Abbott	Clinical Investigation Plan Cover Page

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QuickFlex Micro PAS
QuickFlex Micro Model 1258T – Left Heart Pacing Lead Post Approval Study
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Sponsor

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Cardiac Rhythm Management Division

STUDY PLAN
FOR THE

QuickFlex® µ Model 1258T
Left Heart Pacing Lead Post Approval Study

June 10, 2010

40007524/D-Clinical

[redacted]

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1.0 Introduction

Heart failure (HF) is a major threat to public health affecting 5.3 million individuals in the United States (U.S.). HF is the major cause of mortality, morbidity, and hospitalization in patients aged 65 years and older. In 2008, the estimated direct and indirect cost of HF in the U.S. was 34.8 billion.[1] Several randomized clinical trials have demonstrated the benefits of heart failure patients receiving cardiac resynchronization therapy (CRT) with an implantable cardioverter defibrillator. Implantation of a CRT-D device can make it challenging to place a standard size lead in a small and tortuous vein. St Jude Medical developed a 4.7 Fr CS lead referred to as the QuickFlex®µ 1258T LV Lead. In a premarket IDE clinical trial (G080040), this new lead was successfully implanted in a high percentage of patients, had clinically acceptable bipolar electrical performance, and was associated with a few complications. The goal of this post approval study (PAS) is to characterize the chronic performance of the St Jude Medical (SJM) QuickFlex®µ 1258T lead.

2.0 Purpose

The purpose of this PAS is to evaluate the acute and chronic performance of the SJM QuickFlex®µ 1258T LV lead in a patient population indicated for implantable cardioverter defibrillator and cardiac resynchronization therapy.
The QuickFlex®µ 1258T LV Lead study will be performed in compliance with the Conditions for Approval as agreed upon with the FDA.

3.0 Description of Device

In this study, the QuickFlex®µ 1258T LV Lead will be implanted with compatible legally marketed St. Jude Medical CRT-D devices.

The QuickFlex®µ 1258T left heart lead is a bipolar over–the-wire design, enabling implantation using either stylet or guidewire guided placement. The lead has an open lumen and an opening at the lead tip to allow the use of the guidewire. The lead body has Optim® (Elast-eon) insulation and a maximum lead body diameter of 4.7 Fr. Like the QuickSite® left heart lead family, the distal portion of the QuickFlex®µ 1258T left heart lead is pre-shaped in an "s-curve" configuration. The titanium nitride (TiN) coated platinum/iridium (PtIr) tip electrode contains a molded ring that elutes steroid. Additionally, the surface of the tip electrode is coated with a thin steroid film to provide immediate steroid release. A titanium nitride (TiN) coated platinum/iridium (PtIr) ring electrode is located 20 mm from the tip of the lead. The outer lead body is

[1] Heart disease and Stroke Statistics—2008 Update, American Heart Association

covered with Fast-Pass™ coating to increase lubricity during initial implant. The lead connector complies with the IS-1 connector standard ISO 5841-3.

4.0 Clinical Protocol

4.1 Study Design and Scope

The QuickFlex®µ 1258T LV Lead study is a multi-center post-approval study that will be performed in compliance with the Conditions for Approval as agreed upon with the FDA. Patients may be enrolled in the study in one of two ways. Patients who previously participated in the QuickFlex®µ 1258T LV Lead IDE study and are at a center that is participating in the post approval study may be approached for enrollment into the post approval study. In addition, newly implanted patients will be approached at participating centers for participation in the study until the enrollment criteria is met. New patients who meet inclusion/exclusion criteria will have an attempted implant of the QuickFlex®µ 1258T lead. Patients who have an unsuccessful implant will be followed for 30 days for any adverse events and then withdrawn from the study, or may have an implant reattempted if the physician chooses to do so. Patients who have a successful implant of the LV lead will be considered to have received a successful CRT-D system. Following enrollment, patients will be followed at 6 months, and every 6 months thereafter, for 60 months of follow up (5 years). After patients complete 60 months of follow-up, their participation in the study will be terminated. There will be 1,884 new patients enrolled in the study to achieve an evaluable sample size of 1036 patients. In addition, every effort will be made to enroll existing IDE patients from sites participating in the Post Approval study. [redacted] for a total sample size of 1,955 to 1,991 patients. [redacted] If implantation rate at a study site is higher than the projected estimates, then the study enrollment period will be decreased proportionately. Reporting will occur per section 4.2.3 of the protocol. In order to accomplish this, the study will be conducted at a maximum of 80 study centers.

Definitions: The following definitions will be used in the QuickFlex®µ 1258T post approval study.

Abnormal Lead Pacing Impedance: Measured pacing impedances with values ≤ 200 Ω or ≥ 2000 Ω
Adverse Event: 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 are classified as complications or observations.

Cardiac Tamponade: Confirmed or suspected accumulation of fluid in the pericardial space.

Cardiac Perforation: An excursion of the lead through the cardiac muscle. Signs and symptoms of a perforation by an intra-cardiac lead may include radiographic evidence of excursion of the lead into the pericardial sac, abnormal echocardiography indicative of a perforation, the accumulation of fluid in the pericardium, cardiac tamponade, or patient symptoms such as chest pain and discomfort.

Complication: An adverse event that requires invasive intervention to resolve (e.g., lead fracture).

Diaphragmatic/Phrenic Nerve Stimulation: Electrical activation of the diaphragm muscle by the device output pulse. The abrupt diaphragmatic contraction is noted clinically as hiccups associated with each pacing stimulus. The pacing stimulus may stimulate the diaphragm either directly or indirectly via the phrenic nerve.

Elevated Pacing Thresholds: Voltage thresholds > 3.0V at implant and 2-fold over the first chronic threshold or 3.5V at follow up.
This definition is intended to serve as a guideline and it is understood that individual patients may have unique situations.

Generator Malfunction: Suspected failure of the device to perform as indicated.

Lead Dislodgement: The movement of a pacing lead from its originally implanted position; often indicated by changes in pacing and/or sensing thresholds including loss of sensing and/or capture. Dislodgement can be confirmed by radiographic studies.

