Memorandum

SUMMARY of P880006/S075, P880086/S211, P910023/S279, P970013/S044, P030054/S206, P030035/S089

Ellipse and Fortify Assura ICD, Quadra Assura and Unify Assura CRT-D, Merlin PCS System Model 3330 v 14.1 Software

St. Jude Medical CRMD, Inc.

EXECUTIVE SUMMARY

This PMA supplement was submitted to gain approval for a new version of the Ellipse, Fortify Assura, Quadra Assura, Unify Assura families of ICDs/CRT-D devices. This supplement also includes an update to the Model 3330 Version 14.1 software for the Model 3650 Merlin Patient Care system. The following lists key changes included in this supplement:

- SecureSense Lead Failure Discrimination Algorithm (LFDA)
- Non-sustained Ventricular Tachycardia (NVST) Diagnostics
- RF Telemetry Enhancements
- Merlin Enhanced Diagnostic Report (MED)Enhancements
- New RF Chip
- Increased Memory

The Ellipse family of high voltage devices is based on the currently marketed Fortify family of pulse generators. In addition to the common changes listed above for both families of devices, the Ellipse family of devices are smaller then the previous device. These changes include a new organic hybrid with integrated RF circuitry, a new HV capacitor set, a new battery with QHR chemistry, a new output feedthru, new magnetic components, output and RF Flexes, and a new casted header sub assembly. In addition the sponsor is changing the maximum defibrillation energy from 40J to 36J stating that new lower energy is the same as their Current brand ICD. While they included standards testing showing that the device delivers the specified energy and duration, they did not provide a comparison between the Ellipse, Fortify, and Current devices. They also did not include any waveform analysis to show the equivalence of therapy in the original submission. FDA requested this information and they provided a waveform comparison between the three devices. This included testing waveforms at 3 different energies and with 3 different loads. The information shows that the wave form of the Ellipse device is within a 9% difference to the previous Current device and the Fortify device. This is less then the 15% tolerance limit for defibrillation pulses. The energy delivered and duration is within previously approved devices. There are no additional concerns regarding the safety of the new defibrillation pulse.

The Quadra Assura/Unify Assura/Fortify Assura family is based on the currently marketed Quadra Unify/Unify/Fortify family of pulse generators. The additional changes to this generation of device are minimal. They retain the same form factor, header, and feedthru. There is a new RF Module, an increase in SRAM memory, and a minor change to the hybrid substrate to accommodate the increased memory.

The Model 3650 Merlin Patient Care System (PCS) has been upgraded to Model 3330 version 14.1 of the software to provide support for the Ellipse/Quadra Assura/Unify Assura/Fortify Assura. This includes additional support for the LFDA and NVST features along with MED enhancements.

They have collected 860 clips from 539 patients undergoing VF testing. Of the 860 clips 481 were taken from the Right Ventricle (RV) coil-to-can vector and 379 from the RV tip-to-can. The team feels fairly comfortable with the amount of data provided. However, there were still some concerns regarding the delay in therapy with one of the animals in the animal study. In the sponsors response to our original deficiency they provided additional information regarding the delayed therapy. After analysis of the clip data the sponsor states that the second channel was undersensing due to a charging artifact in the signal. The clips were taken from devices which did not have the LFDA feature which would blank out this type of artifact. The information provided in the response was confusing and a teleconference with the sponsor was setup for April 19th, 2012. The sponsor further explained the undersensing and walked us through several scenarios and provided explanations on the delay of the therapy. They provided additional information regarding the counters and features used seem to ensure the appropriate delivery of therapy and FDA does not have any additional questions regarding this feature.

It was noted in the animal study that two canine failed to defibrillate with full charge (36J) pulses. This raised concern in the original submission that the lower energy may not be appropriate. The sponsor stated that this was due to non-ideal location of the implant in the canine. The location of the implant is based on convenience for the animal and not optimal defibrillation location. Based on the location of the implant, the defibrillation pulse optimized for humans, and the anatomical differences between dogs and humans it is expected that defibrillation would require higher energy. The discussion provided by the sponsor was adequate.

With the change in the RF devices there is also concern with full EMC testing. The EMC consults felt that there was not enough information provided in the original submission about the various wireless components present on the device. They requested additional information regarding how the testing was conducted and correlation between tested devices and the devices that are seeking approval in this submission. The consults also felt that additional labeling should be provided regarding the wireless technologies contained within the device. The sponsor responded with the requested information in amendment 1. A teleconference was held with on April 25th, 2012 to discuss the submitted information. In addition to reviewing what materials were submitted, the sponsor also gave an overview of all the wireless signals within the device and programmer. They explained what each communication device did and how the system operated as a whole. They went over the different standards that they tested and clarified which specific device model was tested. They also clarified how the tested model represents the other models in the family. The EMC consults felt that the testing completed was accurate and adequate. They felt that the labeling contained within the technical manuals was insufficient and that the device should have a strong contraindication statement about being MRI Unsafe. The sponsor includes a statement in their technical manual stating that it is not recommended to be used in an MRI environment. This wording is consistent to what is provided by other sponsors. After review of the consults concerns, it was determined that the MRI labeling provided by the sponsor is consistent to what is currently available from other sponsors and no further additions to the labeling is required.

The updated battery in the Ellipse family is also a slight concern. It seems that the longevity analysis did not include the new LFDA and NVST feature. However, in Amendment 001 they sponsor states the longevity data was established with the LFDA and NVST feature enabled. The sponsor did not mention in the original submission how often they assume the features

will be used during the lifetime of the device and how much battery drain it will cause. The provided additional information stating that the current consumption of the second channel is an additional 0.7 uA. They state that if the second channel is on for 10% of the day or 2.4 hours (which seems like a reasonable overestimate) that the impact to the device would be 10 days total for the life of the device. This seems like a reasonable overestimate of use and limited device longevity impact.

