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: 22 November 2010

From: (b) (6), Biomedical Engineer, FDA/CDRH/ODE/DCD/PDLB

Subject: P960013/S057
St Jude Medical
OptiSense Model 1999 Lead

Contact: Colleen Canan, Regulatory Affairs, St Jude Medical, CRMD

To: The Record

Recommendation: **APPROVAL**

(b) (6) Lead Reviewer, PDLB Date

Mitchell Shein, Chief, PDLB Date

Background/ Reason for Supplement

This PMA supplement was submitted to gain approval for a design change to the header coupling of the OptiSense Model 1999 lead, a bipolar lead used for pacing and sensing in the right atrium. The current header coupling is machined, but the firm proposes to instead mold the component to increase manufacturability. The new molded header coupling requires a change in material (from PEEK (b) to PEEK (b)) and the addition of a chamfer inside the coupling. All other components remain identical, and the functionality of the lead with the proposed molded header coupling will be identical to the functionality of the lead with the currently-approved machined header coupling.

Review Team

Engineering: (b) (6) FDA/CDRH/ODE/DCD/PDLB
Biocompatibility: (b) (6) FDA/CDRH/ODE/DCD/CSPDB

Indications For Use

The St Jude Medical OptiSense Model 1999 lead is intended for chronic pacing and sensing in the right atrium when used in conjunction with a compatible pulse generator.

Device Description

The Model 1999 lead is a device/drug combination product made up of two regulated components: (1) a device (the Model 1999 lead) and (2) a drug component (100 to 700 µg Dexamethasone).The bipolar, silicone insulated, active fixation lead contains an IS-1 bipolar connector and is intended to be used with a 7 French introducer.

Preclinical/Bench

To support approval of the proposed header coupling design, the firm provides documentation of functional/mechanical and biocompatibility testing in addition to a qualification by equivalence assessment for sterilization, packaging, and shelf life.

Mechanical and System Verification Testing

The engineering review was performed by CDRH/ODE reviewer (b) (6) and documented in a review memos dated 02 April 2010 and 13 August 2010. Verification testing evaluated the helix active fixation mechanism, insulation integrity and relevant lead body mechanical properties and strength after preconditioning. All protocols and results were provided.

ENGINEERING REVIEWER COMMENTS: The verification testing included a standard set of tests that thoroughly assesses lead performance and is appropriate for the described design changes to the header coupling. The sample size is acceptable, and the firm has appropriately used the worst case length specimen for all tests. The firm indicates that all samples tested were manufactured using standard procedures. That being said, the initial submission did not include flex fatigue testing of the areas affected by the proposed changes. Concerns with the absence of this testing were communicated in the Major Deficiency Letter sent 09 April 2010. In response to this deficiency (in P960013/S057/A001), the firm provided results from relevant flex testing that indicate all acceptance criteria were met. No concerns remain and; therefore, the engineering testing presented supports approval of the modified header coupling.

Sterilization

The firm assessed sterilization of the OptiSense Model 1999 lead with the proposed molded header coupling by performing bioburden and endotoxin (LAL) testing. No further testing was documented due to the similarity in design to the market-approved predecessor lead that incorporates a machined instead of a molded header coupling.

LEAD REVIEWER COMMENTS: The subject design appears to allow for a tighter fit between the header coupling and the ring electrode, which could theoretically increase the sterilization burden of the device. Initial concerns about the lack of sterilization testing were communicated to the firm in a Major Deficiency Letter sent 09 April 2010. The sponsor confirmed (via email) that AAMI TIR:28 and ISO 1135-1:2007 for production adoption and process equivalency were used to determine the testing required for the modified lead (bioburden and endotoxin). These standards are recognized by the Agency and provide a thorough assessment of sterilization burden. Since no further testing was deemed necessary while applying these two rigorous standards to the proposed changes, the absence of sterilization test results in the subejct submission is acceptable and no concerns remain from a sterilization perspective.

Packaging

The packaging used for the market-approved OptiSense Model 1999 lead with the machined header coupling will be used for the model with the proposed molded header coupling. The double aseptic package is composed of Polyethylene Terephthalate Glycol copolyester (PETG) and includes a Tyvek lid. Four stylets are packaged with the market-approved lead: one in the lead itself and three in a stylet ring. The proposed lead with the header coupling change would be packaged with one additional J-shaped stylet in the stylet ring.

