DEPARTMENT OF HEALTH AND HUMAN SERVICES **M E M O R A N D U M**

Food and Drug Administration
Office of Device Evaluation
10993 New Hampshire Avenue
Silver Spring, MD 20993

DATE: July 9, 2015

FROM: Bradley Quinn, Biomedical Engineer
CDRH/ODE/DCD/CDDB

SUBJECT: P100045/S002/A001 CardioMEMS HF System
I3 Patient Electronics CM100

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TO: The Record

RECOMMENDATION: **APPROVED (APPR)**

Digital Signature Concurrence Table	
Lead Reviewer	Bradley Q. Quinn -S 2015.07.09 22:04:40 -04'00'
Branch Chief	Shawn W. Forrest -S 2015.07.10 09:08:54 -04'00'

SUMMARY

St. Jude Medical has submitted this 180-Day Supplement for changes made to the currently approved I2 Patient Electronics (CM1000 and CM1010). The next generation I3 Patient Electronics (CM1100) includes combining the electronics and pad/pillow into a single unit for ease of use and to increase portability. There are no changes to the indications for use, sensor, delivery catheter, hospital electronics, or website.

The original submission had significant missing information related to the software review, inadequate EMC testing that did not include home-use levels for immunity testing, and concerns with device coexistence. A MAJR Deficiency letter was issued on February 26, 2015.

The sponsor responded to the MAJR deficiency letter on April 14, 2015. The sponsor provided additional software documentation, a revised EMC test report, and a coexistence test report. This software documentation and EMC report were found to be deficient. An interactive teleconference with the sponsor was held on 6/19/15. FDA discussed the EMC deficiencies with the sponsor and helped provided additional solutions. FDA also emailed additional interactive SW deficiencies on 6/22/15. The sponsor provided interactive responses to these deficiencies that were found to be adequate. All issues were resolved.

INDICATIONS FOR USE

The Indications for Use remain unchanged from the PMA Approval. They are:

> The CardioMEMS HF System is indicated for wirelessly measuring and monitoring pulmonary artery (PA) pressure and heart rate in NYHA Class III heart failure patients who have been hospitalized for heart failure in the previous year. The hemodynamic data are used by physicians for heart failure management and with the goal of reducing heart failure hospitalizations.

DEVICE DESCRIPTION

The following device description information was taken from the sponsor's narrative summary in Volume 001.

The CardioMEMS HF System is comprised of the following sub-systems:

- PA Pressure Sensor: A wireless pressure sensor that is permanently implanted within the distal pulmonary artery. The Sensor contains an Inductive/Capacitive (LC) resonant circuit within an oblong fused silica housing. The capacitance of the capacitive element within the LC circuit changes as a function of the pressure in the surrounding environment. As a result, the resonant frequency of the sensor LC circuit various inversely with the pressure in the surrounding environment.
- PA Delivery Catheter: A multi-lumen catheter used by the physician to introduce and deploy the HF Sensor in the target implant location within the distal pulmonary artery.
- Patient or Hospital Electronics: The Hospital Electronics System is used to obtain readings from the Sensor during implant and patient follow-up. The patient uses the Patient Electronics System at home to obtain their own pressure measurements. Both systems provide a means to send pressure data to a custom secure HF Database.
- CardioMEMS HF Website: A secure website that serves as the patient database so that PA monitoring information is available at all times through the Internet. Changes in PA Pressure can be used in conjunction with heart failure signs and symptoms to guide adjustments to medications.