The sponsor also decided to remove Anti-Tachycardia Pacing (ATP) after the device hits ERI. This is due to the smaller battery having lower capacity. This is a concern as some patients may still need ATP prior to having their device replaced. The sponsor states in their response that after ERI, ATP is only unavailable during charging of the high voltage capacitor for VF events. That is if the device detects VF after ERI and starts to charge the high voltage capacitor, ATP therapy will not be delivered. They state that this is similar to device prior to the Unify/Fortify family or having the device with ATP disabled. High voltage therapy is still delivered as normal. The device will exhibit the same behavior for VT before and after ERI. That is ATP will still be delivered for VT episodes after ERI. After speaking with the clinical consultant, she agreed that this is not a concern since ATP is still delivered for VT and a high voltage shock is still delivered for VF.

There was also a concern with single fault testing of the battery and if it causes elevated temperatures inside the can. The sponsor responded stating this risk was evaluated in their risk analysis and was deemed critical, however, improbable. They state they have mitigated the single fault error with a shutdown separator. They also state that the battery used was previously used in the Assura devices and that manufacturing process is proven. This additional information regarding the mitigations seems appropriate and the battery consult had no further questions regarding this issue.

The review team had a few concerns with the original submission; however, the sponsor has provided additional information and testing to alleviate these concerns. After review of the new information and discussion with the sponsor the team feels this product should be approved.

BACKGROUND

The sponsor previously submitted a Pre-IDE [redacted] (b) (4)

(b)(4)

The above questions were evaluated during the original pre-IDE. The sponsor submitted the additional information in the pre-IDE and the information provided was deemed acceptable by the pre-IDE team.

INDICATIONS FOR USE

The Indications for Use for the Ellipse, Fortify Assura, Unify Assura, and Quadra Assura devices are identical to the existing St. Jude Medical pulse generators. It is included here for documentation purposes.

Ellipse Family:

The Ellipse™ DR ICD and Ellipse™ VR ICD pulse generators 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.

Fortify Assura/Unify Assura/Quadra Assura Family:

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.*

Since the Indications for Use have not changed, there are no additional concerns.

CONTRAINDICATIONS

The Contraindications are identical to the currently marketed St. Jude Medical pulse generators and is only provided here for documentation.

Contraindications for use of the pulse generator system include ventricular tachyarrhythmias resulting from transient or correctable factors such as drug toxicity, electrolyte imbalance, or acute myocardial infarction.

Since the Contraindications have not changed, are no additional concerns.

DESCRIPTION OF CHANGES

The following list presents the proposed changes to both the Ellipse and Fortify Assura/Unify Assura/Quadra Assura devices. These changes are common among both device families:

- SecureSense™ (Lead Failure Discrimination Algorithm, or LFDA)
- Non-sustained Ventricular Tachycardia (NSVT) Diagnostics
- RF Telemetry Enhancements
- Merlin Enhanced Diagnostics (MED) Report Enhancements
- New RF chip
- Increased Memory

Ellipse Family Changes

In addition to the changes above, the Ellipse family of ICDs is smaller in size compared to the Fortify devices it is based on. The following changes were also made to the internal components of the Ellipse device:

New organic hybrid with integrated RF circuitry
New HV Capacitor set
New battery with QHR chemistry
New output feedthru
Redesigned magnetic components
Redesigned output and RF flexes
New casted header subassembly utilizing a two-step epoxy casting

The following table shows the model numbers that are included in the Ellipse device family and which header configuration and energy delivered by each device:

Model Name	Model Number	Header Ports	Mechanical Specs
Ellipse™ DR Dual chamber*	CD2275-36 CD2275-36Q	2 DF-1 / 2 IS-1 1 DF4 / 1 IS-1	31 cc volume and 66-68 g weight, 36 J maximum delivered energy
Ellipse™ DR Dual chamber	CD2311-36 CD2311-36Q	2 DF-1 / 2 IS-1 1 DF4 / 1 IS-1	31 cc volume and 66-68 g weight, 36 J maximum delivered energy
Ellipse™ VR Single Chamber*	CD1275-36 CD1275-36Q	2 DF-1 / 1 IS-1 1 DF4	30/31 cc volume and 66-67 g weight, 36 J maximum delivered energy
Ellipse™ VR Single chamber	CD1311-36 CD1311-36Q	2 DF-1 / 1 IS-1 1 DF4	30/31 cc volume and 66-67 g weight, 36 J maximum delivered energy

*Note: These Ellipse™ ICD models do not contain the SecureSense™ or NSVT features.

The sponsor states that the new Ellipse devices deliver a maximum of 36J of energy to the patient. The previous Fortify device (which the Ellipse is based on) delivered 40J of energy. They state that the maximum of 36J is the same as the currently approved Current ICDs.

The changes to the hybrid include a thinner substrate and components that are only attached to a single side, instead of the double side component attache of the Fortify device. The components are now encapsulated the height of the stiffener for structural integrity and allow for the use of a moisture getter or parylene.

The RF module is now integrated onto the hybrid. It utilizes a (b) (4) chip to increase the wakeup range and improve performance in the 2.45GHz band. This band is used to initiate the RF communication. The improvements to the chip also allow for adjustments related to the 2.45GHz wakeup for the life of the device and improve the 400MHz wakeup behavior.

