SUMMARY OF: P910023/S309, P880086/S229, P030035/S107, P880006/S084, P970013/S054, P030054/S238

Ellipse VR ICD (CD1411-36, CD1411-36Q, CD1411-36C, CD1411-36QC), Fortify Assura VR ICD (CD1357-40, CD1357-40Q, CD1357-40C, CD1357-40QC), Ellipse DR ICD (CD2411-36, CD2411-36Q, CD2411-36C, CD2411-36QC), Fortify Assura DR ICD (CD2357-40, CD2357-40Q, CD2357-40C, CD2357-40QC), Unify Assura CRT-D (CD3357-40, CD3357-40Q, CD3357-40C, CD3357-40QC), Quadra Assura CRT-D (CD3365-40, CD3365-40Q, CD3365-40C, CD3365-40QC), Model 3330 Version 17.1 Software for the Model 3650 Merlin Patient Care System Programmer, Model EX2000 Version 6.5 Software for the Models EX1150 and EX1100 Merlin@Home Transmitters, and Model MN5000 Version 6.5 Software for the Merlin.net System

BACKGROUND/ REASON FOR SUPPLEMENT

St. Jude Medical, Cardiac Rhythm Management Division (SJM CRMD) is requesting approval for new Ellipse™ and Fortify Assura™ Dual and Single Chamber Implantable Cardioverter Defibrillators (ICD) and the Unify Assura™ and Quadra Assura™ Cardiac Resynchronization Therapy Defibrillators (CRT-D) device models, which are supported by the Model 3330 v17.1 programmer software, the Model EX2000 v6.5 Merlin@Home software, and the Model MN5000 v6.5 Merlin.net software.

The modified Ellipse and Assura device models are based on the previously FDA approved Ellipse and Unify Assura/Fortify Assura/Quadra Assura high voltage device models (P910023/S279, approved on May 7, 2012).

The key features/modifications proposed in this submission include the following:

- DynamicTx Over-Current Detection (DOCD) Algorithm
- RV to SVC shock configuration (Cold Can)
- (b)(4) Trade Secret coating on the outside of the ICD/CRT-D (b)(4) Trade Secret can

In addition, a minor hardware change was made to support these features:

- Implementation of an updated (b)(4) Trade Secret Transistor (b)(4) Trade Secret
- Added (b)(4) Trade Secret component in the Hybrid Assembly

Software modifications on the Merlin Patient Care System (PCS), Merlin.net system, and Merlin@Home system are also proposed in this submission to support the changes listed above.

The sponsor has provided Risk Management, Hardware/Firmware/Software Verification Testing, System Validation Testing, Animal Study, Biocompatibility, Sterilization, Manufacturing, Packaging and Labeling Information to support these changes. These have been reviewed in subsequent sections of this review memo. No clinical evidence was provided to support the changes.

The main concerns found during this review were in regards to the functionality of the DOCD feature. More specifically, the sponsor had not provided adequate information for FDA to fully

understand how the feature works. Additionally, there were some concerns regarding biocompatibility, labeling, battery longevity estimates, and animal study information. Deficiencies applicable to these concerns were sent to the sponsor on February 12, 2013.

In Amendment 1, the sponsor provided responses to these deficiencies. These responses were determined to be adequate to warrant approval of the supplement.

It should be noted that the sponsor is currently on the OAI list (under a warning letter), and is not able to gain approval for any device manufactured at their OAI facility. Therefore, a consult was sent to the Office of Compliance (OC) to determine if the changes proposed in the supplement warrant approval from a public health standpoint. It was determined, based on review by OC, that although there are remaining concerns with the firms design controls, the new features offer a public health benefit for a select patient population.

INDICATIONS FOR USE

The indications for use of the Ellipse, Fortify Assura, Unify Assura, and Quadra Assura family of devices are identical to existing SJM pulse generators.