The HF Pressure Measurement Electronics uses an antenna located in the vicinity of the Sensor to transmit a 2μs burst of RF energy at periodic intervals approximating (during acquisition) or exactly equal (after lock) to the resonant frequency of the Sensor. During the 2μs burst, the Sensor accumulates energy stored within the LC circuit. After the excitation stops (the RF burst ends), the voltage waveform across the Sensor does not go immediately to zero. Rather, there is a "flywheel" effect, and the sensor voltage keeps oscillating at the excitation frequency of the Sensor– with an exponentially decaying magnitude. The energy within the exponentially decaying sinusoid is re-radiated by the sensor, and is received by the receiver electronics in the main unit. When the main unit is transmitting at precisely the resonant frequency of the sensor, the sensor return will be at the maximum possible amplitude, and the phase of the sensor return will be close to zero degrees with respect to the transmit phase. The sensor return signal is processed via phase-locked loops to steer the frequency and phase of the transmit pulse. Once locked, the averaged frequency of the transmit signal is converted to pressure using the sensor's calibration code. The pressure data is recorded by the electronics over a time window which provides a physiologically meaningful pressure waveform. The electronics then transmits the data to a secure database via modem, wireless transmission, or other means. The database can be accessed by authorized personnel at any time via the internet, cell phone, or other connection, and the pressure waveforms can be analyzed to aid in treatment decisions.

The primary purpose of the I3 patient application software is to control the user interface for the CardioMEMS HF System. More specifically, the I3 patient application software functions are to control the measurement process, provide options for I/O and to control the display, store, and transmit data. The following system diagram identifies the I3 patient application software's role in the system, i.e., the User Interface I/O Processing software and Handheld Firmware. The user interface software and handheld processing firmware were updated to accommodate a handheld display and Wi-Fi. Timing and signal line associations were updated in the processing firmware to accommodate the hardware repackaging.

The I3 Patient Electronics is comprised of the following components:

- Enclosure (ENC):
  - Sets the form factor of the Electronics system.
  - Provides mechanical protection, EMI/EMC protection through internal shielding.
  - Incorporates the user interface touch screen.
- Antenna (ANT):
  - Wirelessly provides power to the sensor and receives signal from the sensor.
  - The antenna element used in the hospital is housed within a handheld wand.
  - The antenna element used in the home is flexible and housed within a soft pillow.
- RF Processing board (RFB):
  - The RF circuitry for interacting with the sensor.
  - Contains the RF transmitting circuitry.
  - Contains the receiver circuitry.
  - Contains the microprocessor to send the frequency data to the SBC.
- Firmware (FW):
  - The firmware for the FPGA and microprocessor on the RF Processing Board
  - Provides the Phase-lock Loop Control for the transmitter and receiver.
  - Provides the timing for the sampling and isolation switching within the receiver.
- Single Board Computer (SBC):
  - The circuit board that contains the hardware required for user interface I/O.
  - Contains the microprocessor used for the user I/O.
  - Contains the physical memory device for software and data.
- User Interface Software (UI):
  - The operating system and application software that controls the user I/O.
  - Converts data from the RF processing board to pressure data.

The following table includes excerpts of a larger table included in Volume 001, starting on PDF pg. 9/698, which compares the characteristics of the I2 and I3 Patient Electronics.

Characteristic	I2	I3	Difference	Note
Technical Feature				
Power Supply	12V 65W Medical Grade	12V 50W Medical Grade	Lower Power	
System Features				
Enclosure	Two piece unit connected by a cable	One piece unit	Redesigned enclosure	The repackaging concept is to reduce the volume of enclosure required for circuit boards and to design the new enclosure to fit inside the antenna pillow.
	Incorporates the user interface touch screen	Incorporates user interface through handheld	Screen and I/O using handheld	The user interface is on a remote handset with touch screen and push button operation.
	Designed so that the system can be placed on a nightstand table	Designed to be an integral part of the antenna pillow	Redesigned enclosure	The user interface is on a remote handset with touch screen and push button operation.
Antenna				
	Connects to the Electronics with a custom cable	Electronics enclosure is directly connected to the antenna	Redundant part	The custom antenna cable is no longer required.
RF Processing Board				
	Contains POTS or GSM modem circuitry	Contains POTS modem circuitry / GSM and Wi-Fi are optional add-ons	USB GSM and Wi-Fi	The GSM Modem and Wi-Fi Circuitry is connected via USB.
Firmware				
	Firmware to interface Remote Button to the microprocessor (SBC) user interface I/O	Remote button replaced with membrane switch	I/O using handheld	I/O is implemented using a handheld.
Usability Features				
Set-up in home	Connect power, antenna, remote button, phone line (or connect GSM antenna)	Connect power, remote button, phone line (or connect GSM antenna)	No need to connect antenna	The custom antenna cable is no longer required.

