatment of these patients. A principal investigator should have experience in and/or will be responsible for:

- Conducting the clinical investigation in accordance with the signed agreement with St. Jude Medical, the investigational plan, all applicable, GCP guidelines, and any conditions of approval imposed by the IRB/MEC
- Providing signed Investigator/Co-Investigator(s) Agreement
- Providing IRB/MEC Approved Informed Consent

- Collection and archiving of data obtained pursuant to the requirements of the investigational plan during the course of the study and after the study has been completed
- Screening and selecting appropriate patients

It is acceptable for the principal investigator to delegate one or more of the above functions to an associate or co-investigator, however, the principal investigator remains responsible for the proper conduct of the clinical investigation, complying with the investigational plan and collecting all required data.

13.0 Monitoring Procedures

St. Jude Medical will serve as the "sponsor" of the Cardiac Lead Assessment Trial. It is the responsibility of St. Jude Medical as the "sponsor" of the study to ensure proper monitoring of the investigation and to see that all the clinical requirements are met.

A St. Jude Medical monitor may visit the investigator or designee periodically during the study to monitor progress, assist in gathering the required data, verify study endpoints, clarify data discrepancies and answer any questions. During these visits, the clinical monitor will review the patient's records to verify that all records and files are up to date, and to assure compliance with all requirements of the protocol,local IRB procedures and applicable FDA regulations. A monitoring report following the on-site visit will be provided to the site to document monitoring findings.

The investigator will make patient and study records available to the clinical monitor for periodic inspection. Clinical monitoring will be conducted as defined in the St. Jude Medical Monitoring Plan for this study.

Responsibility for overall study management will be held by the Director of Clinical Studies, St. Jude Medical.

Clinical Studies Organization
St Jude Medical
15900 Valley View Court
Sylmar, CA 91342
Tel: 800-933-9956
Fax: 866-632-8191

FDA Inspections

The investigator and/or designee should contact St. Jude Medical within 24 hours upon being notified of an impending FDA inspection. A clinical monitor may assist and review study documentation with the investigator and/or designee to prepare for the audit.

An investigator shall permit authorized FDA employees to inspect and copy records that identify subjects, upon notice that FDA has reason to suspect that adequate informed consent was not obtained, or that reports required to be submitted by the investigator to the sponsor or IRB have not been submitted or are incomplete, inaccurate, false, or misleading.

14.0 Consent Materials

Please refer to the attached Statement of Informed Consent in Appendix B to be used for enrolling patients into this study.

Failure to obtain informed consent from a patient prior to study screening and enrollment should be reported to St. Jude Medical within 5 working days and to the reviewing IRB consistent with the IRB's reporting requirements.

Please refer to the attached Informed Consent Addendum for Extended Follow-Up in Appendix C to be used for obtaining consent for only those enrolled patients with QuickSite/QuickFlex leads eligible for extended follow-up (see Section 3.4.5).

Failure to obtain consent from eligible patients prior to conducting extended follow-up visits (42 and 48 month visits) should be reported to St. Jude Medical within 5 working days and to the reviewing IRB consistent with the IRB's reporting requirements.

15.0 IRB Information

IRB/MEC approval for the study and informed consent will be required prior to beginning the study. A copy of the IRB/MEC approval and corresponding informed consent must be forwarded to St. Jude Medical prior to authorization of the institution to begin the study. Any withdrawal of IRB approval should be reported to St. Jude Medical within 5 working days of the withdrawal of approval.

A list of IRBs for Institutions participating in the Clinical Investigation will be provided upon request.

16.0 Other Institutions

The name and address of each institution, at which a part of the investigation may be conducted, that has not been identified under IRB information, will be provided upon request.

17.0 Records and Reports

Clinical investigators of St. Jude Medical investigational products are required to maintain records during the investigation and for a period of two years after the latter of the following two dates: the date on which the investigation is terminated or completed, or the date that the records are no longer required for purposes of supporting a premarket approval application or a notice of completion of a product development protocol.

18.0 References

[1] Duray GZ, Isreal CW, Schmitt J, Hohnloser SH. Implantable cardioverter-defibrillator lead disintegration at the level of the tricuspid valve. Heart Rhythm 2008; 5:1224-1225.