The ICD/CRT-D Systems are intended to provide ventricular antitachycardia pacing and ventricular defibrillation for automated treatment of life-threatening ventricular arrhythmias. AF Suppression™ pacing is indicated for suppression of paroxysmal or persistent atrial fibrillation in patients with the above ICD indication and sinus node dysfunction. In patients indicated for an ICD, the Quadra Assura™ and
Unify Assura™ pulse generators are also intended:

- To provide a reduction of the symptoms of moderate to severe heart failure (NYHA Functional Class III or IV) in those patients who remain symptomatic despite stable, optimal medical therapy and have a left ventricular ejection fraction less than or equal to 35% and a prolonged QRS duration.

- To maintain synchrony of the left and right ventricles in patients who have undergone an AV nodal ablation for chronic (permanent) atrial fibrillation and have NYHA Class II or III heart failure.

DEVICE DESCRIPTION

The new Ellipse and SJM Assura ICD and CRT-D models include limited design changes as compared to the approved Ellipse and SJM Assura models. The key features/modifications are listed below.

- DynamicTx Over-Current Detection (DOCD) Algorithm
- RV to SVC shock configuration (Cold Can)
- (b)(4) Trade Secret coating on the outside of the ICD/CRT-D (b)(4) Trade Secret can

In addition, a minor hardware change was made to support these features:

- Implementation of an updated (b)(4) Trade Secret Transistor ((b)(4) Trade Secret
- Added (b)(4) Trade Secret component in the Hybrid Assembly

These changes are intended to reduce the probability of high voltage lead to lead-to-can abrasion and to improve device response if a high voltage lead problem does occur.

The various families of devices in combination with the compatible commercially available leads constitute the implantable portion of the ICD and CRT-D systems. The compatible RA, RV, and LV leads are implanted using a transvenous technique and/or a transthoracic technique. The SJM Merlin Patient Care System (PCS) Programmer (Model 3650, including Model 3330 v17.1 software), in combination with the Merlin Antenna (Model 3638) and external inductive telemetry wand (Model 3630), constitutes the external portion of the device system and is utilized to interrogate and program these devices.

Remote care support for the implantable devices is provided via the Merlin@Home transmitter devices (Models EX1150 and EX1100, including Model EX2000 v6.5 software) in conjunction with the Merlin.net system (which includes the MN5000 v6.5 software). In this transtelephonic remote follow-up system, the Merlin@Home transmitter device is used as a tool for collecting diagnostics and EGM data from the implantable devices. After collecting data from an implantable device, the Merlin@Home transmitter then transfers the data to an external receiving station (Merlin.net Database) where it is stored. Healthcare providers can view the follow-up data/device data generated by the Merlin.net Model MN5000 software via the SJM web portal (Merlin.net Web Application).

PRECLINICAL/BENCH

BIOCOMPATIBILITY/MATERIALS

The sponsor has provided a certification that all blood/tissue contact materials used in the new Ellipse and SJM Assura device models are identical materials used in previously approved Ellipse and SJM Assura devices with the exception of the (b)(4) Trade Secret coating, which is used in other legally marketed SJM devices. Because of this, the sponsor states that additional biocompatibility testing is not necessary, as the materials have been previously tested and approved for their biocompatibility in other devices. The sponsor has provided a table in the submission that lists the materials used for each component of the device, the predicate device the material was used in, and the PMA number in which this material was approved:

A consult was issued to a materials engineer to review to biocompatibility section of this submission. He had several concerns with the sponsor's claim that biocompatibility testing was not necessary, based on the information provided. He provided a deficiency which was sent to the sponsor via e-mail on December 13, 2013. This deficiency focused on the manufacturing processes, chemical characterization, interactive chemistry and starting materials of the new Ellipse and SJM Assura devices, as compared to the predicates.