User Interface	Touch screen on enclosure	Implementation of Touch Screen	I/O using handheld	The user interface is on a remote handset with touch screen and push button operation.
Measurement Button	Remote Button Firmware	Remote Handset	I/O using handheld	I/O is implemented using a handheld.

The following are pictures of the I2 and I3 Patient Electronics:

I2 Patient Electronics

I3 Patient Electronics

REVIEW

Note: The original electronics and software review was completed under M080008/M003. P100045/S002 is the first engineering review since the original.

Electrical Safety

The sponsor provided an Electrical Safety test report from (b) (4) demonstrating conformance to IEC 60601-1:2005 + CORR. 1 (2006) + CORR. 2 (2007). This document can be found in Volume 001, Attachment A, PDF pg. 28/698.

Original Lead Reviewer Comment: The sponsor's Electrical Safety testing information appears to be adequate. The Electrical Safety test report performed by (b) (4) for SJM states that all applicable clauses passed. Additionally, all components appeared to have been included in the testing.

While the (b) (4) test report tests a non-recognized version of the Electrical Safety standard, Attachment No. 4 includes the National Deviations for United States (US) for ANSI/AAMI ES60601-1:2005 + A2:2010/(R)2012. All applicable clauses in Attachment No. 4 passed.

EMC & Wireless

The sponsor provided an EMC test report from (b) (4) demonstrating conformance to IEC 60601-1-2 ed3.0 (2007-03). This document can be found in Volume 001, Attachment E, PDF pg. 243/698. The test report evaluated the following:

- Harmonics
- Flicker
- ESD Immunity
- Radiated RF Electromagnetic Immunity
- Electrical Fast Transient/Burst Immunity
- Immunity to Surges

- Conducted RF Electromagnetic Immunity
- Power Frequency Magnetic Field Immunity
- Voltage Dips/Interruptions Immunity

The sponsor stated that all testing passed. Additionally, the sponsor identified that Radiated Emissions and AC Mains Conducted Emissions were not tested as part of this test report. The test report also defines the Essential Performance specific to the device, which stated: "Under typical operating conditions, the System shall read (b) (4) over the entire pressure range. Over the range of environmental test conditions, the electronics will measure (b) (4) ."

Original Lead Reviewer Comment: While the majority of the tests in the report complied with the standard, the Conducted RF Electromagnetic Immunity test results were out of specification in the exclusion band (b) (4) . The test report did not identify how the device performed in this band and did not identify if the device still performed safely. The sponsor will be asked to clarify the device status for this out of spec result. Please see Original Deficiency #1.b. It should be noted that for the Voltage Dip/Interruption Immunity tests, at (b) (4) , the device lost power but was restored using the ON button. While technically a failure, I believe this is acceptable since the device does not provide active therapy and the user could initiate another recording session if power was lost.

The report also identified that Radiated Emissions and AC Mains Conducted Emissions were not tested as part of the 60601-1-2 test report. The sponsor elected to perform the emissions testing covered in the following review section. Please see the following review section for the assessment of the emissions testing.

The EMC test levels used in the report are reflective of the 3rd edition of the standard and the sponsor has not evaluated the device using test levels representative of home use. The sponsor will be asked to update their EMC testing using home-use levels for ESD, Power frequency magnetic fields, Conducted RF, and Radiated RF. Please see Original Deficiency #1.c.

It is also unclear from the test report if the equipment under test included the landline, the GSM, or the WiFi dongle. The sponsor will be asked to clarify and ensure that all versions were tested. Please see Original Deficiency #1.a..

*The table on PDF pg. 293 includes the table identifying the Emissions Test, Compliance Level, and EM Environment Guidance. The bottom row includes the following statement, "The i3 Pressure Monitoring System is suitable for use in all establishments, **other than** domestic, and those directly connected to the public low-voltage power supply network that supplies buildings used for domestic purposes." There is no additional explanation of this statement and it appears to be a significant issue. Please see Original Deficiency #1.d.*

Additionally, the EMC table from the test report in this submission identifies that the Harmonic Emissions and Flicker limits are Class A. However, the three labeling manuals indicates the compliance levels are Class B. The sponsor will be asked to update their labeling with the appropriate limits supported by their testing. Please see Original Deficiency #1.e.