Lead Fracture: A break in a conduction coil of a pacing or defibrillation lead typically evidenced by an increase in impedance, intermittent or complete loss of capture, intermittent or complete loss of sensing, noise on the intra-cardiac electrogram and visual signs of conductor coil fracture on x-ray.

Lead Implant Attempt: An insertion of the lead into the vasculature and into the heart for positioning within a single procedure. A second attempt occurs when the lead is completely removed from the vasculature and is reinserted, or a new lead is inserted.

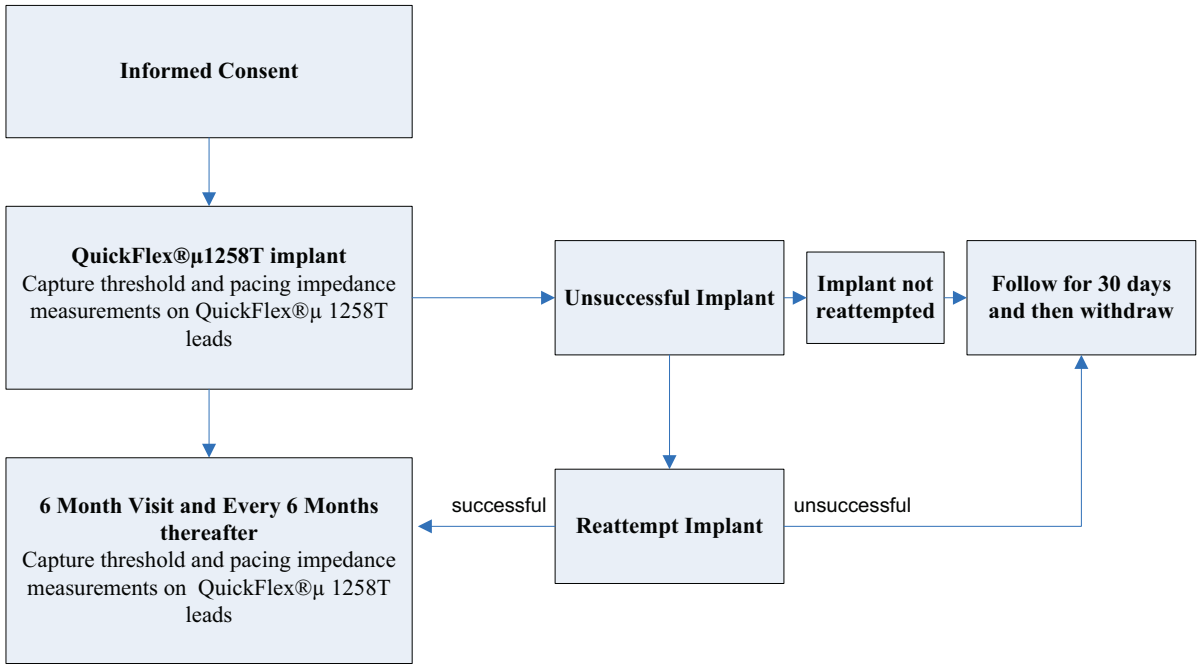
Lead Insulation Damage: A disruption to the integrity of the lead insulation without disruption of the conductor coil. An insulation break may be indicated by a drop in impedance, and can cause loss of capture or sensing problems.

Loss of Capture: The inability of the device's output pulse to result in depolarization and contraction of the appropriate cardiac chamber. Causes include insufficient stimulus strength, separation of the electrode from the myocardium and placement of the stimulating electrode in contact with a non-responsive portion of the myocardium such as scar tissue.

Loss of Sensing: A condition in which the pulse generator is unable to sense intrinsic cardiac signals (applicable to RA and RV lead(s)).

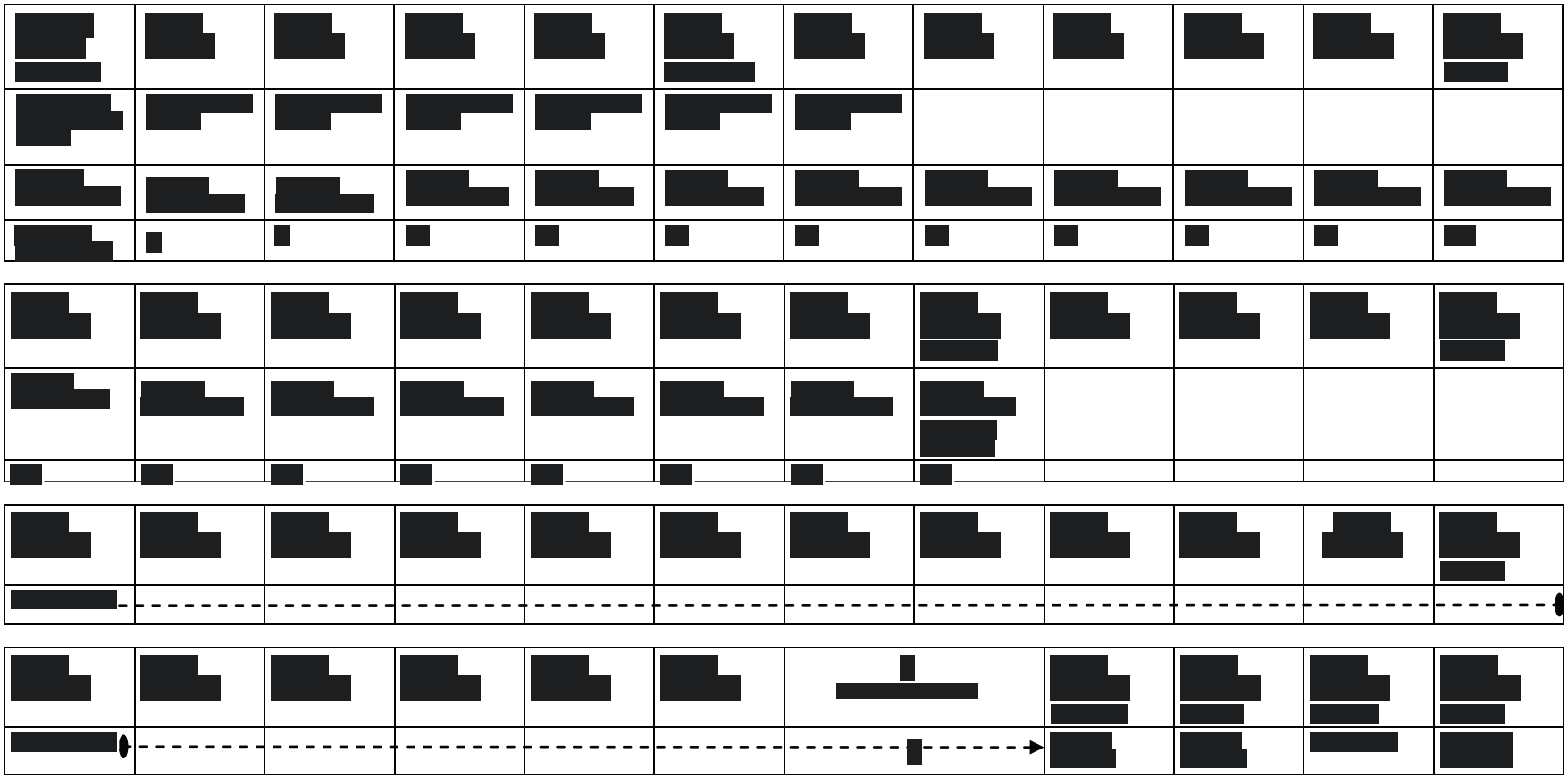
Observation: Adverse events that can be managed without invasive intervention (e.g., over-sensing or loss of pacing capture, which is remedied by reprogramming of the pulse generator).
Over-sensing: The detection of inappropriate electrical signals by the pulse generator's sense amplifier. These signals, such as myopotentials, electromagnetic interference, T waves or crosstalk between atrial and ventricular channels, must be of sufficient duration to interfere with normal device function. (applicable to RA and RV lead(s)
Pneumothorax: An accumulation or suspected accumulation of air in the pleural cavity.
Successful Implant: A SJM CRT-D system with an implanted QuickFlex®µ 1258T lead.
System Implant Attempt: A procedure in which a QuickFlex®µ 1258T lead implant is attempted.
Under-sensing: The failure of the pulse generator to sense P or R waves, causing delivery of inappropriately timed, asynchronous or competitive output pulses. Under-sensing can sometimes be corrected by programming the device to a more sensitive setting, i.e., decreasing the millivolt (mV) value (applicable to RA and RV lead(s)).
Unsuccessful Implant: An attempted implant that does not result in a successful QuickFlex®µ 1258T lead implant.