LEAD REVIEWER COMMENTS: The sponsor provides sufficient justification for qualification by equivalence with respect to packaging. The design and manufacturing changes subject in this submission should not affect the ability of the market-approved package to maintain a sterile barrier under standard storage and transportation conditions. A minor change in packaging was being evaluated during the review of P960013/S057, so the firm was asked to provide an update on the status of that review in the Major Deficiency Letter sent 09 April 2010. The firm indicated in A001 the packaging change was approved under P960013/S058 on May 19, 2010. No concerns remain regarding the packaging of the subject lead.

Shelf Life

The market-approved OptiSense Model 1999 lead with a machined header coupling has a three year shelf life, and the firm believes this shelf life is also appropriate for the proposed lead with a molded header coupling. The new material, PEEK(b) , is injection molded and, according to the material vendor, can withstand storage in dark, dry conditions at ambient temperature for at least 20 years without effects on the viscosity of the polymer.

LEAD REVIEWER COMMENTS: The qualification by similarity is, I believe, appropriate for the shelf life of the lead with the proposed header coupling. The material vendor's certification of shelf life was provided in the initial submission, and confirmation was provided in A001 that the vendor's recommended storage conditions are adhered to. Since the raw material is stored and processed according the vendor's recommendations, the provided vendor certification for the raw material is applicable to the OptiSense lead as well. I have no further concerns about the sponsor's request for a 3 year shelf life.

Risk Management

The firm documented a risk analysis guided by ISO 14971 and an internal SOP. The final assessment indicates that the residual risks are acceptable given the medical benefits provided by the device. Appendix A of the document lists, in table format, the five new risks introduced with the design and manufacturing process changes associated with the proposed molded header coupling.

LEAD REVIEWER COMMENTS: The firm appears to have adequately assessed the risks involved with the proposed changes. I believe the new risks that the proposed changes introduce have been appropriately mitigated by the testing documented in this submission.

Manufacturing

The OptiSense Model 1999 lead with the proposed molded header coupling will be manufactured and sterilized at both the St Jude Medical Veddesta and Sylmar FDA-approved facilities. No further information is provided concerning the manufacture of the leads incorporating the subject changes.

LEAD REVIEWER COMMENTS: The firm provides the locations of the manufacturing sites for the leads that incorporate the subject design and manufacturing changes. These facilities have already been approved by FDA, and, therefore, I have no further concerns about the manufacture of the OptiSense Model 1999 lead.

Biocompatibility

The firm provides a summary of the biocompatibility testing completed on the new PEEK(b) material used in the molded header coupling, which included cytotoxicity, hemolysis, and material mediated rabbit pyrogen tests.

BIOCOMPATIBILITY REVIEWER COMMENTS: The summary of testing provided initially was insufficient to allow review of the biocompatibility of the new material, (b) PEEK. Test reports for the tests conducted were requested in the Major Deficiency Letter sent 09 April 2010. In addition, the firm was asked to perform several additional biocompatibility tests required by the Agency for all permanent implants contacting circulating blood. The test reports for all requested tests were provided in A001. During review of the data in those test reports, three

additional concerns were found regarding test extract preparation, use of controls, and use of nonpolar in addition to polar extracts. These concerns were communicated in the second deficiency letter sent 18 Aug 2010. The firm's responses were reviewed as indicated in the 22 Nov 2010 biocompatibility review memo and found to be acceptable based on the unfiltered nature of the extracts, additional testing of the comparative control, and test specimen selection. No concerns remain with the biocompatibility of the subject material and device.

Labeling

The indications for use, contraindications, warnings and precautions for the OptiSense Model 1999 lead will not change as a result of the subject design and manufacturing changes. The market-approved language will remain in the user's manual and labels.

LEAD REVIEWER COMMENTS: The changes described in this submission do not affect the labeling of the device. I have no concerns about the user manual, IFU, and label sets.

Summary of interactive review/correspondence

12 March 2010: File submitted
09 April 2010: Major Deficiency Letter sent
24 June 2010: Major Deficiency responses received in P960013/S057/A001
18 Aug 2010: Deficiency Letter sent regarding A001
17 Sept 2010: Deficiency responses received in P960013/S057/A002
12 Nov 2010: Additional Information questions sent via email
19 Nov 2010: Additional Information email responses received

Conclusion

This submission requests approval for design and manufacturing changes to the header coupling of the OptiSense Model 1999 pacing and sensing lead. The firm provided testing, rationale for qualification by equivalence, and a risk assessment to demonstrate that the proposed design and manufacturing changes do not negatively impact the mechanical functionality, sterilization, packaging, shelf life, or biocompatibility of the OptiSense Model 1999 pacing and sensing lead. Initial concerns with engineering test selection, sterilization validation procedures, and biocompatibility were sufficiently addressed in amendments A001 and A002. No concerns remain with the submission; therefore, I recommend approval of P960013/S057.