The Ellipse devices use a new Q High Rate (QHR) Battery provided by (b) (4)
This battery chemistry was previously used in the Unify/Fortify family of devices ((b) (4)
The sponsor states that the change is intended to provide greater device longevity and enable faster charge times. They are using the same method to attach the battery to the hybrid by using gold plated battery posts into spring connectors. However, they are resistance welding a gold plated pin to the anode wire exiting the battery instead of using a bent anode wire configuration.

The HV capacitor features a new case and lid closure design along with an updated form factor for greater packaging efficiency. The new capacitor has a nominal operating voltage of 800 volts and the capability of charging to 875 volts to deliver a 36J “Safety Shock” in the ICD.

The Ellipse family of devices uses a new casted header subassembly utilizing a two-step epoxy casting process. The sponsor states the headers are manufactured using similar molds and tooling to current processes. The header is attached using the same method of backfilling epoxy material to cast headers onto the device. This is historically the same method used to attach the header.

The header thickness has been reduced from 14mm to 10mm and incorporates new connector blocks with offset setscrews compared to the bore axes. The have also changed the electrical connections of the header from platinum-iridium wires to titanium ribbons. The electrical connection to the feedthru will be made through the laser welding of Ti weld sleeves to the Ti ribbon and the platinum-iridium wires of the feedthru.

Fortify Assura/Unify Assura/Quadra Assura Family Device Changes
The Fortify Assura/Unify Assura/Quadra Assura retain the same external mechanical package and form factor as the Unify/Quadra Unify/Fortify devices including the header and feedthru. This has limited the device changes compared to the Unify Quadra/Unify/Fortify devices that it is based on. The only internal changes are the new RF module and the increased memory size. The increased memory size required a minor change to the hybrid circuit. The sponsor notes that

the upgraded SRAM was approved for use in the Promote Q device (P030054/S713). The RF module change and the increased memory is shared by the Ellipse

The following table shows the model number and header configurations for the Fortify Assura/Unify Assura/Quadra Assura device family including the energy delivered:

Model Name	Model Number	Header Ports	Mechanical Specs
Quadra Assura™ ICD w/ CRT	CD3265-40 CD3265-40Q	2 DF-1 / 2 IS-1/ 1 IS4 1 DF4 / 1 IS-1/ 1 IS4	38-40 cc volume and 81-83 g weight, 40 J maximum delivered energy
Unify Assura™ ICD w/ CRT	CD3257-40 CD3257-40Q	2 DF-1 / 3 IS-1 1 DF4 / 2 IS-1	36 cc volume and 77-78 g weight, 40 J maximum delivered energy
Fortify Assura™ Dual Chamber	CD2257-40 CD2257-40Q	2 DF-1 / 2 IS-1 1 DF4 / 1 IS-1	35 cc volume and 75-76 g weight, 40 J maximum delivered energy
Fortify Assura™ Single Chamber	CD1257-40 CD1257-40Q	2 DF-1 / 1 IS-1 1 DF4	35 cc volume and 75-76 g weight, 40 J maximum delivered energy

SOFTWARE

Implant Software

The sponsor has updated the software embedded in the device as well as the programmer software used on the Merlin Programmer. The embedded firmware in the current submission is Unity 2.0. This version of the firmware is based on Unity 1.6+ which was approved under P030054/S173.

The firmware information for the subject device is provided in Volume IV. The sponsor states that the firmware features for ST monitoring, Chamber Onset, Far-field morphology/enhance morphology, and Store EGM libraries are not available and locked out in the Model 3330 v14.1 programmer software.

Version: Unity 2.0 – Embedded firmware for the Ellipse/Fortify Assura/Unify Assura/Quadra Assura device		
Level of Concern: Major (This is appropriate for this type of device and is consistent with other similar devices)		
	Yes	**No**

Software/Firmware Description: The proposed version of the software includes the addition of the following requirements from the previously approved software (Unity 1.6+): SecureSense - Added the ability to determine if detection of a Ventricular Tachycardia or Fibrillation (VT/VF) is due to sustained noise (such as that caused by lead failure). The physician can configure the device to inhibit therapy associated with a VT/VF due to sustained noise. Non-Sustained Ventricular Tachycardia (NSVT) Diagnostic - Enhanced ventricular rhythm detection to identify and record periods of arrhythmia that are not long enough to be classified as Ventricular Tachycardia (VT) or Ventricular Fibrillation (VF). Modified Merlin Enhanced Diagnostics (MED) – including the following: • increased the recording frequency of all yearly trends • added a yearly ST Monitoring trend that indicates when ST episodes have been detected • added a yearly trend that records when programming, interrogation, and certain clinical alerts occur • modified the Atrial Tachycardia/Atrial Fibrillation (AT/AF) Trend to include the mean duration for AT/AF Episodes lasting an entire day Include date and time for all clinical alerts used by the remote care system. Currently many of the alerts do not include the date and time. Added capability to clear stored electrograms (SEGM) based on type (VT/VF vs Auto Mode Switch EGMs). Currently the only option is to clear all SEGMs. Optimized RF communication to improve transmission of real time ECG data. Added capability to maintain counters related to VF/VT episodes for the life of the device. Currently the counter can be cleared and are not stored for the life of the device. Added a capability, in support of the new Ellipse/Fortify Assura/Unify Assura/ Quadra Assura family of devices which have a smaller battery, to disable anti-tachycardia pacing (ATP) in the ventricular fibrillation (VF) zone after the Elective Replacement Indicator (ERI) has been reached. *REVIEWER COMMENTS: The above listed changes are the major changes that are provided in the submission. While most of them were described in the submission and are related to new features that the sponsor is adding, the last change was not previously described. The sponsor indicates that the device will no longer deliver anti-tachycardia pacing (ATP) while in the VF zone after the device has entered ERI. This seems like a safety hazard as patients who have a device implanted may not receive therapy if VF is detected. The sponsor states that with the smaller battery there is not enough capacity to allow ATP and RF telemetry after ERI. They have chosen to remove therapy without any information regarding any mitigation that is taken for patients who would need therapy before device replacement. A deficiency will be addressed to the sponsor.* ***The sponsor addressed this concern by stating that ATP is still available for VT episodes and that only for VF episodes ATP will not be delivered. They also state that this is similar behavior to previous devices. After consulting the clinician regarding this issue there are no further concerns regarding safety or efficacy for this issue.***	X	

