DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION
CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

Division of Cardiovascular Devices
Pacing, Defibrillator & Leads Branch

Date:	6 May 2010
From:	(b)(6) Mechanical Engineer, FDA/CDRH/ODE/DCD/PDLB
Subject:	P030054/S130 St. Jude Medical QuickFlex µ Model 1258T left ventricular pacing lead
Submission Date: **Amended:**	16 July 2009 23 September 2009, 10 March 2010, 22 March 2010, 5 April 2010, 5 May 2010
Contact:	Colleen Canan
To:	The Record
Recommendation:	Approval

Background/ Reason for Supplement

St. Jude submitted this PMA supplement to request approval of the QuickFlex µ Model 1258T left ventricular lead (1258T lead). This lead model is based upon the U.S. market approved 1056T, 1058T, and 1158T left ventricular lead models.

Review Team

Lead Reviewer: (b)(6) PE, FDA/CDRH/ODE/DCD/PDLB
Clinical: (b)(6) MD, FDA/CDRH/ODE/DCD/PDLB
Engineering: (b)(6) FDA/CDRH/ODE/DCD/PDLB
Epidemiology: (b)(6) MD MPH, FDA/CDRH/OSB/Epi

Marketing History

The QuickFlex 1258T lead received CE mark on 29 Sep 08 and is currently marketed outside the United States in the European Union. The firm states that the lead has not been withdrawn for the market in any country for any reason related to safety and effectiveness of the device.

Indications For Use

The following indications/intended use statement is presented in the submission and included in the User's Manual for the Model 1258T lead:

The QuickFlex™ µ Model 1258T leads are 4.7 French, transvenous, steroid eluting, bipolar, IS-1 compatible, S-shaped curve, passive fixation leads intended for permanent sensing and pacing of the left ventricle when used with a compatible St. Jude Medical® biventricular system.

This intended use statement is detailed, complete, and acceptable.

Device Description

The Quickflex µ Model 1258T is a steroid eluting, bipolar over-the-wire left heart lead design, enabling implantation using either stylet or guidewire guided placement. The lead has an open lumen inside the electrode coil along its length, and a slit seal/opening at the lead distal tip to allow the use of the guidewire. The lead body is formed with Optim (Elast-eon) silicone-polyurethane co-polymer material with a maximum lead body diameter of 4.7 F. Like the Quicksite left heart lead family, the distal portion of the Quickflex µ Model 1258T left heart lead is pre-shaped in an "s-curve" configuration. The distal tip of 1258T is identical to the approved 1158T. The titanium nitride (TiN) coated platinum/iridium (Pt/Ir) tip electrode contains a molded ring (MCRD) that elutes the steroid dexamethasone sodium phosphate (DSP). Additionally, the surface of the tip electrode is coated with a thin DSP steroid film to provide immediate steroid release. A titanium nitride (TiN) coated platinum/iridium (Pt/Ir) ring electrode is located 20 mm from the tip of the lead. The outer lead body is covered with Fast-Pass™ coating to increase the lubricity during initial implant. The lead connector complies with the IS-1 connector standard ISO 5841-3.

The lead body of 1258T has been modified compared with 1158T. The primary changes are a reduction of the lead body diameter, change to flat coil wire for the tip electrode, use of single (rather than dual) ring electrode cable, and use of Optim outer tubing material.

> *The firm provided an acceptable description of the new 1258T lead and the differences between the market approved 1056T, 1058T, and 1158T lead models. The firm provided additional information regarding accessory design characteristics, dimensions, materials, and part numbers under an amendment to this PMA supplement. The firm confirmed that the device to be marketed is unchanged from the IDE study device.*

Drug Component

The firm did not initially provide and specific information concerning the drug or drug component. Detailed information was provided by amendment to this PMA supplement. The 1258T lead tip and tip electrode is identical to the 1158T lead tip and electrode. The drug MCRD and tip electrode drug coating are identical to what is approved for the SJM 1158T lead. The firm provided documentation of the measured drug dose of the MCRD, coating, and total dose. The labeling and packaging was updated to include the specific drug dose information under amendment to this PMA supplement. SJM is in the process of updating their specifications and methods regarding pacemaker lead drug components and drug coatings. As a condition of approval for this supplement, the firm agreed to the same schedule to update drug specifications and methods, and stability. The agreement and condition of approval text was reviewed and found acceptable by CDER.

> *The firm provided full documentation for the drug MCRD and coating and updated the labeling to include the nominal dose. The firm agreed to conditions of approval to update steroid drug specification, methods, and stability for the 1258T lead. CDER agreed to the condition of approval text. All issues regarding the drug component and coating are resolved.*

Packaging

The firm describes the packaging as being PETG with a Tyvek lid. The firm states that the packaging is identical to that used for Model 1158T. The firm provided detailed information on the packaging design, materials, part numbers and similarity to approved SJM packaging under an amendment to this PMA supplement.