In response to the deficiency, the sponsor provided (via e-mail on January 18, 2013) a table comparing the subject and predicater materials and manufacturing processes. After evaluation of these minor differences and based on the historical use of the (b)(4) Trade Secret coating for similar indications as the Ellipse devices, the information provided in this response was

found to be acceptable. One issue remained regarding the use of a medical adhesive in the subject devices that was not used in predicate devices. The sponsor was asked, in the Major Deficiency Letter, to provide the name of the Medical Adhesive, if it is directly contacting the blood/tissue of the patient, and justify why its inclusion into the manufacturing processes of the subject devices does not alter the safety and effectiveness of the device.

The biocompatibility reviewer was again consulted to review the sponsor's response regarding the medical adhesive in Amendment 1. According to his memo, he finds the information acceptable and believes the use of the medical adhesive does not affect the safety and effectiveness of the device. This information is acceptable and I have no further concerns with this section of the review.

ANIMAL STUDIES

An acute canine study was conducted in accordance with Good Laboratory Practices (GLP), to evaluate if the (b)(4) Trade Secret coating impacts high voltage lead impedance, defibrillation therapy success, and other algorithms that use unipolar sensing or EGM signals. Specifically, the study evaluated the following:

1. Pacing and sensing functionality, including pacing lead impedances, pacing thresholds (including AutoCapture and Cap Confirm function), and sensed amplitudes.
2. High voltage therapy functionality, including high voltage lead impedance measurement, induction, charging, and delivered energy or pulse width, with SecureSense and Far Field Morphology enabled as well.

A consult was issued to a veterinarian to review the acute animal study provided in this submission. A minor deficiency was sent to the sponsor in the February 2013 correspondence that requested pathology reports, color photographs, histopathology, and data collected during the GLP study. Overall, the consulting reviewer accepts the sponsor's response to the deficiency and has no further concerns. She did express that the study was limited by its acute nature and its lack of testing of the DOCD feature. I agree with the reviewer's comments and I have no further concerns.

ELECTRICAL SAFETY

The following tests were performed to verify the electrical performance of the listed components and features:

(b)(4) Trade Secret

- Electrical Tests

Hybrid Assembly:

- Electrical Function Test
- High Voltage Stress Test

Tachycardia:

- Functional Tests
- Measurement of HV Output, Delivered Energy, Pulse Width, and Charge Time
- Shock Delivery Load Range
- Over Current Detection (OCD) Tests
- Dynamic OCD Tests
- High Voltage Lead Impedance
- High Voltage Lead Integrity Check
- DC Fibber Test
- Backup Defib Operation Tests
- Inductive/RF Telemetry
- Distance Tests

An electrical engineer was issued a consult to review the tests listed above. According to his review, it appears that the appropriate testing was completed successfully. He did not have any further concerns. A deficiency was not sent to the sponsor regarding the electrical testing. This information is acceptable.

MECHANICAL SAFETY

The following tests were performed to verify the mechanical performance of the components listed.

(b)(4) Trade Secret

- Environmental Tests
  - Stabilization Bake
  - Temperature Cycling
- Life Test
- Mechanical Tests
  - Wire Bonding
  - Wire Bond Pull Test
  - Die Shear Strength Test

Hybrid Assembly:

- Visual Inspection
- Temperature Cycling
- Acceleration
- Mechanical Tests – Wire Pull and Die Shears

A mechanical engineer was issued a consult to review the test reports listed above. One failure was noted during testing. The component was examined and was found to have (b)(4) Trade Secret coverage underneath. It was determined that the root cause was due to the (b)(4) Trade Secret placement. The mechanical engineer had no concerns with this failure and no further concerns with this section of the review. I agree with the engineer's assessment and find this information acceptable.