4.1.1 Study Flow Diagram



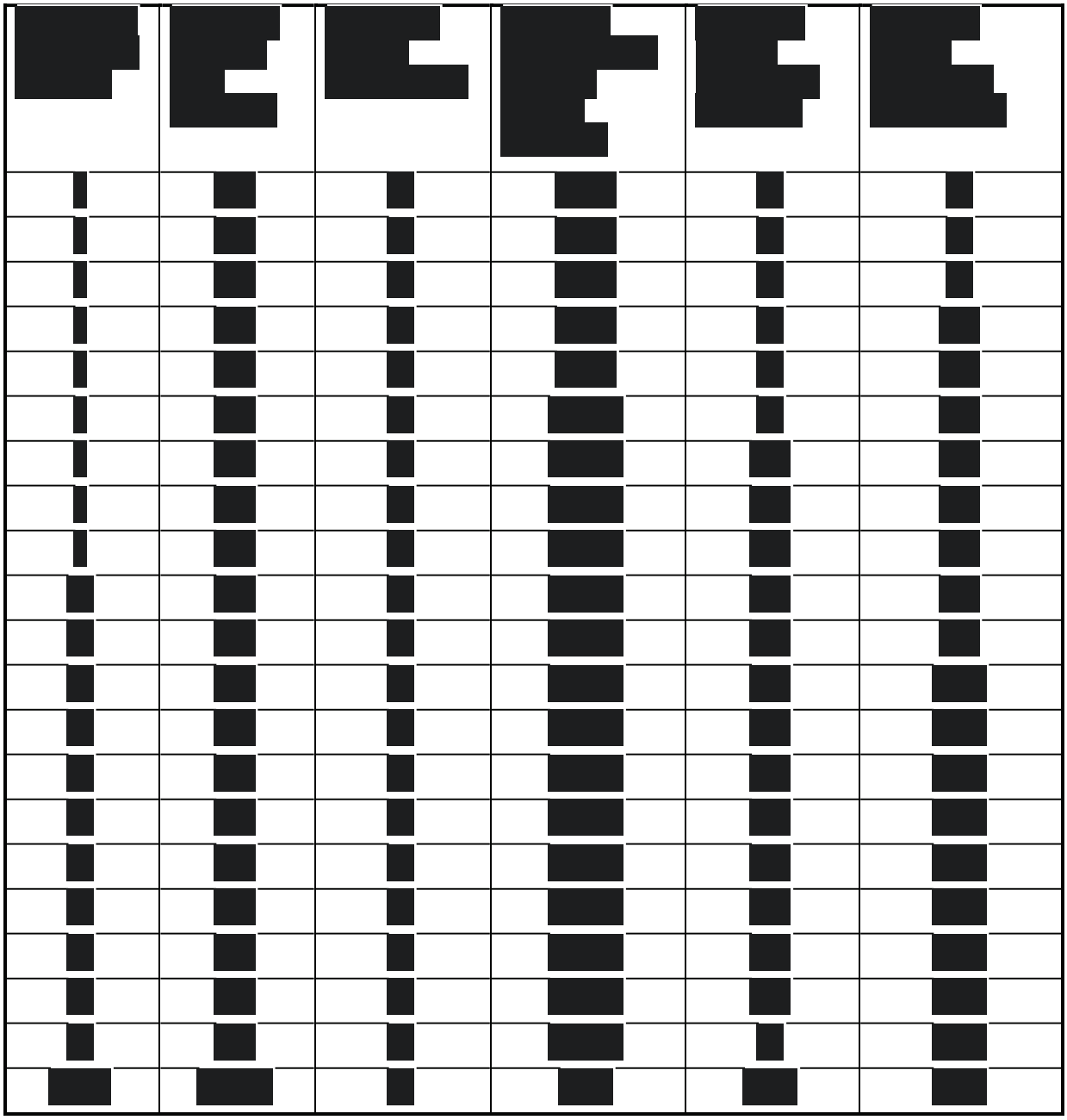
4.1.2 Projected Study Timeline

A timeline for the QuickFlex®µ 1258T LV Lead post approval study is provided below. This timeline is based on initiating the study in the third quarter of 2010; dates will change based on the actual start date of the study, the date enrollment begins, and/or the actual enrollment rate.