> *The updated packaging information was reviewed and found acceptable as it is identical to approved packaging for other SJM left ventricular leads.*

Sterilization

The firm describes the sterilization method and cycle for the 1258T lead in the submission. The sterilization and packaging of the 1258T lead is identical to the packaging, sterilization, and process of other SJM market approved leads. The firm provided a sterilization assessment concluding the 1258T lead was a lesser sterilization burden than the lead model used to validate the sterilization cycle. The firm provided validation testing including bioburden and particulate.

The sterilization information was reviewed. The sterilization assessment justified use of the validated and approved 1158T EtO sterilization cycle. Sterilization validation testing for 1258T was reviewed and found acceptable.

Shelf Life

The firm provided documentation of previous and current shelf life testing of the device, drug component, and packaging to justify a shelf life of 3 years for 1258T. Additional information was provided by supplement regarding package testing and drug component stability testing.

The device and package shelf life testing was reviewed and found acceptable to support a 3 year shelf life. CDER considered the drug stability testing acceptable for a 3 year shelf life on an interim basis, based on previous approval of the same component for 3 years for 1158T. Per a prior agreement with FDA, SJM agreed to update their stability testing methods and protocol, and to confirm shelf life testing as a condition of approval to this supplement. The agreement and condition of approval text was found acceptable to CDER.

Biocompatibility

The firm presented a summary of biocompatibility documentation in the submission and copies of test reports. A listing of tissue/blood contacting materials was provided. The electrode, outer insulation, connector boot, and suture sleeve materials are all previously approved and used on other St. Jude pacemaker and ICD leads. The firm provided a Biocompatability Certification for all tissue contacting materials.

The biocompatibility test reports, justification and certification were reviewed and found acceptable.

Labeling

The firm provided draft copies of the Model 1258T user manual, specification sheet, and package labels. The information in the user manual included the device description, indications for use, contraindications, contents, package instructions, storage, sterilization, handling, and lead implantation, potential adverse events, and clinician use instructions. The information is all consistent with that of the previous QuickFlex lead models and other marketed leads. The labeling was updated to include changes to the clinical study summary report and drug labeling under amendments.

The final labeling was reviewed. The labeling included updates to address all identified deficiencies and found acceptable.

Summary of Studies

To support the approval of the 1258T lead, the firm presented a comprehensive program of analysis, development, and study. A risk analysis was provided to identify and assess potential risks and to document mitigation steps to reduce identified risks to acceptable levels. Mitigation steps included bench testing, animal studies, and a 3 month human clinical study. The scope of this information was considered acceptable to support approval of the 1258T left ventricular lead design differences from the previously approved 1158T LV lead family. The review of supplied premarket information concluded that concerns for future chronic performance of the 1258T LV lead could be addressed by conducting a confirmatory post-approval study. The 1258T supporting analyses and testing provided in this PMA supplement is summarized in the sections below.

Risk Assesment

The firm evaluated the 1258T lead for potential hazards and residual risks and found them similar to their legally marketed 1056T, 1058T and 1158T left heart leads. No new risks were identified in the Risk Assessment Report. The qualification testing, animal study testing, and premarket clinical study data are used to verify that known risks are mitigated to acceptable levels. The risk assessment was augmented with comprehensive testing for acute bend, crush, and suture sleeve zone testing.

The risk assessment, mitigation steps, and residual risk assessments were reviewed and found acceptable.

Qualification Bench Testing

The firm presents a summary of their qualification testing in the main submission and detailed test reports in Appendices. In addition, the firm submitted (b)(4) cycle testing for a final lead body orientation not completed at the time of the original PMA/S submission. Test reports were presented for (b)(4) test flows. The sponsor documents that the lead samples were sterilized (b)(4) and exposed to temperature storage and temperature shock conditions prior to testing. The sponsor documented that the test samples were made under production manufacturing conditions with production operators using the production procedures and equipment. The sponsor indicates that testing was conducted utilizing 92 cm and 75 cm leads and represents the 86 cm lead length by similarity, which is acceptable. The sponsor provided a sample size justification for the test flows. The sponsor's analysis required a minimum of (b)(4) samples to provide the required (b)(4) confidence that at least (b)(4) of the production population meets or exceeds the minimum acceptable test requirements. The sponsor elected to use a sample size of (b)(4) for the primary test flow and flex fatigue test flow with allowance for no failures.

Functional Testing Test Flow

The functional testing presented was previously reviewed to support IDE approval under G080040. The primary test flow sequence included preconditioning, polarization, dimensional check, DC resistance, stylet testing, guidewire testing, suture sleeve testing, tip shape retention testings, connector testing, sensing impedence, dry and wet hipot, tensile testing, current leakage, and document compliance.