LEAD ABRASION TESTING

The purpose of this testing was to document comparative lead-to-can abrasion tests for Riata ST and Durata High Voltage Leads. The test protocol was identical between the two provided reports. The testing was used to compare abrasion cycles to failure for the two lead types against (b)(4) Trade Secret coated test plates vs. uncoated (control) test plates. A mechanical engineer was issued a consult to review this testing. Based on his review, the sample, size, protocol, and acceptance criteria were appropriate to demonstrate if there was a statistical significance between the tested samples and the control samples. The testing was a test to failure. The number of cycles until a conductor shorted to the (b)(4) Trade Secret can was counted. The acceptance criteria were stated as "a statistically significant improvement in lead-to-can abrasion cycles to failure". From the results it appears there was a statistically significant improvement in the number of cycles to failure for both leads that were abraded against both the coated and un-coated plates. While the testing was informative, it does not fully addresse the issue of lead cable externalization and abrasion. The (b)(4) Trade Secret coating on the can appears to delay the abrasion. The consulting engineer had no concerns with this testing, however, he recommends reviewing the labeling carefully to ensure there are no claims about preventing lead abrasion.. I agree with the engineer's assessment of the lead-to-can abrasion testing. I have reviewed the labeling to ensure that there are no claims about preventing lead abrasion in the subject devices. This information is acceptable.

FIRMWARE

Both the new Ellipse and new Quadra Assura/Unify Assura/Fortify Assura device models utilize the Unity 2.3 Firmware. The Unity 2.3 Firmware is based on Unity 2.0 Firmware (P910023/S279, approved May 7, 2012).

All changes to the functionality of the firmware were reviewed by a clinician to determine if the new functionality was clinically acceptable. The clinician had several clarification questions that were sent to the sponsor in the February 2013 Major Deficiency Letter. These questions were in regards to the specific functionality of the feature, what constitutes "over current", the types of lead failures that would be detected with DOCD, and the effects on patient safety and device effectiveness. The sponsor responded adequately to these questions in Amendment 1. The clinician had one further question regarding the patient alert feature of DOCD, which was resolved interactively.

The sponsor provided the Level of Concern, Firmware Requirements Specification, Device Hazard Analysis, Architecture Design Chart, Traceability Analysis, Firmware Development Environment Description, and Firmware Verification in support of the Unity 2.3 Firmware in the submission. All documentation was found to be acceptable with the exception of the Architecture Design Chart, and a deficiency was sent to the sponsor in the February 2013 Major Deficiency Letter to address the lack of information in the chart and features affected by changes made for the DOCD feature. The sponsor responded adequately to this deficiency in Amendment 1 by providing an updated chart and explanations of all changes to features affected by the implementation of DOCD. This information was found to be acceptable and there were no further concerns with the firmware section of the submission.

SOFTWARE

The Model 3330 version 17.1 software is based on Model 3330 versions 16.1.1 and 14.1.1 software (P030054/S230 and P030054/S211, respectively). It should be noted that the Model 3330 Version 17.1 software does not support wired or wireless network connections for the Merlin PCS programmer, and the existing methods for data transfer remain unchanged.

A clinician reviewed the changes made to the software to determine their clinical acceptability. In the first round of review, the sponsor had a concern about changes to the Non-Sustained Lead Noise (NSLN) feature and a deficiency was sent to the sponsor regarding this concern. The sponsor responded to this deficiency in Amendment 1; however, there were remaining concerns from the clinician and a teleconference was held on May 15, 2013 to discuss this feature. The sponsor clarified the changes and the clinician found them to be acceptable. He has no further concerns with the software section of the submission.

The sponsor provided the Level of Concern, Software Requirements Specification, Device Hazard Analysis, Architecture Design Chart, Traceability Analysis, Software Development Environment Description, and Software Verification in support of the Version 17.1 Software in the submission.

CLINICAL DATA

The sponsor did not provide clinical data to support this supplement.

CONCLUSION

All issues have been resolved regarding deficiencies sent on February 12, 2013. There are no remaining issues. The features included in these new device models are intended to protect patients with failed/broken leads. Although I do not believe that these features will completely mitigate for these failures, they seem to provide further safety benefits for patients. Additionally, I agree with the Office of Compliance's decision to move forward with the approval of this submission, although the sponsor remains on the OAI list. Therefore, I recommend approval of this supplement.