The sponsor has listed 11 other minor updates to the device firmware. Most of these updates are related to increasing the reliability of the RF link and wake up at both the 2.45 GHz and 400MHz channel. The changes also include support of the new RF chip described in the hardware changes. The new RF chip allows for an enhanced telemetry signal strength indicator. They have also made improvements with the communication link by reducing data sent and received during noisy communication. These upgrades seem appropriate for the new chip and if the EMC and EMI testing show that there are no other issues, these changes seem appropriate and I have no further concerns with the RF enhancements made in the software.

The sponsor addressed this concern by providing samples of therapy and binning "issues" with the current method. They also provided details regarding the device will behave with the new implementation. After discussion with the clinician about this change there are no further concerns with this feature. The device will reset counter appropriately and deliver therapy as needed.

There are 5 additional changes for features that are for OUS devices. These features are locked out by the Merlin 3330 programmer. The changes are listed as changes #20-#25. The changes are related to far-field morphology and ST monitoring segments which are not currently approved for US devices. Since these features are not for US devices only a cursory review was conducted to see if there would be any impact to other changes. It does not seem that there is any sort of interaction between these changes and other changes made to the firmware and there are no additional concerns regarding these specific changes.

The sponsor has also provided fixes for field related problems. These fixes are listed in table 13 in Volume IV. The changes are:

Enhanced Over Current Detection (OCD) – Currently the OCD bit is not masked during normal use. The device will set the bit if there is a detection of current greater then 60 Amps. If an external defibrillation shock is given to the patient the device may set the OCD bit thinking that there was an over current situation with the device. The sponsor is proposing masking the OCD bit and only unmasking during a device initiated shock. This would allow the device to accurately determine a device specific over current condition. The sponsor states that this is not a safety issue, since the device takes looks for an over current situation for each device generated defibrillation pulse. The external defibrillation does not affect the hardware and the device will still deliver therapy. This only produces clinical alerts within the device. This seems like an acceptable fix as they have provided additional testing and validation for this condition. It is unsure if the sponsor is going to provide fixes for devices currently in the field a general deficiency will be sent to the sponsor regarding all of the field reported issues that have been fixed.

Ensure High Voltage Lead Impedance (HVLI) measurements are only taken after implant – Currently HVLI measurements may be taken pre-implant. This will lead to incorrectly delivered alerts and patient notifications that the lead impedance is out of range. It was assumed the clinician would clear device data before implant. This change will prevent the pre-implant measurements of the HVLI to be considered for the HVLI out-of-range condition. The sponsor has provided extra validation and testing for this change and seems to be appropriate. Other then the concern about

current devices in the field, I have no additional concerns regarding this change. *Improved High Voltage charging capability during low battery situations – Currently there are 5 MDRs and 3 complaints out* (b) (4) *devices sold worldwide regarding this issue. The device will receive an interrupt from the HV hardware and proceed with a firmware reset, after the reset the firmware still detects the interrupt from the HV hardware and does a second firmware reset which causes the device to go into hardware back up mode. The proposed change allows the firmware to ignore the interrupt given by the HV hardware after the firmware requests the HV chip to turnoff. It also requires the HV hardware to be initialized after the interrupts are cleared during restart. It is unclear how long the firmware will ignore interrupts from the HV chip and if there could be possible problems with the HV hardware during this time. If there is a problem with the HV hardware and the firmware ignores the interrupt, it seems therapy would not be delivered. It is also unclear what happens to the device while in the hardware back up mode and if the device will still deliver therapy if needed. A deficiency will be addressed to the sponsor* ***The sponsor addressed this issue by stating that the interrupts are not ignored during normal operation. This would only occur if the firmware requested the HV chip to turnoff. The response the sponsor provided is adequate and there are no further concerns with this issue.*** *Corrected rounding error for Activity Sensor Rate Histogram – This change fixes an issue that caused the Sensor Indicated Rate Histogram to place events into a slower rate bin for the histogram. It is unclear from the submission how this information is used. After discussion with Dr. Brian Lewis regarding this correction and he stated that the rate bin correction is not a major issue. I do not have any further concerns with this change.* *Updated the Non-Maskable Interrupt (NMI) handler to operate during Pre-Implant (shipping) Mode – The sponsor states that the device will not correct memory errors if it is in the shipped setting state. This leads to problems with the RF telemetry function after implant. The sponsor stated this was a logic error introduced in a previous project and that they have implemented a new integration test to induce a NMI while in the shipped setting state. This seems like a reasonable solution and the additional testing provides a check to make sure this will not occur with future revisions.*		
Device Hazard Analysis: St. Jude Medical states that the risk/hazard analysis is done at the system level which is provided in Appendix 10. The risk analysis has been updated the subject devices which covers the changes included in this submission. *REVIEWER COMMENTS: The risk analysis is appropriate for this type of system. It seems all identified system hazard scenarios have been mitigated or are at an acceptable level of risk.*	X	
Software Requirements Specifications: The sponsor has provided the Software Requirement Specifications (SRS). The sponsor has included the new features that are presented in the submission. *REVIEWER COMMENTS: The requirements appear to adequately define the software functionality associated with the implant. This seems adequate for the submission as it ties in with the system traceability analysis for the requirements.*	X	