Finally, the sponsor has not addressed exposure to known sources of EMI. While the labeling does address some sources and warns against their interference, not all sources are identified and not all sources can be warned against (e.g., RFID). The sponsor will be asked to provide EMI testing. Please see Original Deficiency #2.

A001 MAJR Deficiency Response:

In response to Deficiency #1.a., the sponsor clarified that the WiFi dongle and GSM cellular modem were present during all EMI and EMC testing. The test report, TR-1011-022, A001

Attachment A, was updated to include this response.

In response to Deficiency #1.b., the sponsor clarified that the device continued to operate without any effect on safety or effectiveness. The sponsor also stated that while the performance goal of (b) (4) in the exclusion band), the device still operated within the overall (b) (4) product specification.

In response to Deficiency #1.c., the sponsor provided an updated EMC Test Report that included the home-use limits for ESD, Power Frequency Magnetic Fields, Conducted RF, and Radiated RF.

In response to Deficiency #1.d., the sponsor stated the original report included an error, which was revised by (b) (4) to reflect the Class B Emission Levels.

In response to Deficiency #1.e., the sponsor restated that the limits were in fact tested to Class B levels and an updated manual was provided that reflected the correct EMC information.

In response to Deficiency #2, the sponsor included a warning in the labeling against the use of the device in the presence of MRI, CT, diathermy, RFID, and ESS.

A001 Lead Reviewer Comment: The sponsor appears to have adequately clarified the issues identified in Deficiency #1.a., b, d, and e. The sponsor's inclusion of a warning against use in potentially harmful EMI environments also appears to adequately warn users against failures of the device.

However, the sponsor's updated EMC Test Report is not adequate in that there were multiple failures of the device to meet the home-use limits. For the ESD testing, the handheld component failed to meet the (b) (4) air discharge limit, the handheld display degraded over the course of the testing, and ultimately experienced a catastrophic failure and required component replacement. For the Radiated RF testing, the AC Adapter component failed to meet the (b) (4) at a specific frequency. The AC Adapter failed and the device was not recoverable.

The failed EMC Test Report was discussed with the sponsor and led to a teleconference on June 19, 2015. During the discussion, FDA explained that these limits were appropriate given the intended use environment of the device and that a satisfactory 60601-1-2 test report was needed for conformance. FDA proposed multiple solutions that included additional investigative testing, modifications to the handheld component and storage area, and a new power supply. The sponsor stated they would consider the information discussed and follow-up with FDA.

Interactive Review:

The sponsor provided an email response on July 3, 2015 in response to the June 19th teleconference. This updated response included a new EMC Test Report and a Narrative Summary that explained the design changes made to the I3 component in order for it to meet the home-use limits. The design changes included adding a protective cover on the cradle for the handheld and including (b) (4) on the handheld cable and AC Adapter cable. The sponsor's conclusion section of the narrative response indicates that the modifications will be implemented for all I3 patient electronics.

Interactive Lead Reviewer Comment: The ESD testing was repeated using two scenarios: (1) (b) (4). In the first scenario, there were multiple instances where the handheld reset and recovered on its own. In the second scenario, the handheld reset and recovered on its own, on the (b) (4) the device blanked out but was recoverable by the user, and on the (b) (4) the device blanked out but was recoverable by the user. While these are less than ideal, the fact that the majority of issues were

recoverable by the device and a few required user interventions appears to be adequate. There is no direct therapy associated with use of the device and the user would clearly be aware that the display stopped working.

The Radiated RF testing was repeated and the reading pasued and recovered on its own for horizontal application of the field in the (b) (4) *range and the unit changed font size without affecting performance at the horizontal* (b) *orientation at the* (b) (4) *range. The font size reverted after cycling the power. Again, while these are less than ideal, appear to be adequate. The failures were either self-recoverable or could be corrected by the user.*

The new EMC testing appears to be adequate.