The testing methods and results were reviewed and found complete and acceptable.

Flex Fatigue Test Flow

The flex fatigue test flow sequence is included the following tests: preconditioning, shipping, connector flex fatigue, distal tip flex fatigue, and lead body flex fatigue. Testing was performed at (b)(4) lead body orientations which is appropriate for non-symmetrical leads. A deficiency for missing evaluation of the small 1258T lead body to damage by acute bend, crush loading, and flex fatigue at the suture sleeve were addressed by submission of additional testing under amendments to the submission. Flex testing following severe lead manipulation including acute bend, crush, and suture sleeve area was provided for multiple axes.

The test methods and results were reviewed and found thorough and acceptable.

GLP Animal Study

The firm conducted a GLP animal study using the 1258T lead to support approval of IDE study G080040. The animal study collecting data on (b)(4) for a period of 6 months. The 1258T lead was implanted as part of a CRT-D system which included a Model 1581 Riata RV lead, a Model 1688 Tendril Right atrial lead, and an Epic II HF Model V-355 CRT-D. Data collected included implant and handling information as well as pacing thresholds, p-wave amplitudes, R-wave amplitude and pacing impedance. The final report for GMP animal study (b)(4) was presented in this PMA supplement.

The animal study information was reviewed under G080040 and no further review was considered necessary as the information was identical. The animal study results provide early support of good handling, good electrical performance, and low complications for in-vivo use of the 1258T lead.

Clinical Study

The clinical review was performed by Dr. (b)(6) as documented in a review memo dated 13 Nov 2009. The QuickFlex Model 1258T clinical study was a prospective, multi-center non-randomized clinical study to evaluate the safety and effectiveness of the QuickFlex Model 1258T left ventricular lead in a heart failure patient population. The study was conducted under G080040. A total of (b)(4) patients were enrolled at (b)(4) clinical sties. The total time to followup was (b)(4) patient months. The average follow-up was (b)(4) patient months (range (b)(4) to (b)(4). The primary safety endpoint was freedom from LV lead related complications through 3 months. The firm initially reported no complications, but later updated the clinical study analyses and report by converting two observations to complications under amendment to this PMA supplement. The clinical study primary effectiveness endpoints were LV lead implant success rate and LV lead bipolar pacing capture threshold. The study LV lead implant success rate was (b)(4) with a (b)(4) statistical lower confidence bound of (b)(4). The mean LV voltage threshold was (b)(4) with (b)(4) upper confidence bound of (b)(4).

The clinical reviewer found the updated reporting of complications acceptable. The clinical study implant success rate and mean LV voltage thresholds were well below the prespecified acceptance criteria. Dr. (b)(6) found the study results and study report acceptable to support 1258T market approval.

Manufacturing

The firm states on page 27 that the Model 1258T leads will be manufactured at approved SJM CRMD manufacturing facilities. The firm provided full documentation of manufacturing locations, addresses, facility numbers, and inspection status, and manufacturing process changes for 1258T in an amendment to this PMA supplement.

The manufacturing section and additional information were reviewed and found complete and acceptable.

Post-Market Study

A post-market study of the 1258T lead was considered necessary by the review team to verify the predicted good chronic performance of this modified LV lead design. This recommendation was initially provided to the firm as a future concern under the IDE study. The epidemiology review was performed by Dr. (b)(6) as documented in review memos of 18 Nov 2009, 19 Mar 2010, 12 Apr 2010 and 3 May 2010. The initial post-approval study proposal was a part of SJM's existing SCORE Registry. Upon review this study vehicle did not meet the FDA study requirements and a new post-approval study protocol was submitted as an amendment to the PMA supplement. The firm addressed multiple study protocol and case report form deficiencies through an interactive process with ODE and OSB/Epidemology reviewers. The firm agreed to fully power the study with new enrollees but to also re-consent and follow IDE subjects as a post-approval study subgroup. After interactive review and updates, the firm submitted a final post-approval study protocol and final case report forms.

> *ODE and OSB/Epi reviewed the final protocol dated 30 April 2010 and final case report forms dated 30 April 2010 and found them acceptable. In the final amendment, the firm provided written agreement to a condition of approval to conduct the post-approval study.*

Recommendation

The model 1258T lead is a left ventricular lead based upon the market approved 1058T and 1158T left ventricular lead models. The firm submitted comprehensive bench testing, animal study testing and clinical study testing to demonstrate the safety and effectiveness of the 1258T lead for its intended use. The information was reviewed and found complete and acceptable for market approval. The review team recommends approval of the 1258T lead with the conditions of conducting a post-approval study and updating the drug methods, specifications and stability testing. St. Jude has provided written agreement to these conditions.

(b)(6) Lead Reviewer, PDLB Date

Mitchell Shein, Chief, PDLB Date