Architecture Design Chart: An architecture design chart is provided for the implant software and is included in Appendix 16. The architecture design chart is combined with the Software Design Specifications and Software Requirements Specification which includes typical diagrams and flowcharts. *REVIEWERS COMMENTS: The architectural information provided for the implant seems adequate. The changes made in this submission build on the previous architecture and do not depart from it in any major way. All of the changes were highlighted in the submission and seem appropriate. The sponsor provided information is adequate.*	X	
Design Specifications: The software design specifications are identified in the traceability analysis. Each software change has its own design specifications which are included in the traceability analysis. St. Jude Medical provided a sample of the design specification. The specification document lists all of the requirements for the software and what is needed to meet the requirements. *REVIEWER COMMENTS: The sponsor seems to have provided a complete Design specification document for the IMD and Programmer. The sponsor provided information is adequate.*	X	
Traceability Analysis/Matrix: The sponsor has provided a traceability matrix in Volume IV. This includes traceability for each software change and connection to the hazard/risk analysis for the device, the specific design specification, test number, and result of testing. *REVIEWER COMMENTS: The information provided shows the link between each change, the risk, the design specification, testing, and testing results. The table is complete. However, there are still concerns regarding some of the changes (as mentioned above). Please see deficiencies regarding Software changes that address these concerns.*	X	
Development Environment: The overall software development environment has not changed as compared to the Unity 1.6+ Firmware for the changes / enhancements in this software version. REVIEWER COMMENT: The sponsor provided information is adequate.	X	
Verification & Validation Testing: The sponsor has provided the verification and validation test results for final version of the software. The Software Verification Report is provided in Appendix 13. *REVIEWER COMMENT: The Software Verification Report contains an overview of which tests were run and the outcomes of all of the testing. All of the testing was reported as passed. Although there seems to be some issues with some of the software testing as mentioned above, the testing seems to be complete and covers the range of changes to the firmware. Also, it seems full verification of the device testing was done both as the firmware and as complete functional device. This seems appropriate for the types of changes to the device. Since all testing is stated as passing, I do not have any further concerns.*	X	

Revision Level History: In Volume IV Table 16 provides the revision history for the Unity 2.0 Firmware. This shows all the additions of various features and final release for formal verification. *REVIEWER COMMENTS: The sponsor provided information is adequate.*	X	
Unresolved anomalies: Table 15 in the submission states that there are still 2 unresolved anomalies in the implant software. The anomalies in the table do not provide a Severity Level, Probability Level, or Risk Classification and only provide justification for postponing the anomaly. *REVIEWER COMMENT: While the sponsor provides justification for postponing these software anomalies, they do not provide a Severity, Probability Level or Risk Classification. The first anomaly states that the Ventricular Pacing could exceed the maximum tracking rate for one cycle when the device enters Atrial Noise Reversion. The sponsor does not state how often the device enters Atrial Noise Reversion during typical use of the device. They state that the device hardware has a built-in protection system to prevent pacing at unsafe high rates and states that one fast pacing cycle will not induce arrhythmia. They also state that since the device is still sensing the ventricle pacing on a T wave following the sensed P is not a concern. The sponsor should provide additional information regarding how often this anomaly could occur.* *The second anomaly is related to the new Lead Failure Discrimination Algorithm (LFDA). The sponsor states that if the device detects lead failure, then an actual VF episode, followed by another positive lead noise detection, the Lead Failure Discriminator Timeout (the period of time where the LFDA will stop detecting sustained lead noise after which normal VF/VT detection and therapy will proceed) will be ignored, while the device is charging to deliver therapy, causing a possible additional delay in therapy. The sponsor does not state how often this occurs, or how long of a delay there will be before therapy is delivered. The sponsor also states: "*therapy will continue to be inhibited during the episode, as long as the device is diagnosing lead noise without undersensing." *This seems probable that with intermittent detection of lead failure, therapy could be indefinitely withheld. While tape testing provided by the sponsor shows minimal delays in therapy delivery when required, this seems like a potential issue without knowing the possible frequency of this condition. A deficiency will be addressed to the sponsor.* ***The sponsor addressed the concern by providing additional detail regarding the anomalies. They state that both anomalies have a low rate of occurrence and that the first anomaly would only result in 1 interval being paced incorrectly. The second anomaly can only occur due to a race condition and that it would result in clinically appropriate behavior. There are no further concerns with these anomalies.***	X	

Programmer Software

The sponsor has updated the programmer software to Model 3330 version 14.1. The updated version is based off the Model 3330 version 13.1.1 software and is designed to run on the Model 3650 Merlin Patient Care System (PCS) programmer. The Merlin PCS has the same intended use as before.