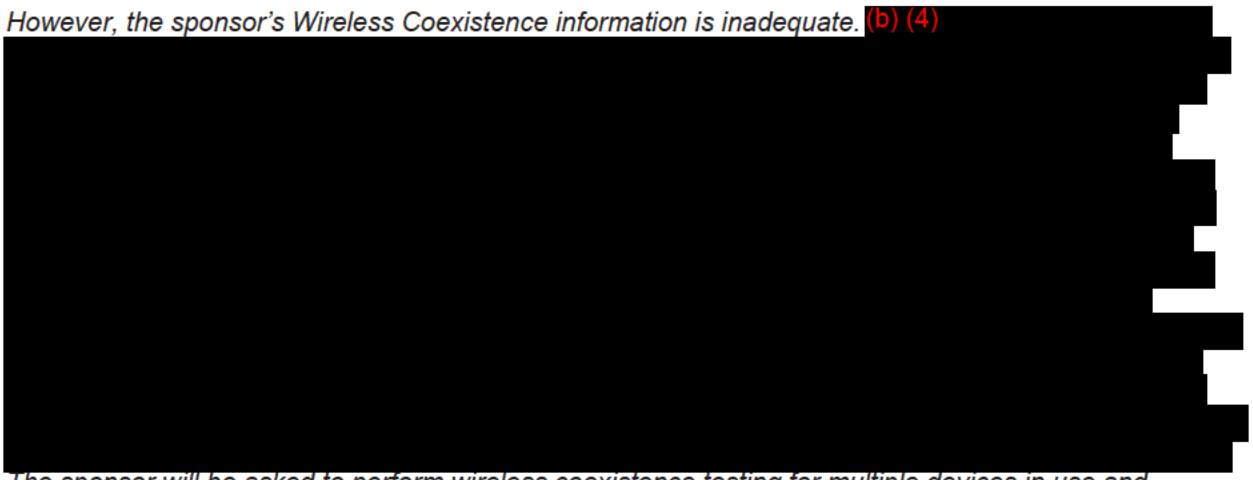
Attachment F, HF Electronics Electrical Safety and EMI/EMC Testing, is a high level overview of the electronics testing for the submission.

PDF Pg. 324/698 discusses information recommended in FDA's Radio Frequency Wireless Technology in Medical Devices Guidance Document. The sponsor addressed the wireless Quality of Service, a rationale for not performing full wireless coexistence testing, an explanation of security for signals and data, EMC, setup, and maintenance.

PDF Pg. 310/698 references Pacemaker/ICD Compatibility testing included in report TR-1000-11. Attachment F includes a very brief, high level summary of the testing. The actual test report does not appear to be included in the submission.

Original Lead Reviewer Comment: The sponsor does not fully and adequately address FDA's recommendations in the Wireless Guidance document. The sponsor's Quality of Service discussion relies on the fact that the pressure data is only a piece of HF management and care provided by the physician and that delays in data transmission would not create a hazardous situation if a patient receives standard of care treatment.

However, the sponsor's Wireless Coexistence information is inadequate. (b) (4)



The sponsor will be asked to perform wireless coexistence testing for multiple devices in use and establish the minimum separation distance and ensure it is adequate given the intended use environments. Please see Original Deficiency #3.

The sponsor states that Set-up, Operation, and Maintenance are covered in the Instructions for Use. This information is present in the revised versions of the manuals and appears to be adequate.

The sponsor's Pacemaker/ICD compatibility testing, included in TR-1000-11, does not appear to be included in the submission. The sponsor will be asked to provide this missing information. Please see

Original Deficiency #4.

A001 MAJR Deficiency Response:

In response to Deficiency #3, the sponsor cited current warnings in the labeling against two devices interfering with each other and operation of multiple devices within the same general vicinity. The sponsor also provided additional coexistence testing, I3 Coexistence Test Report, TR-1011-036, which identified that the separation distance between I3 electronics operating at the same time without artifact present on the waveform is (b)

In response to Deficiency #4, the sponsor included the test report TR-1000-011, In Vitro Study of the Interactions between a Pressure Measurement System and Implantable Medical Devices. The sponsor clarified that this testing has been previously submitted and reviewed. The sponsor also stated that there have been no changes to the power levels, communication technique, antenna type or topology of the power amplifiers between the I2 and I3 that would invalidate the original testing. The report concluded there is no interaction between the device and pacemakers and ICDs.

