DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

MEMORANDUM

DATE: March 6, 2012

TO: The Record

FROM: [redacted], Lead Reviewer
CDRH/ODE/DCD/PDLB

SUBJECT: P030054/S196/A001
P910023/S270/A001
CorVue Thoracic Impedance Monitoring
St. Jude Medical

CONTACT: Sonali Dewan
St. Jude Medical Cardiac Rhythm Management Division
701 East Evelyn Avenue
Sunnyvale, CA 94086

Phone: (408) 522-6154
Fax: (408) 522-6440
Email: sdewan@sjm.com

RECOMMENDATION: APPROVAL

Signature	*Date*	*Signature*	*Date*
[redacted]		[redacted]	
Lead Reviewer, PDLB		Branch Chief, PDLB	

BACKGROUND

This supplement was originally submitted to request approval for a Merlin.net Version 5.0(B) and Model 3330 Version 12.1.4 Programmer software for the Model 3650 Merlin Patient Care System which will enable the CorVue Congestion Monitoring Feature in the Unify, Fortify, and Quadra family of devices. The Unify and Fortify devices with CorVue received CE mark approval on January 29, 2010; the Promote Quadra received CE mark approval April 29, 2010; and Unify Quadra received CE mark approval on March 15, 2011.

St. Jude Medical also submitted an amendment supplement to address the deficiency letter received on October 27, 2011. This supplement now requests approval for Merlin.net Version 5.0(B) and Model 3330 Version 12.1.4.2 Programmer Software for the Model 3650 Merlin Patient Care System which will enable the CorVue Thoracic Impedance Monitoring Feature in the Unify, Fortify, and Quadra family of devices.

REVIEW TEAM

The following CDRH individuals contributed to the review of this submission:

[redacted]

ODE/DCD/PDLB – lead reviewer
ODE/DCD/PDLB – original lead reviewer
ODE/DCD/PDLB – Clinical reviewer
OSB/DBS/DDB – Statistical reviewer
ODE/DCD – Informal reviewer present during team discussions

DEVICE DESCRIPTION

CorVue Thoracic Impedance Monitoring tracks potential fluid changes by monitoring intrathoracic impedance which may assist in the detection of impending heart failure.

The thoracic impedance readings work in tandem with other patient/cardiac measures to provide a more complete, objective picture of patient status.

CorVue measures the patient's intrathoracic impedance and compares it to a reference value which is a moving average. It then displays the accumulation of time that the measured impedance is below the reference impedance.

Amendment (A001) addresses the concerns raised by FDA in the deficiency letter dated October 27, 2011. The clinical study results demonstrated that CorVue is similar in performance to OptiVol; (b) (4) [redacted] For the programmer, the colored bar below the graph has also been modified in accordance with FDA's suggestions to show a constant blue color and does not transition to orange. The remote monitoring (Merlin.net) screen was further modified to remove the colored bar based on interactive feedback from FDA.

In amendment (A001), the sponsor had mistakenly included the wrong screen shot of the programmer. The correct version was emailed to FDA on January 18, 2012.

BENCH TESTING

Software

In amendment (A001), the sponsor submitted an addendum to the Software Verification Report. This addendum describes the changes made to Merlin 3330 version 12.1.4.2 as a result of the changes made to address FDA's deficiencies. This document was reviewed and found acceptable.

The sponsor also submitted another addendum interactively due to FDA requested changes to the Merlin.net Remote Monitoring System. This document was reviewed and found acceptable.

The modifications and testing completed to upgrade the software for the Merlin.net remote monitoring system and to upgrade the software on the Merlin PCS Programmer to display the CorVue feature were also reviewed in the original submission for any major concerns. The information provided by the sponsor did follow FDA's guidance document for Software Contained in Medical Devices. The information was reviewed and found acceptable.

STATISTICAL

The statistical data was reviewed by [redacted] and by [redacted] during his clinical review. The main concerns regarding the statistical analysis were that there were multiple analyses submitted that were not prespecified and FDA was unsure of how or why they were chosen. The sponsor was asked to

submit one primary analysis that is based on the prespecified analysis decided on in the IDE study and any additional analyses they wish to submit with an explanation on why they are relevant analyses to review.

The sponsor has removed (b) (4) from their displays and has replaced it with Thoracic Impedance Monitoring. Due to these changes, the statistical review to the sponsor's responses is no longer necessary as found in deficiency response review email.

CLINICAL

St. Jude sponsored the DEFEAT-PE (Detect Fluid Early from Intro-thoracic Impedance Monitoring) IDE study (G080193). This pivotal study was designed to demonstrate the safety and effectiveness of the CorVue Congestion Monitoring algorithm in the devices listed above. The study was a non-randomized, multi-center pivotal study to collect information on intrathoracic impedance measurements from St. Jude ICD and CRT-D devices. The study was conducted at 34 US centers and enrolled 162 (81 ICD and 81 CRT-D) patients. The CorVue Congestion Monitoring Algorithm was turned on at enrollment. The Congestion Trigger parameter was programmed to a fixed value of 13 days for the ICD cohort and 14 days for the CRT-D cohort. Patient follow-up visits were performed at baseline, three months after baseline, and every three months following until the completion of the study. Patient enrollment began on June 9, 2009 and ended June 30, 2010. Average duration for the CRT-D cohort was 9.2 ± 5.4 patient-months and the ICD cohort had an average follow-up time of 11.3 ± 3.9. provided a clinical consult for the file. He had an area of concern regarding the display. Because the sponsor failed to meet the endpoints of the trial, FDA was concerned that the current data does not support the use of a graph and a colored bar chart as proposed. The bar displays an orange color when congestion is detected. This is very easy for a physician to see when looking at the display and there is concern over the fact that the data shows that the feature has very low sensitivity and coupled with a high rate of false positives, this will cause the rate of detected events that are positive detections to be very low. With the current display as it is, physicians can be misinformed more easily about the acute HF status of a patient.