Version: Model 3330 Version 14.1 – Programming software for various devices.		
Level of Concern: Major (This is appropriate for this type of device and is consistent with other similar devices)		
	Yes	**No**
Software/Firmware Description: The version 14.1 software uses the version 13.1.1 software as a "predicate" version. Volume VI table 17 contains a list of all the changes. The major changes for the software include support of the Ellipse/Fortify Assura/Unify Assura/Quadra Assura devices. In total 21 changes were made to the software including 9 field related issues. The highlights of the changes include the addition of DirectTrend data for up to 1 year (previously only 3 months) for additional devices, increased upper limit of VT rate zone parameter to 260 bpm, display/printing of EGM, minor display improvements on the programmer, added missing legally marketed leads to drop down list (7170/7171 Durata). *REVIEWER COMMENTS: The table shows all of the changes and gives an engineering reason why the change was made. All changes seem reasonable for a new version of software. The field related issues seem to be relatively minor changes to display issues and minor alerts for devices. The bug fixes seem appropriate software enhancements. I have no further concerns regarding the programmer software changes*	X	
Device Hazard Analysis: St. Jude Medical does a system level device hazard analysis. Their analysis includes a section for software risks and is provided in Appendix 21. *REVIEWER COMMENTS: The risk analysis is appropriate for this type of system. All identified system hazard scenarios have been mitigated or are at an acceptable level of risk.*	X	
Software Requirements Specifications: The sponsor has provided the Software Requirement Specifications (SRS) for the programmer which includes functional requirements, user interface requirements, and non-functional requirements. *REVIEWER COMMENTS: The requirements appear to adequately define the software functionality associated with the implant. The requirements describe the user requirements that the system must meet and the description of the system features and components that satisfy these requirements. The software requirement specification defines functionality, response to inputs, and external interfaces. The information contained and provided is adequate.*	X	
Architecture Design Chart: An architecture design chart is provided for the programmer software and is included in Appendix 22. *REVIEWERS COMMENTS: The architectural information provided for the implant seems adequate. The changes made in this submission build on the previous architecture and do not depart from it in any major way. All of the changes were highlighted in the submission and seem appropriate. The sponsor provided information is adequate.*	X	

Design Specifications: The software design specifications are provided in Appendix 24. All of the changes to the design specification are also listed in the Traceability Analysis section. *REVIEWER COMMENTS: The sponsor seems to have provided a complete Design specification document for the programmer. The sponsor provided information is adequate.*	X	
Traceability Analysis/Matrix: A traceability analysis was provided in Volume VI section 6.3. The traceability analysis reports the testing requirements and software specifications for each software change in the programmer. The main change is the addition of new devices to the programmer software. *REVIEWER COMMENTS: This information demonstrates that the requirements were tested during verification and the sponsor provided information is adequate.*	X	
Development Environment: The overall software development environment has not changed as compared to version 13.1.1 for the changes / enhancements in this software version. REVIEWER COMMENT: The sponsor provided information is adequate.	X	
Verification & Validation Testing: The sponsor has provided the verification and validation test results for final version of the Model 3330 Version 14.1 programmer software The software test plan is included in Appendix 19. *REVIEWER COMMENT: The Software Verification Reports were reviewed and the results look appropriate. The testing was done in-line with their usual testing for the programmer and seems complete. They have included their standard testing along with additional testing for changes. This seems acceptable.*	X	
Revision Level History: A software revision history is provided in Volume VI Table 21 *REVIEWER COMMENTS: The sponsor provided information is adequate.*	X	
Unresolved anomalies: The unresolved anomaly is listed in Volume VI Table 20. They have a single anomaly where the new Ellipse device does not show up in alphabetical order in the Sessions Record Menu. *REVIEWER COMMENT: After review of the anomalies they all seem to be low risk to the patient. I have no further concerns regarding the anomalies listed.*	X	

The software testing seems to be complete and in-line with this type of upgrade to the product. They have followed there usual battery of tests and included updates for the RF devices. All reported anomalies seem to be a minor concern to patient safety or efficacy of the device. It seems that the testing is complete and I have no further questions.

EMC/EMI TESTING

The sponsor provided testing in accordance with EN45502-2-2:2008 and ANSI/AAMI PC69:2007 standards. They also provided electronic article surveillance system and RFID testing. The consult reviewers seem to feel that there is some variation and deviations in some of the testing. They feel the sponsor has not provided adequate information regarding which devices were tested and how they apply to all of the devices under consideration for this PMA/S. There is also concern from the consults that the wireless coexistence testing is insufficient. The device contains three separate RF components, one at 64kHz, one at 402-405 MHz, and one at 2.45Ghz. There is concern that interference may degrade performance of the communication link. According to the consult there is also a lack of labeling included in the patient/clinician manual regarding the effects of the wireless communication. In addition to the wireless labeling, the consults pointed out discrepancies regarding MRI labeling in the submission. While the sponsor is not seeking MRI compatibility in this submission for this device, there seems to be a few tests done regarding MRI environments. These seem to be reasonable concerns and it seems the sponsor has provided somewhat limited information regarding the EMC/EMI capabilities of the device.

All of the concerns regarding the EMC/EMI and Wireless testing were resolved in an Amendment to the file and through interactive review. The sponsor provided adequate testing and there are no further concerns with EMC/EMI and wireless issues.

ELECTRICAL VERIFICATION AND VALIDATION TESTING

Component Level Testing
All of the components that have been revised or changed for the Ellipse device were tested both electrically and mechanically. This includes the following components:

64K Telemetry Coil
HV Transformer/Aux Coil
HV Capacitor
Feedthru Verification
Output and RF Flexes
Battery Verification (Component and Device level)
Hybrid Verification

During the testing of the 64K telemetry coil the sponsor found an issue with the mechanical shock testing once the coil was mounted. The sponsor noticed the epoxy had cracked on one of the tested devices. They revised their drawings and added additional epoxy to the base of the coil and around coil pins and soldering pins. The sponsor then conducted a die shear strength comparison between the old method and the new method with additional epoxy. This testing showed the additional epoxy increased the shear strength by a factor of 2. One concern regarding this test is that there is no information if this process was added into the manufacturing of the part and hybrid component.

This concern was addressed by the sponsor in Amendment 1. They stated that no changes were made prior to final testing and provided updated testing information for the changes. There are no further concerns with this deficiency.