A001 Lead Reviewer Comment: The sponsor's response to Deficiencies #3 and #4 appear to be adequate.

The results of the additional wireless demonstrate the device's ability to operate effectively in the presence of another device/interferer. The sponsor also demonstrated the I3's ability to lock to the appropriate/linked implant and maintain the lock in the presence of an interfering I3 unit set to the same frequency. This testing appears to invalidate the information in the (b) (4), which did not include any hard evidence of failures.

The missing pacer/ICD compatibility test report was provided and the sponsor clarified that this testing was previously submitted to FDA. I agree with the sponsor's rationale that no factors have been altered that would invalidate the previous testing.

Emissions Testing

The sponsor provided Emissions test reports from (b) (4) in Volume 001, Attachments C and D, PDF pg. 203/698. Attachment C evaluated FCC Part 18 Radiated and Conducted Emissions and ETSI EN 302 510-2 Maximum ERP of Fundamental, Unwanted Emissions in the Spurious Domain, and Spurious Radiation of Receivers. Attachment D evaluated FCC Part 15.107/EN 55022 Conducted Emissions and FCC Part 15.109/EN 55022 Radiated Emissions.

Original Lead Reviewer Comment: The sponsor's Emission testing is not adequate. It is unclear why the sponsor has not performed Emissions testing in the IEC 60601-1-2 testing and why they have elected to use other emissions test reports. Attachment F included the Electronics ES and EMC overview and did not provide any specifics or justifications for why different emissions testing were performed for the i3. Additionally, the FCC testing does not take into account Immunity issues. The sponsor will be asked to provide a rationale for why the alternative testing is appropriate and explain how the results sufficiently address EMC concerns. Please see Original Deficiency #5.

I spoke with Dr. Seth Seidman about this issue in the curbside consult. He stated that Emissions should be evaluated under IEC 60601-1-2 and that a detailed rationale would need to be provided if they did not do so.

A001 MAJR Deficiency Response:

In response to Deficiency #5, the sponsor stated that (b) (4) reviewed the Emissions testing performed separately by PCTEST. The sponsor also stated that the emissions were tested against CISPR22 limits. These limits were identified as being identical to those required by IEC 60601-1-2.

A001 Lead Reviewer Comment: The sponsor's response to Deficiency #5 appears to be adequate. The sponsor clarified how the emissions testing was performed and stated that the test limits used were identical to those of 60601-1-2.

Design Verification Testing

The sponsor provided a Design Verification Test Report, TR-1011-012, in Volume 001, Attachment G, PDF Pg. 333. The test report evaluated accuracy, repeatability, noise, distance, locking capability, resolution, barometric pressure, user interface, and frequency range. The tests were completed under different stages including Final Test, New Patient Data File, Initial Implant, Follow-up, and Home Modes. The actual results for the testing are included in Appendices to TR-1011-012 and did not appear to be included.

Original Lead Reviewer Comment: The sponsor's test report only includes summary information on the results and is missing most of the supporting details. For example, the statistical rationale for the test sample sizes is included in the Test Protocol TP-1011-012. Additionally, the raw data was included in Appendices that were not part of the submission. The sponsor will be asked to provide this missing information. Please see Original Deficiency #6.

As identified in the wireless section above, FDA received (b) (4) *The sponsor will be asked to explain how they are able to identify the implanted sensor and demonstrate performance when two patients with implants share a bed and obtain their readings. Please see Original Deficiency #7.*

A001 MAJR Deficiency Response:

In response to Deficiency #6, the sponsor provided the missing appendices that included the raw data supporting the results in TP-1011-012.

In response to Deficiency #7, the sponsor clarified that there is a unique calibration frequency for each sensor and that it is paired with a specific I3 Electronics unit that is exclusive to each patient. If two patients have the CardioMEMS HF System and live together, each will have their own I3 Electronics unit.