[redacted]

[redacted]



4.2 Study Endpoints/Objectives

The endpoints of the study are:

- Complication free survival rate at 5 years for complications related to the LV lead
- Electrical performance (capture threshold) of St. Jude Medical's QuickFlex®µ 1258T LV Lead

The study will also characterize the complication rates and perform a trend analysis for all complications related to the LV lead.

4.2.1 Primary Endpoint 1 – Freedom from LV Lead-Related Complications

We will test the following hypothesis for LV lead related complication free survival at 5 years:

H_0: Complication free survival at 5 years ≤ 92.5%
H_1: Complication free survival at 5 years > 92.5%

The desired outcome is to reject the null hypothesis. The null hypothesis will be rejected at the 5% significance level if the 95% Lower Confidence Bound (LCB) for the freedom from complications is greater than 92.5%.

Sample Size

[redacted]

Analysis
All complications will be classified as related to the LV lead or as unrelated. The following complications will be included in the LV lead related analysis:

- Cardiac perforation
- Lead dislodgement that occurred greater than 30 days after implant
- Lead insulation damage
- Lead fracture
- Diaphragmatic/Phrenic nerve stimulation

- Abnormal LV lead performance (abnormal lead pacing impedance, elevated pacing thresholds, and loss of capture,)
- Other unexpected complications that are considered related to the LV lead

All patients who had an attempted implant of the QuickFlex µ 1258T LV Lead will be included in the analysis of this endpoint. The survival time for all patients will be calculated as the number of days from implant or attempted implant to the date the complication was first discovered. For patients who do not experience a complication related to the LV lead at the time of their withdrawal, the survival time will be censored on the date of their withdrawal. For patients who have not experienced any complication related to the LV lead at the time of analysis, the survival time will be censored on the date of analysis. This analysis will also include all IDE study patients from sites that agree to participate in the PAS study. Patients from these sites who participated in the IDE study, but who do not consent to participate in the PAS study will be included in the analysis. If event free, they will be censored at the time of approval of the QuickFlex®µ 1258T LV Lead or the last IDE follow-up visit (whichever is later). This will ensure that there is no bias in the estimates of complication rates; site selection criteria are independent of complication rates. The endpoint will be evaluated using the Kaplan-Meier method and the 95% lower confidence bound (LCB) will be obtained by transformation from its log scale, based on Peto et al[2]. The null hypothesis will be rejected if the 95% LCB is greater than 92.5%. Kaplan-Meier curves will also be presented for each adverse event category of complication listed above.

A sub-group analysis will be performed to compare the LV lead related complication rates in patients rolled over from the IDE study to newly enrolled patients. Complication free survival estimates will also be estimated for the newly enrolled and IDE subjects by stratification in the Kaplan Meier analysis. The two groups will be compared using the log-rank test. As with the primary analysis, the sub-group analysis will include all IDE study patients from sites that agree to participate in the PAS study. Patients from these sites who participated in the IDE study, but who do not consent to participate in the PAS study will be included in the analysis. If event free, they will be censored at the time of approval of the QuickFlex®µ 1258T LV Lead or the last IDE follow-up visit (whichever is later). This will ensure that there is no bias in the estimates of complication rates; site selection criteria are independent of complication rates.

[2] Peto R, et al. Design and analysis of randomized clinical trials requiring prolonged observation of each patient: II. Analysis and examples. *British Journal Cancer* 1977, 35:1-39

4.2.2 Primary Endpoint 2 – LV Bipolar Capture Thresholds

LV lead bipolar pacing capture threshold at 5 years at 0.5 ms pulse width

The hypothesis is as follows:

H_0: Mean LV lead bipolar pacing capture threshold at 5 years ≥ 3.5V
H_1: Mean LV lead bipolar pacing capture threshold at 5 years < 3.5V

The objective performance criterion of 3.5V is based on an acceptable LV capture threshold of 3.5V.

The desired outcome is to reject the null hypothesis.

Sample Size

Patient Group
All patients who complete a 5 year follow-up and have a LV lead capture threshold at 0.5 ms pulse width will be included in the analysis.

Analysis
The sample average and sample standard deviation will be calculated for LV lead capture threshold. The 95% UCB for the mean LV lead capture threshold at 5 years at 0.5 ms pulse width will be calculated based on a t-distribution. The null hypothesis will be rejected if the 95% UCB is less than 3.5V. Summary statistics for LV lead bipolar capture thresholds will also be broken down and presented separately for the roll over and new enrolled patients.

[3] Rhythm ICD/QuickSite Model 1056T Final Report. IDE G020114S/28.July 28, 2005

4.2.3 Secondary Objective – LV Lead Related Complication Rates

Complication rates for complications related to the LV lead

The objective is to characterize the complication rate of the QuickFlex®µ 1258T lead, and to perform a trend analysis of all complications. All complications will be evaluated for their relationship to the LV lead, reported and summarized for all patients and will also be broken out by gender. In addition, separate summaries will be presented for rollover patients and newly enrolled patients. The following complications will be reported as related to the LV lead:

- Cardiac perforation
- Lead dislodgement that occurred greater than 30 days after implant
- Lead insulation damage
- Lead fracture
- Diaphragmatic/Phrenic nerve stimulation
- Abnormal LV lead performance (abnormal lead pacing impedance, elevated pacing thresholds, and loss of capture)
- Other unexpected complications that are considered related to the LV lead

Table 2: Summary of LV Lead Related Complications

Description of Complication	Number of Patients with Comp (No. of pts = X)	% of Patients with Comp	Number of Comps	# Comps/pt-years (Total pt-years = X)
Cardiac perforation	X	X%	X	X
Lead dislodgement that occurred greater than 30 days after implant	X	X%	X	X
Lead insulation damage	X	X%	X	X
Lead fracture	X	X%	X	X
Abnormal LV lead performance	X	X%	X	X
Diaphragmatic/Phrenic nerve stimulation	X	X%	X	X
Other unexpected complications that are considered related to the LV lead	X	X%	X	X
Total	**X**	**X%**	**X**	**X**

Sample Size [redacted]

[redacted]

[redacted]

[redacted]

Sample size accounting for patient attrition

[redacted]

Patient Group

All patients who are implanted or attempted to be implanted with the QuickFlex®µ 1258T LV Lead will be included in this analysis.