The sponsor also conducted device level testing which included the following Electrical Verification:

Functional
Detection Intervals
Sensitivity
PVARP
P-V Delay
Escape Interval

Sensing/Pacing Refractory Period
A -V Delay
Pacing Pulse (Intervals, Width, Amplitude)
Burst Fibber Pacing (Intervals, Width, Amplitude)
NIPS Intervals
Shock-on-T Fibber Intervals
DC Fibber Amplitude
ATP Intervals
Minimum BCL and Synch to R-Wave
Pacing Lead Impedance
Accelerometer
Hardware Backup Pacing

The sponsor provided two sections which included the testing listed above. One was for the Ellipse family of devices while the second was with the Fortify Assura/Unify Assura/Quadra Assura family of device. While the sponsor did provided functional testing according the applicable standards (EN 45502-2-2, EN 45502-1, etc) they did not provide a comparison of the defibrillation waveforms between the Ellipse, the current Fortify, and the Current ICD. The sponsor states that the Ellipse defibrillation pulse of 36J is the same as the Current ICD device. The current device on the market, the Fortify device, delivers a 40J defibrillation pulse. The electrical testing seems to be congruent with device features and meets the design specifications as well as the standards. It does not appear any modifications were necessary for the device to meet the standards and this testing seems appropriate. There are no additional concerns regarding the electrical functional testing of the device.

Battery Analysis

A review of the battery testing and the device longevity analysis found 3 issues with the testing. The sponsor did not include testing of the single fault hazard resulting from a short circuit test. They have also not included information as to how much the device would heat up in this type of situation. The submission included a statement that ATP is removed after the device hits ERI. This is a concern found in the firmware testing as well and will be addressed to the sponsor in the firmware portion of the deficiencies. In addition it was also noted that the longevity calculations, while meeting the 3 month specification, do not offer a wide margin of error. The DR/VR models are estimated to only last 3.6-3.9 months. There is also concern that the sponsor may not have included features such as NSVT and LFDA in the calculations for longevity. Combined with the removal of ATP pacing there is a safety concern that the device may not last as long as indicated.

The sponsor addressed all of the above concerns in Amendment 1. They provided an explanation, as mentioned above, regarding ATP after ERI. They stated that ATP is still available for VT episodes, and that VF is still treated. They provided calculations for the NSVT and LFDA features and incorporated it into the longevity calculations. They also provided appropriate mitigations for the single fault hazard. After review of Amendment 1 there were no additional concerns with the battery analysis.

MECHANICAL TESTING

The Ellipse family of devices has gone through a significant mechanical change. The overall package size has been reduced and a new header design has been incorporated. The sponsor provided mechanical testing data for the device.

In particular to this mechanical engineering review, the Ellipse cans are smaller in size than their predecessors and incorporate electrical component changes to the internal mechanical package (hybrid has a single-sided assembly with new solder pastes for component attach). In addition,

the headers of the subject devices have been modified to accommodate the newly designed cases and provide "compatibility with future designs." As indicated by the sponsor:

> "There are a total of four (4) header designs for the Ellipse family of ICDs. Two (2) headers are DR and VR headers containing standard IS-1 and DF-1 bores. Two (2) headers are DR and VR headers containing DF4-LLHH bores." The header and feedthru for the Quadra Assura/Unify Assura/ Fortify Assura family of ICDs are unchanged relative to the predecessor.

- Header thickness reduced from 14 mm on Fortify to 10mm (plus septum protrusions) on Ellipse
- New connector blocks are used on Ellipse which offset the setscrews relation to the bore axes
- Ti ribbons are used instead of Pt-Ir wires of predecessor devices
- New feedthru includes six output wires which are short on the header side and spaced to allow for laser welding to header

The sponsor completed expected tests regarding the new design however some of the test parameters and acceptance criteria were questionable. It was necessary to clarify with the sponsor if any changes were made due to field related issues and provided comment on some additional squeeze testing for the can.

The sponsor provided additional information regarding the mechanical testing in Amendment 1. After a brief interactive review with the sponsor all mechanical concerns were addressed. There are no further concerns with the mechanical review.

BIOCOMPATIBILITY/MATERIALS

The sponsor states that all of the materials for the updated device are identical to the previous devices. The sponsor has provided biocompatibility certificates stating that the devices use the same materials for the case, header, and septum assemblies. They have also included statements saying that the formulation, processing, and sterilization of each material is the exact same with no other chemical being added (e.g., plasticizers, fillers, color additives, cleaning agents, mold release agents, etc.).

Since the Ellipse, Fortify Assura/Unify Assura/Paradym RF device uses the exact same materials as the devices that St. Jude Medical currently manufactures; additional biocompatibility testing is not necessary. They have stated that there are no new chemicals or processing and that the sterilization is the same as before. There are no further concerns regarding the biocompatibility of this device.

PACKAGING, SHELF LIFE, AND STERILIZATION

According to the sponsor the updated devices will have the same 18 month Shelf-Life as the current Fortify devices. They have provided longevity calculations for the device which includes the 18month shelf life requirement.

The sponsor has a new battery type and capacity for the Ellipse device, this brings up a concern because the battery material and capacity has changed compared to the previous device. This may have an impact on the longevity and the shelf life of the device. The sponsor has completed a battery longevity calculation based on several parameters and battery depletion information provided by the battery provider, (b) (4) This information is included in the Vol III Page 316. The sponsor used several maintenance charge frequency for the capacitor maintenance in the calculations. They have stated that only 2 charges are

used per year during pre-implant and during BOL to ERI. They have also stated that there are 12 charges per year after the device reaches ERI. During the battery review it was noted that the for the new QHR battery it is not necessary to perform additional reforms for battery conditioning. The longevity estimates provided by the sponsor take into account an 18 month shelf-life.