[2] Mehta D, Nayak H, Singson M, Chao S, Jorge E, Camunas L, Gomes J. Late Complications in Patients with Pectoral Defibrillator Implants with Transvenous Defibrillator Lead Systems: High Incidence of Insulation Breakdown. *PACE,*1998; 21:1893-1900.

[3] De Lurgio D, Sathavorn C, Mera F, Leon A, Walter P, Langberg J. Incidence and Implications of Abrasion of Implantable Cardioverter-Defibrillator Leads. *American Journal of Cardiology*,1997, 79:1409-1411.

[4] Pavia S, Saliba W, Wilkoff B. Lead System Dysfunction, Diagnosis, and Therapy. In: Pacifico A. ed-in-chief. *Implantable Defibrillator Therapy: A Clinical Guide*. Norwell, Ma. Kluwer Academic Publishers 2002:259-278.

[5] Kleemann T, Becker T, Doenges K, Vater M, Senges J, Schneider S, Saggau W, Weisse U, Seidl K. Annual Rate of Transvenous Defibrillation Lead Defects in Implantable Cardioverter-Defibrillators over a Period > 10 years. *Circulation*. 2007;115:2474-2480.

[6] Blommaert D, Louagie Y, Eucher P, Collet B, Mancini I, Govarets G, Leclercq C, De Roy L. Are Cardioverter-Defibrillator Leads Reliable Over time? *NASPE Abstracts*, 2003, 26:1123.

[7] Degeratu F, Khalighi K, Peters R, Shorofsky S, Gold M. Sensing Lead Failure in Implantable Defibrillators: A Comparison of Two Commonly Used Leads. *J Cardiovasc Electrophysiol*, 2000, 11:21-24.

[8] Liu J, Rattan R, Adelstein E, et al. Fluoroscopic screening of asymptomatic patients implanted with the recalled Riata lead family. Circ Arrhythm Electrophysiol. 2012 Aug 1;5(4):809-14.

[9] Shen S, Bhave P, Giedrimas E, et al. Prevalence and Predictors of Cable Extrusion and Loss of Electrical Integrity with the Riata Defibrillator Lead. J Cardiovasc Electrophysiol. 2012 May 15.

[10] Parvathaneni SV, Ellis CR, Rottman JN. High prevalence of insulation failure with externalized cables in St. Jude Medical Riata family ICD leads: Fluoroscopic grading scale and correlation to extracted leads. Heart Rhythm. 2012 Aug;9(8):1218-24. Epub 2012 Mar 23.

[11]Corbisiero R, Armbruster R. Incidence of Externalized Conductors in ICD Leads Using PA and Lateral Chest X-Ray Imaging. Heart Rhythm 2012;9(5):S236.

[12]Ha A, Vezi BZ, Keren A, et al. Predictors of Fracture Risk of a Small Caliber Implantable Cardioverter Defibrillator Lead. *PACE*, 2010;33(4):437-443.

Appendix A: Details About Lead Compromise

Lead Compromise as evidenced by imaging includes externalized conductors or other visual lead anomalies. The types, extent and location of these anomalies in high voltage (HV) leads are listed below:

Type	Extent	Location on the lead (see figure below)
Externalized Conductors	- Apparent width and length of externalized conductors on fluoroscopy	- Region 1 - Region 2 - Region 3 - Region 4
Other Visual Lead Anomalies	- Fracture - Subclavian crush - Kink - Broken filars on a shocking coil - Other irregularities	- Region 1 - Region 2 - Region 3 - Region 4 - RV coil - SVC coil - Distal to RV coil - Proximal to region 1

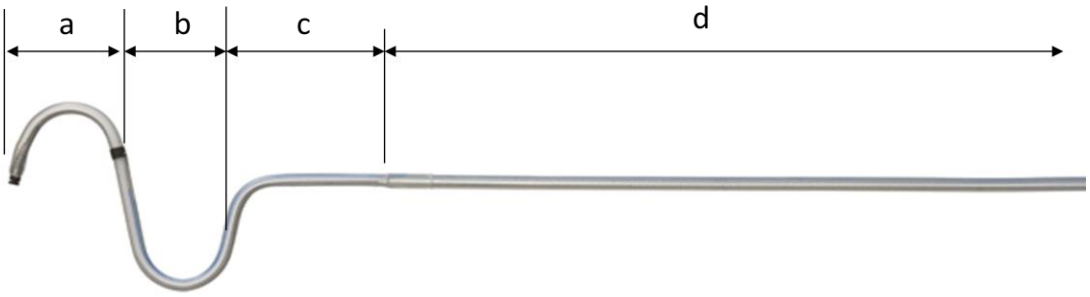
Single Coil Riata Lead

Dual Coil Riata Lead

Similarly, the type, extent and location of these anomalies in CRT leads are listed below:

Type	Extent	Location on the lead (see figure below)
Externalized Conductors	- Apparent width and length of externalized conductors on fluoroscopy	- Region a - Region b - Region c - Region d
Other Visual Lead Anomalies	- Fracture - Kink - Subclavian crush - Other irregularities	- Region a - Region b - Region c - Region d

.



Appendix B: Statement of Informed Consent

Statement of Informed Consent

Study Title: ST. JUDE MEDICAL CARDIAC LEAD ASSESSMENT STUDY

Introduction

You are being asked to take part in this research study because your doctor has determined that you may qualify to take part in the St. Jude Medical (SJM) Cardiac Lead Assessment Study. The SJM Cardiac Lead Assessment Study is sponsored by SJM and constitutes the modification of the "Riata Lead Evaluation Study". This form explains why this research is being done and what your role will be if you decide to participate. This form also talks about the possible risks that may happen if you take part in this study. This study is sponsored by St. Jude Medical.

Please read this form, and ask your study doctor any questions about the study so that you can have your questions answered before you decide if you want to take part in the study. Please take your time and talk about this information with your family, friend, or family doctor.

This consent form may contain some words that you do not understand. Please ask the study doctor or the study staff to explain any words or information that you do not understand.

If you agree to be in the study, you will need to sign this form. Taking part in this study is entirely voluntary. You may decide not to participate without penalty or loss of benefits to which you are otherwise entitled.

What is the purpose of the study?

The purpose of this study is to determine the prevalence of wires being visible outside the lead insulation body (externalized conductors) or other forms of visual compromise in the Riata®, Riata® ST silicone ICD, QuickSite®/QuickFlex® CRT and Durata® ICD leads. In order to evaluate the prevalence of externalized conductors or other forms of visual compromise in the Riata, Riata ST silicone ICD, QuickSite/QuickFlex CRT and Durata ICD leads, cinefluoroscopy (i.e. video or x-ray) will be taken to determine the prevalence of externalized conductors or other forms of visual compromise of the lead. This study **does not** involve any investigational product (medical device) or procedures.

Approximately 1500 patients (500 with Riata or Riata ST leads, 500 with QuickSite/QuickFlex leads and 500 with Durata leads) will be enrolled in this non-randomized, multi-center, international post market study at up to 60 sites.

In order to determine the risk that externalized conductors will result in an electrical malfunction, all patients will be followed every 6 months for a three-year period (36 months) in the study.

What will happen if you take part in the research study?

If you decide to take part in this study, some tests will be done to help your doctor determine if you qualify. You must have a market released SJM ICD or CRT-D already implanted and also have a market released Riata ICD, Riata ST silicone ICD, QuickSite/QuickFlex CRT or Durata ICD lead. Once all of the tests have been completed, your doctor will decide if you qualify to take part in the SJM Cardiac Lead Assessment Study. If you do not qualify for the study, your participation will end.

If your doctor determines that you qualify, and you decide to take part in this study, the following procedure(s) will be performed. You will be screened for evidence of externalized conductors forms of visual compromise of the lead through cinefluoroscopy (i.e. X-ray, video, etc.), demographics (gender, age, medical history, history of electrical malfunctions in the past, etc.) and lead electrical performance will also be evaluated.

There may be a representative of the sponsor at your study visits and the representative may carry out some of the study procedures. The study doctor may direct a representative from the sponsor to collect the signal information. At the study doctor's direction, the sponsor representative may also program your device or run tests to see if your device is working as expected. The sponsor's representative will work under the direction of your study doctor or other care provider.

How long will study last?

You will be followed for a period of three years. Data will be collected at 6, 12, 18, 24, 30 and 36 months post enrollment.