Analysis and reporting

Interim Reports and Trend Analysis

[redacted]

[4] Hahn, G.J. and Meeker, W.Q. Statistical Intervals: A Guide for Practitioners. Wiley Series in Probability and Mathematical Statistics. 1991.

[redacted]

[redacted]

Final Report
The number and proportion of patients who experience each type of complication in Table 2 at 5 years will be presented, along with the 95% confidence intervals for the proportion based on the Clopper-Pearson exact Binomial method.

4.2.4 Additional Data

- Demographic data including gender, age, ethnicity, tobacco use, cardiovascular history, arrhythmia history, NYHA functional classification, left ventricular ejection fraction, QRS duration, cardiomyopathy classification, cardiac medications, and continuous variables will be summarized by average and standard deviation. Categorical variables will be summarized by frequency and percentage.
- Capture thresholds using a pulse width of 0.5ms for LV leads at enrollment/implant and at each follow-up visit – the average threshold along with standard error bars will be plotted for each visit. LV threshold testing must be performed in bipolar configuration.
- Pacing lead impedance for LV leads at enrollment and at each follow-up visit – the average lead impedance along with standard error bars will be plotted for each visit. LV threshold testing must be performed in bipolar configuration.
- LV lead handling characteristics
- LV lead implanting tools/accessories
- LV lead venous access location
- LV lead implant attempts and repositions during procedure
- LV lead implant procedure and fluoroscopy time

- Final LV lead location
- Final programming for LV pacing configuration
- Reasons for unsuccessful LV lead implant
- Mortality
- Adverse Events
- LV lead implant attempts – the average, standard deviation and range of number of LV lead implant attempts will be reported
- Mortality – a Kaplan-Meier analysis will be performed for all-cause death
- Adverse Events will be classified and reported as complications or observations. Interim and Final reports will summarize all adverse events. Observations and complications will also be classified as related to the LV lead or unrelated to the LV lead and reported in the following categories.
    a. LV lead related complications include:
        i. Diaphragmatic/Phrenic nerve stimulation
        ii. Lead dislodgement that occurred greater than 30 days after implant
        iii. Lead insulation damage
        iv. Lead fracture
        v. Elevated pacing threshold
        vi. Loss of capture
        vii. Cardiac perforation
        viii. Other unexpected complications that are considered related to the LV lead

    b. Complications that are unrelated to the LV lead include:
        i. Pneumothorax
        ii. Infection
        iii. Bleeding/Hematoma requiring pocket revision
        iv. Cardiac Perforation
        v. CS dissection/perforation
        vi. Cardiac vein thrombosis
        vii. Lead dislodgement occurring in the peri-operative period (within 30 days of implant)
        viii. Elevated pacing thresholds due to patient's venous anatomy
        ix. Loss of capture unrelated to lead fracture or dislodgement
        x. Abnormal Lead pacing impedance ($\leq 200\ \Omega$ or $\geq 2000\ \Omega$) unrelated to lead fracture or dislodgement
        xi. Complications related to other implanted leads (right atrial or right ventricular)

4.3 Site Selection

Centers will be selected for participation in the study based on their ability to screen and enroll eligible patients, and perform the required study procedures outlined in sections 4.5 and 4.5.1. SJM will attempt to have a diversified group of centers participating in the study in the United States, including academic and non-academic institutions, [redacted] To ensure a widespread distribution of data and minimize site bias, a maximum of approximately 15% of the total enrollment will be allowed at a single site.

The sites who have participated in the QuickFlex® µ 1258T Investigational Device Exemption (IDE) study will be invited to participate in this post market study. Sites who agree to participate will be instructed to approach all patients who were previously enrolled in the QuickFlex® µ 1258T Investigational Device Exemption (IDE) study for participation in the post market study for further data collection.

4.4 Patient Selection

4.4.1 Inclusion Criteria

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

1. Have an approved indication per ACC/AHA/HRS guidelines for implantation of a CRT-D system or participated in the QuickFlex® µ1258T IDE study
2. Have the ability to provide informed consent for study participation and be willing and able to comply with the prescribed follow-up tests and schedule of evaluations

4.4.2 Exclusion Criteria

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

1. Have a hypersensitivity to a single 1.0mg dose of dexamethasone sodium phosphate or short term contact with heparin
2. Have a life expectancy of less than 5 years due to any condition
3. Be less than 18 years of age

4.5 Study Procedures

All required study procedures at each specified interval are outlined in the sections below.

Table 3: Schedule of Evaluations Summary

Evaluation	Enrollment/ Implant	6 months	12months	Every 6 months through 5 years
Inclusion/Exclusion Evaluation	√			
Bipolar LV Lead capture threshold testing using a pulse width @ 0.5 ms and LV lead impedance. **Bipolar pacing configuration is required.**	√	√	√	√
**Unipolar LV lead capture threshold testing using a pulse width @ 0.5 ms and LV lead impedance. Only for patients programmed to LV unipolar pacing configuration	√	√	√	√
Real time measurements and trends for all implanted leads	√	√	√	√

4.5.1 Enrollment Requirements

4.5.1.1 Enrollment

Patients will undergo screening evaluations as outlined by the inclusion/exclusion criteria. The proportion of male and female patients enrolled over time will be carefully monitored to ensure a representative sampling that is consistent with clinical practice. In both the SJM sponsored Post Approval Study, and the Attain Model 4193 LV lead study, male patients comprised 60%-70% of the study cohort. It is expected that the proportion of male patients in this study will be comparable.