In Amendment A001, the sponsor's response to a clinical deficiency is summarized below:

> *The CorVue feature has been modified based on the FDA's guidance. It has been renamed CorVue Thoracic Impedance Monitoring and is an indicator of when the patient's daily impedance measure falls below the reference impedance. The modified CorVue feature is no longer represented as a (b) (4), and will track a patient's daily impedance and compare it to the patient's reference impedance.*
>
> *The transition of the colored bar from (b) (4) has also been removed. As demonstrated by the clinical data, the CorVue feature performs similarly to the current market offering. There is clinical evidence which suggests there is utility in using an impedance monitor combined with a programmable threshold to gain additional insight into the heart failure population. The remote monitoring (Merlin.net) screen was further modified (b) (4) based on interactive feedback from FDA.*

provided the clinical review to the sponsor's deficiency responses in his review memo dated February 21, 2012. He found that the modifications made by the sponsor for the programmer display were acceptable. For the Remote Monitor Display (Merlin.net), the sponsor's proposal was not acceptable. (b) (4) This concern was identified to the sponsor and resolved interactively. The sponsor made further modifications to their remote monitoring system and modified the manuals further for this change. These changes were reviewed and found acceptable.

also had a concern with using the term CorVue Threshold for the selectable duration which defines episodes sufficiently long to be logged. The sponsor was asked if a better term was available. The sponsor could not find an adequate replacement term. This response was deemed acceptable.

There are no further questions regarding the clinical data.

LABELING

FDA initially had concerns with the data presented and had requested additional information to be able to better determine the study outcomes and labelling needed to be addressed in the future. The current data did not support use of the feature as proposed. Clarified analyses were requested from the sponsor to better allow FDA to evaluate the study data and to address labelling for the feature.

The sponsor provided updated corrections to the Programmer Help Manual and the Merlin.Net Manual in Amendment A001. The changes made to the manuals were in response the sponsor's final implementation of the Thoracic Impedance Monitoring feature. During the review of the Programmer Help Manual, an error was found where the sponsor still used the term (b) (4) The sponsor was notified and a corrected page was sent by email on February 3, 2012. The corrected page was reviewed and found acceptable.

The sponsor also had to make further changes (b) (4) in the Merlin.net Remote Monitor. These changes were sent to the FDA and found to be acceptable.

There are no further concerns regarding labeling.

INDICATIONS FOR USE

The Indications for Use are identical to the 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.

The CRT-Ds 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.

HARDWARE / FIRMWARE TESTING

There were no changes relevant to this issue. This section is not applicable to this submission.

EMC/EMI TESTING

There were no changes relevant to this issue. This section is not applicable to this submission.

BIOCOMPATIBILITY

The device remains the same as the previously approved Unify, Quadra, and Fortify devices. Therefore, no biocompatibility testing was required.

ANIMAL TESTING

An animal study was performed on 8 canines to demonstrate a relationship between transthoracic impedance measurements obtained by the CRT-D device and physiologic parameters derived from echocardiography and invasive pressure measurements during induction and exacerbation of heart failure. A rapid ventricular pacing induced HF model was used in combination with a terminal acute fluid overload

HF exacerbation phase. Impedance values trended downward during the rapid pacing phase in all canines.

PACKAGING, STERILIZATION, AND SHELF-LIFE

There were no changes to the sterilization or packaging of the devices.

POST APPROVAL STUDY

SJM originally discussed the possibility of a PAS during a conference call with FDA in G080193/S002 (DEFEAT-PE IDE Study), but no SJM feels it is no longer necessary due to changes to the CorVue Thoracic Impedance feature. SJM has provided justification on why they feel the PAS is not longer beneficial.

A discussion with [redacted] was held on February 24, 2012. During this discussion it was confirmed that he no longer believes that a Post Approval Study is necessary based on the final implementation of the Thoracic Impedance Monitoring function by St. Jude Medical.

Based on this discussion and SJM's justification, FDA believes that a Post Approval Study is no longer necessary.

SUMMARY OF INTERACTIONS

Oct 27, 2011:	Major deficiency letter sent
Jan 5, 2012:	SJM response to deficiencies
Jan 18, 2012:	Email from SJM with corrected screen shot from the programmer
Feb 3, 2012:	Email from SJM with corrected Programmer Help Manual
Feb 21, 2012:	Telephone discussion with SJM to provide final decision guidance
Feb 23, 2012:	Telephone discussion with SJM where SJM's target date to submit final information is Mar 5, 2012
Mar 2, 2012:	Email from SJM with final Merlin.net manual, final Merlin.net screenshot, software verification report addendum, and PAS justification

CONCLUSION/RECOMMENDATION

All deficiencies from FDA's October 27, 2011 Major Deficiency letter were adequately addressed by the sponsor in amendment A001 and by subsequent information which was submitted interactively. After the modifications made by SJM to the Thoracic Impedance Measurement function, SJM reduced the functionality of the feature and it is no longer referred to as (b) (4) [redacted]. SJM has not claimed any clinical utility for the Thoracic Impedance measurement feature. The labeling accurately reflects the function of this feature as a "tool" that may contribute to standard management for heart failure patients. I believe that St. Jude Medical has shown that the Thoracic Impedance measurement feature is safe and can effectively measure and display Thoracic Impedance.

I recommend that the sponsor receive an **APPROVAL** letter.