There are a few concerns regarding the battery life testing and longevity estimates. However, it seems that the 18 month shelf-life for the battery should be adequate.

The sponsor states that the sterilization process is the exact same as before. They have verified the sterilization of the new packaging with a Bioburden Assay and Ethylene Oxide and Ethylene Chorohydrin Residuals test. The results of the test are provided in Volume III page 307. They state the following:

> The bioburden met the requirement of less than 100 colony forming units. The total bioburden CFU per device was 0.0 cfu.
>
> The EO residual met ISO 10993-7:2008 (Corr. 2009) requirements. The ethylene oxide maximum was (b) (4) and no ethylene chloroydrin residuals were detected after total extraction.

They have also stated that the packaging materials and configuration is the same as previous devices. They also state load and density configuration is the same.

The sterilization data seems to be adequate. Since the packaging and materials are the same and EtO and ECH residuals passed the standard testing I have no further concerns with their sterilization information.

MANUFACTURING DATA

The sponsor claims that the overall manufacturing of the Ellipse device has not changed compared to the previous device. They state that minor modifications were made for the single side attached hybrid (instead of dual sided). They also state that the manufacturing process for the Fortify Assura/Unify Assura/Quadra Assura devices has not changed from the previous device.

The sponsor states that the devices in this submission are manufactured similar to the previous device. However they have not provided any information regarding the differences between the manufacturing processes.

The sponsor provided the updated information regarding their manufacturing process. The updates were minor and there were no further concerns regarding the manufacturing information provided.

ANIMAL STUDIES

The sponsor provided animal testing data for the device. The animal study was done to evaluate several different features of the device including OUS features. The features include:

SecureSense
NSVT Diagnostics
SEGM Data Library
Monitor Zone Improvements

DirectTrend expansion
Far Field Morphology
Chamber Onset
Enhanced ST Monitoring Diagnostics

Of these features, only SecureSense and NSVT Diagnostics are included in the submission for approval. NSVT is a diagnostic feature which would not need evaluation in an animal study. The ST Monitoring and other features that were studied in the animal testing are for future applications or current IDE devices. The sponsor did not provide real-time data to show that the device would inhibit therapy if it detects a lead fracture. Within in the animal study it was noted that two of the canines failed to defibrillate with the highest programmed energy of 36J.

The sponsor provided waveform data in Amendment 1 and provided justification as to the failure to convert the animals. The information provided was adequate and there were no further concerns with the animal study.

LABELING

The labeling section was reviewed by the clinical consult. She did not find any major issues with the labeling; however she did notice a lack of data regarding the LFDA and NSVT features and their out of box settings. She also mentioned that there was no information on how to verify that the amplitude on the second channel is adequate. Her concerns are addressed in the clinical deficiencies.

CLINICAL DATA

Although clinical data was not included in this submission as established in the pre-IDE meeting (I090676), a clinical consult was established to evaluate the new SecureSense Lead Failure Detection Algorithm (LFDA) and Non-Sustained Ventricular Tachycardia (NSVT) diagnostic. The sponsor has provided tape (or clip) testing to show the safety and effectiveness of the LFDA feature.

> They studied 481 VF clips (RV coil-can) and 379 VF clips (RV tip-can) from 539 patients undergoing VF testing.
>
> Of these 860 clips, 7 were not detected as VT/VF with LFDA off. The remaining 853 clips were run through with LFDA on. 851 (99.8%) had VF as the initial diagnosis and the other 2 had VF as a final diagnosis. Regarding these 2 clips; (1) had undersensing on the 2nd channel due to low amplitude signals which was detected on the 3rd redetection round. Therapy was delayed by 12 cycles or 1.9 sec. (2) had oversensing on pacing stimulus prior to VF and properly diagnosed VF during redetection which delayed VF diagnosis by 6 cycles or 1 sec.
>
> Time to diagnosis was compared between LFDA on and LFDA off and found that the upper 95% confidence bound was 0.019 sec. 3 clips had a delay 1-1.5 sec and 1 clip had a 2 sec delay.
>
> They also induced noise with pocket manipulation in 90 patients to obtain 653 noise sequences. Of these, 222 had sustained noise RV coil-can, 29 had sustained noise RV tip-can, and 54 had non-sustained noise.

6 out of 251 (222+29) were excluded for not detecting VF with LFDA off and another 7 were excluded for unrealistic artifact. 91.2% (217) had successful LFDA inhibition of therapy for the duration of the episode.

For the 54 nonsustained episodes, the specificity for detection of noise was 90.4%.

The information provided by the sponsor compelling and the safety of the device fairly robust. There were only 2 events out of 853 were not diagnosed as VF initially but eventually making the correct diagnosis within two seconds. The safety of the device would be how many times the device missed or under sensed a VF episode. The feature, during tape testing only delayed therapy by less then 2 seconds (typically less then 1 second) which is clinically acceptable. Additional data from the animal testing and a further explanation of the initial settings of the device and the LFDA self-check mechanism were necessary. There were a few questions about the NSVT feature including out of box settings and programming questions. Also a concern regarding battery life with this feature on in a patient with a high number of NSVT was conveyed to the sponsor.

The sponsor responded with adequate information to address the concerns of the team. They provided additional information regarding timeout scenarios and their tape testing. After Amendment 1 and the interactive review there were no further concerns regarding the clinical information.

CONCLUSIONS

The sponsor has provided a majority of the testing required to show safety and effectiveness of the new features. The sponsor has appropriately described the changes to the device and provided adequate testing and discussion regarding the devices performance, safety, and effectiveness.