Data will be collected on the patient's gender, age, ethnicity, tobacco use, cardiovascular history, arrhythmia history, NYHA functional classification, left ventricular ejection fraction, QRS duration, cardiomyopathy classification, and cardiac medications.

Patients who meet inclusion/exclusion criteria, sign an IRB/MEC approved informed consent, and have an implant or attempted implant of the QuickFlex® µ 1258T LV lead will be considered enrolled in the

study. The enrollment date for patients in the study will be the date of implant or attempted implant.

The IDE cohort patients will be eligible to rollover into the post approval study after signing consent for further data collection. The enrollment date for these patients will be the date of signing consent.

Complete and submit a Patient Status, Enrollment and Implant Case Report Form(s). If an adverse event or protocol deviation occurred during this visit, complete an Adverse Event and/or Deviation Case Report Form. Send the forms to St. Jude Medical, CRMD Sunnyvale, CA.

*Do not complete an Enrollment or Implant Case Report Form for the IDE rollover patients.

4.5.1.2 Implant Procedures

The implant procedure will be performed according to standard of care. Consult the User's Manual for implantation guidelines, appropriate lead/device connections and general handling information.

Left Ventricular Lead Placement

To facilitate the introduction of the QuickFlex® µ 1258T left heart lead into the coronary sinus, the physician can use any appropriate delivery system that is legally marketed by SJM or other manufacturers.

Electrical Measurements at Implant

After connection of the device to the leads, the following electrical measurements must be performed with the device at implant: capture threshold testing for the LV lead using a bipolar configuration and a pulse width of 0.5ms, and pacing lead impedance for the LV lead. All electrical measurements for the LV lead must be completed in the bipolar configuration.

**If final programming for LV pacing configuration is unipolar, perform electrical measurements (i.e. capture threshold test using a pulse width of 0.5ms and pacing lead impedance) in the selected unipolar vector.

***Note:** As referenced under the Definitions in section 4.1: Study Design and Scope, abnormal pacing lead impedances are defined as measured pacing impedances with values ≤ 200 Ω or ≥ 2000 Ω. Pacing

lead impedances measured up to 1999 Ω are considered to be within the normal bounds of the performance of the LV lead because characteristics such as lead position, orientation of the electrodes, previous tissue injuries, etc., specific to each patient have been known to produce measured pacing impedances that are higher than anticipated. Should the LV lead pacing impedance be measured at ≤ 200 Ω or ≥ 2000 Ω, exhibit increase or decrease of 25-30% in an acute setting, or between consecutive visits, the investigator should refer to the Users Manual, St. Jude Medical technical support or other St. Jude Medical clinical support personnel to diagnose potential lead failures.

Device diagnostics and archives of LV lead impedance values may also be used to diagnose potential lead failures. This information will be available for viewing on the SJM Model 3510 and/or the Merlin Patient Care System Model 3650 programmers or device print-outs. Alternatively, the investigator should refer to the Users Manual, St. Jude Medical technical support or other St. Jude Medical clinical support personnel to diagnose potential lead failures.

Complete an Implant Case Report Form and record all results. If an adverse event or protocol deviation occurred during the implant procedure, complete an Adverse Event and/or Deviation Case Report Form. Send the forms to St. Jude Medical, CRMD Sunnyvale, CA.

Download and export the following device session records to St. Jude Medical.
1. Initial and Final Programmed Parameters
2. Real-Time Measurements and Trends for all implanted leads
3. Capture threshold testing printout for LV lead (bipolar configuration)
4. Capture threshold testing printout for LV lead (unipolar configuration) **Only for those patients programmed to a unipolar vector for LV pacing
5. All stored IEGM(s)

4.5.1.3 Unsuccessful Implant

Patients who have an unsuccessful implantation of a St. Jude Medical CRT-D system will be followed for a period of 30 days for adverse events and then withdrawn from the study unless the implant will be re-attempted.

Complete Patient Status, Enrollment, Implant and Product Out of Service (if applicable) Case Report Forms and record all results. If an adverse event or protocol deviation occurred during the attempted implant procedure, complete an Adverse Event and/or Deviation Case

Report Form. Send the forms to St. Jude Medical, CRMD Sunnyvale, CA.

After 30 days, complete a Withdrawal Case Report Form and Adverse Event Case Report Form (if applicable) and record all results. Send the forms to St. Jude Medical, CRMD Sunnyvale, CA.

If the physician chooses to re-attempt the implantation of a St. Jude Medical CRT-D system, complete an Implant Case Report Form and Product Out of Service Case Report Form (if applicable) and record all results. If an adverse event or protocol deviation occurred during the implant procedure, complete an Adverse Event and/or Deviation Case Report Form. Send the forms to St. Jude Medical, CRMD Sunnyvale, CA.

4.5.2 System Revisions

For all system/lead revisions, complete the applicable testing as outlined in section 4.5.1.2. Any explanted devices or leads (including damaged leads, lead segments and lead fragments) should be returned to St. Jude Medical for analysis promptly. Any changes to the status of the lead (i.e., capped or removed) will be documented on the Product Out of Service Case Report Form. Complete an Adverse Event, System Revision, and Product Out of Service (if applicable) Case Report Forms. If an adverse event or protocol deviation occurred during the system revision procedure, complete an Adverse Event and/or Deviation Case Report Form. Send the forms to St. Jude Medical, CRMD Sunnyvale, CA.

4.5.3 Follow-Up Requirements

Patients who have a successful system implant will be seen at 6 months after implant and every 6 months thereafter until the patient reaches the 5 year visit.

The schedule of follow-up visits is based on the date of successful LV lead implant for new patients and the date of signing consent for the IDE rollover patients. Table 4 outlines the time window that is permitted for each of the study interval visits.

Table 4: Study Interval Time Windows

6 months	Every 6 months thereafter until 5 years
± 45 days	± 60 days

4.5.3.1 6-Month Visit and Every 6 Months thereafter until 5 years

Perform a device follow-up and interrogate the device.
Perform the following electrical measurements: capture threshold testing for the LV lead using a pulse width of 0.5 ms and pacing lead impedance for the LV lead. All electrical measurements for the LV lead must be completed in the bipolar configuration.