You will be screened for evidence of externalized conductors or other forms of visual compromise of the lead through cinefluoroscopy (i.e. X-ray, video, etc.) every 12 months including the final study visit at 36 months.

What are possible discomforts or risks?

There may be risks associated with (a small amount of radiation) exposure to cinefluoroscopy which may increase your risk of cancer. The estimated fluoroscopy time required is approximately 45 seconds per visit.

Risk for women of childbearing age?

If you are pregnant or plan to become pregnant in the next 6 months, you should discuss your participation with your study doctor. Patients who become pregnant while taking part in the study should contact the study doctor right away.

What are the possible benefits to you or to others?

If you decide to take part in this study, you may encounter an additional benefit if the incidence of externalized conductors is identified. You may also be more closely monitored by your physician.

The sponsor of this study is paying for cost of data capture and items that are not deemed standard of care/routine care in the study. St. Jude Medical will pay the study center where the study is being conducted.

If you do not want to take part in this study, what other options are available to you?

Your doctor will discuss other options available to you.

How will your privacy and the confidentiality of your research records be protected?

If you decide to take part in this study, your medical records and personal information will be kept private to the extent allowed by federal, state, and local law. No personal information about you, your illness, or your treatment will be made public.

Information (data) collected from the study will be sent to St. Jude Medical. A special code (letter and number combination) will be used to identify your personal information.

The data may be given to governmental agencies, for example: the Food and Drug Administration (FDA) or similar government agencies in other countries. Only information about your medical condition as it relates to the Riata®/ Riata® ST Silicone Leads, Quicksite/Quickflex or Durata lead will be provided to St. Jude Medical. In order to verify study data, monitors from governmental agencies (for example: FDA), St. Jude Medical, and the Institutional Review Board (IRB)/Ethics Committee (EC) will also have the right to review your medical records as they relate to this study. In addition, publication(s) using data collected during the study will not include your name or any information that can identify you.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This web site will not include information that can identify you. At most, the web site will include a summary of the results. You can search this web site at any time.

St. Jude Medical may export data to countries where different data protection laws apply.

If you receive medical care from a doctor other than your study doctor while taking part in this study, you agree that your medical records will be made available for the collection of data related to this study.

If you choose to take part in this study, will it cost you anything?

You and your insurance company are responsible for the costs of all standard of care tests, procedures, and devices. There is no guarantee that your insurance company will cover 100% of these costs. You should check with your insurance company to verify coverage or payments of these procedures.

Will you receive compensation (payment) for taking part in this study?

No payment will be made to you for taking part in this study.

What if the device needs to be removed?

In the event your Riata®, Riata® ST Silicone lead, Durata lead or QuickSite/QuickFlex bipolar silicone CRT lead or any part has to be removed, it will be returned to St. Jude Medical for analysis. Should you withdraw from this study and choose to have your RiataICD, Riata ST silicone ICD, QuickSite/QuickFlex CRT or Durata ICD lead or any part of it removed, the cost will be your responsibility.

In the event of your death, your implanted Riata ICD, Riata ST silicone ICD, QuickSite/QuickFlex CRT or Durata ICD leadmay be removed and returned to St. Jude Medical for analysis. The study doctor will get your family's approval prior to removing the device.

What if you are injured because of the study?

If you are injured as a direct result of taking part in this study, medical treatment will be available to you. You, or your insurance company, will be responsible for all costs incurred as a result of that treatment. No other arrangement has been made for financial payments or other forms of compensation (such as lost wages, lost time or discomfort) with respect to such injuries. You do not waive any legal rights by signing this consent form.

During the study, if you experience any medical problems or illnesses from taking part in this study, please contact Dr. _____ at ___-___-_____.

What are your rights if you decide to take part in this study?

Your signature on this consent form means that you have received information about this research study and that you agree to be a part of the study.
You may stop taking part in the study at any time without penalty or loss of benefits to which you are otherwise entitled. If you wish to stop taking part in this research study for any reason, you should contact Dr. _____ at ___-___-_____. A decision to withdraw or to not take part in the study will not affect the quality of medical care that

you receive. Your decision will not result in any penalty or loss of benefits to which you are otherwise entitled or affect your future medical care.

Your doctor or the sponsor, St Jude Medical, may decide to withdraw you from the study at any time without your consent. If it is felt to be in your best interest, or if the study is stopped, your doctor may withdraw you from this research. If you have a problem as described in the risks section, or if you become ill during the research, you may have to stop participating in the study, even if you would like to continue. Your study doctor will make this decision. Your study doctor or designee will discuss with you what follow-up is required if you decide to withdraw, or are withdrawn from the study before the study is finished.

If important information is learned during the course of this study, your doctor will be notified by St. Jude Medical. You will be told of any important new information that is learned during the course of this research study that may affect your condition or your willingness to continue to take part in this study.

Who can you contact for study information?

If you have any questions about the study or taking part in this study, please contact Dr. _____ at ___-___-_____.

In addition, if you have questions about your rights as a research patient, or if you have complaints, concerns, or questions about the research, please contact _____ at ___-___-_____.

You are making a decision on whether or not to take part in the study. Your signature indicates that you have read the information in this form and have decided to take part in the study. You will be given a signed copy of this form to keep.

_____
Printed Name of Patient

_____ _____
Signature of Patient Date

_____ _____
Signature of Person Obtaining Consent Date

Appendix C: Informed Consent Addendum for Extended Follow-up

Informed Consent Addendum for Extended Follow-up

Study Title: ST. JUDE MEDICAL CARDIAC LEAD ASSESSMENT STUDY

Introduction

This Addendum contains important information regarding your participation in this research study, the St. Jude Medical (SJM) Cardiac Lead Assessment Study. Due to a shortage of enrollments of patients implanted with certain QuickSite/QuickFlex leads, only those patients already enrolled with these specific leads will be asked to extend their follow-up duration for one (1) additional year in order to have enough data to meet the study objectives.

You are being asked to extend participation in this study because your study doctor has determined that you have a qualifying QuickSite/QuickFlex lead. If you agree to extend your participation in the study, you will need to sign this form. Extending your participation in this study is entirely voluntary. You may decide not to extend your participation without penalty or loss of benefits to which you are otherwise entitled and continue to participate according to the original follow-up duration.

Please read this form, and ask your study doctor any questions about the study so that you can have your questions answered before you decide if you want to extend your participation in the study. Please take your time and talk about this information with your family, friend, or family doctor.

This form may contain some words that you do not understand. Please ask the study doctor or the study staff to explain any words or information that you do not understand.

The language in this Addendum may replace statements made in the existing Informed Consent Form that you previously signed.

Extended Follow-Up

If you extend your participation in this study for one (1) additional year, data will also be collected at 42 and 48 months post enrollment. At the 42 and 48 month visits, lead electrical performance will be evaluated. At the final 48 month visit, you will also be screened for evidence of externalized conductors or other forms of visual compromise of the lead through cinefluoroscopy (i.e. X-ray, video, etc.).

Who can you contact for study information?

If you have any questions about the study or taking part in this study, please contact Dr. _____ at ___-___-_____.

In addition, if you have questions about your rights as a research patient, or if you have complaints, concerns, or questions about the research, please contact _____ at ___-___-_____.

Agreement of Decision to Extend Participation

Taking part in this extended follow-up is entirely voluntary. You are making a decision on whether or not to take part in the extended follow-up for this study. Your signature indicates that you have read the information in this form and have decided to extend your participation for this study. You will be given a signed copy of this form to keep.

_____
Printed Name of Patient

_____ _____
Signature of Patient Date

_____ _____
Signature of Person Obtaining Consent Date

Appendix D: Revision History

Revision History				
Amendment Number	Version	Date	Rationale	Details
2	K	18Sept2015	• Change lead subgroup cohort defined by lead implant date to age of lead at enrollment (in years) and added Riata leads implanted in 2002 and 2003 to the eligible leads for enrollment in order to complete enrollments in a timely manner while adhering to the original 522 order study design (analyses of lead subgroups by age of lead). • Increased number of sites from 50 to 60 to increase enrollment rate • Added extended follow-up for eligible patients already enrolled with QuickSite/QuickFlex leads in order to address challenges with completing enrollments with this lead group/sub-groups.	Updates: • Table 1 and 2 • Enrollment Timeline • Sections 3.2.1, 3.3.1 • Sections 3.1, Appendix B. • Sections 3.2.1, 3.2.2, 3.4, 3.4.5, 14.0, Appendix C • Tables 3 and 5