**If final programming for LV pacing configuration is unipolar, perform electrical measurements (i.e. capture threshold test using a pulse width of 0.5ms and pacing lead impedance) in the selected unipolar vector.

***Note:** As referenced under the Definitions in section 4.1: Study Design and Scope, abnormal pacing lead impedances are defined as measured pacing impedances with values ≤ 200 Ω or ≥ 2000 Ω. Pacing lead impedances measured up to 1999 Ω are considered to be within the normal bounds of the performance of the LV lead because characteristics such as lead position, orientation of the electrodes, previous tissue injuries, etc., specific to each patient have been known to produce measured pacing impedances that are higher than anticipated. Should an LV lead pacing impedance be measured at ≤ 200 Ω or ≥ 2000 Ω, exhibit increase or decrease of 25-30% in an acute setting, or between consecutive visits, the investigator should refer to the Users Manual, St. Jude Medical technical support or other St. Jude Medical clinical support personnel to diagnose potential lead failures.

Device diagnostics and archives of LV lead impedance values may also be used to diagnose potential lead failures. This information will be available for viewing on the SJM Model 3510 and/or the Merlin Patient Care System Model 3650 programmers or device print-outs. Alternatively, the investigator should refer to the Users Manual, St. Jude Medical technical support or other St. Jude Medical clinical support personnel to diagnose potential lead failures.

The site will report all adverse event(s) that have occurred between scheduled study follow-up visits. Complete a Follow-up Case Report Form and record all results. If the patient experienced adverse event(s), or protocol deviation, complete an Adverse Event and/or Deviation Case Report Form. Send the forms to St. Jude Medical, CRMD Sunnyvale, CA.

Download and export the following device session records to St. Jude Medical.

1. Initial and Final Programmed Parameters
2. Real-Time Measurements and Trends for all implanted leads
3. Capture threshold testing print-out for LV lead (bipolar configuration)
4. Capture threshold testing printout for LV lead (unipolar configuration) **Only for those patients programmed to a unipolar vector for LV pacing
5. All “new" stored IEGM(s) since previous session

5.0 Protocol Deviations

Investigators are required to adhere to the protocol, 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 clinical protocol was not followed. All deviations from the protocol must be reported to St. Jude Medical per 21 CFR §812.150. In addition, all deviations must be reported to the reviewing IRB/MEC per the IRB/MEC’s reporting requirements.

The investigator must notify St. Jude Medical and the reviewing IRB/MEC of any deviation from the protocol plan to protect the life or physical well-being of a subject in an emergency as soon as possible, but no later than 5 working days after the deviation has occurred, or no later than 5 working days after the investigator becomes aware of the deviation.

Should a deviation occur, complete a Deviation Case Report Form and submit to St. Jude Medical. If a deviation occurs between scheduled visits, the event should be reported at the next scheduled visit.

6.0 Adverse Events

QuickFlex® µ 1258T Investigational Device Exemption (IDE) sites who agree to participate in the post approval study will be instructed to report all adverse events on IDE patients who are consented for participation in the post market study starting from the date of the last IDE follow up visit to ensure that all adverse events are reported. Adverse events will then continue to be reported every 6 months for the duration of the patient’s participation in the study.

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 to resolve (e.g. lead dislodgment requiring repositioning).
Each complication will be reported in one of the following categories for analysis purposes:

a) LV lead related complication: A complication that is related to the LV lead.
b) Device related: A complication related to the device.
c) Other system related complication: A complication that is related to the RV or RA lead.
d) Procedure related complication: A complication related to an implant or system revision procedure.
e) Other complication: Any complication that does not fall into one of the categories listed above.

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). Observations will be reported in one of the following categories:

a) LV lead related observation: An observation that is related to the LV lead
b) Device related: An observation related to the device
c) Other system related observation: An observation that is related to the RV or RA lead.
d) Procedure related observation: An observation related to an implant or system revision procedure.
e) Other observation: Any observation that does not fall into one of the categories listed above.

As defined in 21 CFR §812.3, unanticipated adverse device effects (UADE) are defined as any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

If an unanticipated adverse device effect occurs, the investigator must notify St. Jude Medical and the IRB/MEC immediately, but no later than 10 working days of the investigator's knowledge of the event, as required by 21 CFR §812.150. St. Jude Medical will take any steps necessary to investigate the event, and will be responsible for notifying FDA and all other participating IRBs/MECs and investigators.

Should St. Jude Medical determine, either through physician reports or in-house testing, that an unanticipated adverse event presents an unreasonable risk to participating patients, St. Jude Medical will suspend the clinical investigation and notify all participating investigators, IRBs/MECs and the FDA.

For unexpected failure modes or unexpected adverse events, the site should follow their standard reporting practices for medical device reporting (MDR). As defined in 21 CFR 803, a MDR reportable event (or reportable event) means: An event that device user facilities become aware of that reasonably suggests that a device has or may have caused or contributed to a death or serious injury. A device user facility must report deaths and serious injuries that a device has or may have caused or contributed to, establish and maintain adverse event files, and submit summary annual reports to FDA.

Potential adverse events associated with the use of left ventricular leads include:

- Allergic reaction to contrast media
- Bodily rejection phenomena
- Cardiac/coronary sinus dissection
- Cardiac/coronary sinus perforation
- Cardiac tamponade
- Coronary sinus or cardiac vein thrombosis
- Death
- Endocarditis
- Excessive bleeding
- Hematoma/seroma
- Induced atrial or ventricular arrhythmias
- Infection
- Lead dislodgement
- Local tissue reaction; formation of fibrotic tissue
- Loss of pacing and / or sensing due to dislodgement or mechanical malfunction of the pacing lead
- Myocardial irritability
- Myopotential sensing
- Pectoral/diaphragmatic/phrenic nerve stimulation
- Pericardial effusion
- Pericardial rub
- Pnemothorax/hemothorax
- Prolonged exposure to fluoroscopic radiation
- Pulmonary edema
- Renal failure from contrast media used to visualize coronary veins
- Rise in threshold and exit block
- Thrombolytic or air embolism
- Valve damage

Performance of a coronary sinus venogram is unique to lead placement in the cardiac venous system, and carries risks.

Potential complications reported with direct subclavian venipuncture include hemothorax, laceration of the subclavian artery, arteriovenous fistula, neural damage, thoracic duct injury, cannulation of other vessels, massive hemorrhage, and rarely, death.

Should an adverse event occur, complete an Adverse Event form and submit to St. Jude Medical. If an adverse event occurs between scheduled visits, the event should be reported at the next scheduled visit. 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 are 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 investigation must be reported to St. Jude Medical as soon as possible. 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 (Death form, Withdrawal form, and Product Out of Service form). A Mortality Committee will review and classify all patient deaths. It is the investigator's responsibility to notify the IRB/MEC per the IRB/MEC policy. 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 and time 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 (include any available documentation)
- 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 (including damaged leads, lead segments and lead fragments) 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 Patient Relocation

If a patient moves from the geographic area of the investigator, then SJM will first attempt to place the patient with another QuickFlex® µ 1258T® PAS investigator. If it is not possible to place the patient with another QuickFlex® µ 1258T PAS investigator, SJM will request that the patient's new physician forward the patient's study information to the investigator. See definition for patients lost to follow-up in Section 10.0.

10.0 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:

- Heart Transplant
- Patient Death
- Patient and/or Family Request
- Patient Lost to Follow-Up - Defined as the following: Patient will be considered "lost to follow-up" after a minimum of two documented phone calls were made by personnel at the study center to the patient or emergency contact, a certified letter was sent to the last known address, and two consecutive visits pass without an investigator receiving data
- Patient Non-compliance
- Patient Participation terminated by Investigator
- Sponsor Request
- System explanted without a system replacement
- Unsuccessful Implant
- Removal of the QuickFlex® µ 1258T lead without a QuickFlex® µ 1258T lead replacement

Complete a Withdrawal Case Report Form and record all results. If the patient experienced an adverse event or protocol deviation, complete an Adverse Event and/or Deviation Case Report Form. Send the forms to St. Jude Medical, CRMD Sunnyvale, CA.

11.0 Risk Analysis

The risks associated with the use of the QuickFlex Model® µ 1258T LV lead in a CRT-D indicated patient population with advanced heart failure are anticipated to be comparable to those associated with the use of other SJM legally marketed LV leads. Patients participating in this study are clinically indicated for a CRT-D system as part of their medical management and are subject to the risks associated with an implant procedure (refer to Section 6.0). There are no expected additional risks associated with this study beyond those found with device testing at implant and follow up visits.

12.0 Investigator Information

This post approval study will be conducted by investigators with experience and/or willingness to be trained in the use of CRT-D devices. 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 protocol, all applicable FDA regulations (21 CFR Parts 50, 54, 56, 812), GCP guidelines, and any conditions of approval imposed by the IRB/MEC
- Providing signed Investigator/Co-Investigator (s) Agreement
- Providing signed Financial Disclosure Form for Clinical Investigators
- Providing IRB/MEC approval for study protocol and approved informed consent
- Collection and archiving of data obtained pursuant to the requirements of the protocol during the course of the study and after the study has been completed
- Strict adherence to the post approval study testing requirements
- 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 post approval study and collecting all required data.

13.0 Monitoring Procedures

St. Jude Medical will serve as the "sponsor" of the QuickFlex® µ 1258T Post Approval Study. 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.

Prior to beginning the study, a St. Jude Medical monitor will contact the investigator or designee to discuss the protocol and to review the data requirements in detail. A St. Jude Medical monitor will visit the investigator or designee periodically during the study to monitor progress, to assist in gathering the required data and to 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 ensure compliance with all requirements of the protocol and FDA regulations.

The investigator will make patient and study records available to the clinical monitor for periodic inspection. Clinical monitoring will be conducted under the St. Jude Medical standard operating procedure 9.4.3 (Clinical Monitoring Procedure).

Responsibility for overall study management will be held by the Sr. Vice President of Clinical Affairs, St. Jude Medical, CRMD.

Clinical Affairs
St. Jude Medical CRMD
15900 Valley View Court
Sylmar, CA 91342
TEL: (800) 423-5611 ext. 2739 or 2872
FAX: (800) 254-6411

FDA Inspections

The investigator and /or designee should contact St. Jude Medical at 1-800-733-3455 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, at reasonable times and in a reasonable manner, to enter and inspect any establishment where post approval study devices are used and to inspect and copy all records relating to the study.

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/MEC have not been submitted or are incomplete, inaccurate, false, or misleading.

14.0 Labeling

Please refer to the Users Manual for appropriate handling and implant technique of the QuickFlex® µ 1258T left heart pacing lead.

15.0 Consent Materials

See attached consent in Appendix A.

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

16.0 IRB/MEC 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/MEC approval should be reported to St. Jude Medical within 5 working days of the withdrawal of approval.

Institutional Review Board (IRB/MEC) for participating Institutions
A list of IRB/MEC's for Institutions participating in the Clinical Investigation will be provided upon request.

17.0 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/MEC information, will be provided upon request.

18.0 Records and Reports

Clinical investigators of post approval studies performed as a condition of FDA approval are required to maintain records, prepare and submit reports, and permit FDA Bioresearch Monitoring Inspections relating to the investigator's participation in and conduct of the study.

18.1 Custody

An investigator may withdraw from the responsibility to maintain records for the period required and transfer custody of the records to any other person who will accept responsibility for them as described, including the requirements regarding FDA inspection. Notice of transfer shall be given to St. Jude Medical and FDA no later than ten working days after transfer occurs.

18.2 Retention Period

Clinical investigators in the QuickFlex® µ 1258T LV Lead study are required to maintain records during the investigation and for a period of at least two years after the date on which the post approval study is terminated or completed.

Appendix A: Consent Form

Statement of Informed Consent

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

APPENDIX B: Detailed Sample Size Calculations

[redacted]

Detailed Sample Size Calculations for Complication rate

[redacted]

[redacted]

Simulation:
For a particular sample size (n), generate 10,000 random binomial samples with $p = 0.4\%$.

[redacted]

Output:

[redacted]