The sponsor also referenced the I3 Coexistence Test Report that was provided in response to Deficiency #3.

A001 Lead Reviewer Comment: The sponsor's responses to Deficiencies #6 and #7 appear to be adequate.

The sponsor provided all the raw test data in Attachment G. There was a significant amount of

information that was presented in a very technical format without much explanation. It would have been preferable to have a quick primer or explanation on the way in which the data was presented. However, upon detailed examination, the various raw data appears to indicate all samples passed, which is supported by the previously submitted summary document. Ask and ye shall receive.

As stated above regarding the response to Deficiency #3, the sponsor's I3 Coexistence Test Report includes supporting testing which appears to demonstrate the device functions appropriately in the presence of other I3 units. (b) (4) [redacted].

Mechanical (including thermal and antenna/pad)

The sponsor provided a test report for IEC 60601-1-11, Medical Electrical Equipment – Part 1-11: General requirements for basic safety and essential performance – Collateral Standard: Requirements for medical electrical equipment and medical electrical systems used in the home healthcare environment, in Attachment H, PDF Pg. 362/698. This test report evaluated shock and vibration, atmospheric pressure, environmental conditions of transport and storage between uses, temperature and humidity, IP testing, Leakage current, dielectric test, push, impact, and drop. The testing was performed by (b) (4) [redacted]

The sponsor also included an I3 Mechanical Test Report, TR-1011-016, in Attachment I, PDF. Pg. 421/698, and was intended to test the mechanical/physical characteristics of the I3. Nearly all the testing in this report references mechanical testing completed per standards elsewhere in the submission (IEC 60601-1-11).

Original Lead Reviewer Comment: The sponsor's 60601-1-11 test report appears to be inadequate. PDF Pg. 381/698 Clause 12 states that the Emissions classification is Class B according to (b) (4) [redacted]. *However, this information is not supported by the current IEC 60601-1-2 test report. Additionally, the test data for 10.1.2 Mechanical Strength for Non-Transit-Operable ME Equipment, indicated that the device "passed" the Vertical Axis orientation, but had a comment that the unit did not initial function and was* (b) (4) [redacted]. *It then functioned, maintained performance, and safety after the test. A subsequent image depicts the* (b) (4) [redacted] *" and appears to be the ensuing fix. The report states the repair was allowed as the structural deficiency would be corrected in the final version of the product. It is unclear if the device was retested to obtain a passing result or how they concluded it was adequate. Please see Original Deficiency #8.*

The sponsor's I3 Mechanical Test Report appears to be adequate assuming that the IEC 60601-1-11 report is revised based on the issues previously identified.

A001 MAJR Deficiency Response:

In response to Deficiency #8, the sponsor restated that there was an error in the initial test report and that Class B Limits were tested.

The sponsor also provided a detailed explanation for why the (b) (4) [redacted] was an acceptable practice for the testing. The sponsor also stated that (b) (4) [redacted]

The sponsor also provided an updated Mechanical Strength for Non-Transit-Operable ME Equipment test report which confirmed that the repair was not relevant to the results.

A001 Lead Reviewer Comment: While the sponsor's explanation for the acceptability of the SMD teepee is slightly confusing, the repeated testing appears to be adequate to demonstrate that the test passed without the need for any modifications.

Shipping

The sponsor performed Shipping Tests per ISTA 3A 2008 in Attachment J, PDF Pg. 450/698. The testing was performed by (b) (4) Multiple test reports were provided for varying device configurations and environmental conditions.

Original Lead Reviewer Comment: The sponsor's shipping tests appear to be adequate.

Biocompatibility

The sponsor included a Biocompatibility Analysis and Letter from NAMSA in Attachment K, PDF Pg. 628/698. The Analysis identifies all the patient contacting materials and assesses the risks of patient exposure. The letter from NAMSA identifies that the sponsor has performed the appropriate biocompatibility risk analysis and that there are no new risks that require evaluation.

Original Lead Reviewer Comment: The sponsor's biocompatibility analysis appears to be adequate. There are no new risks as identified in their risk analysis and the patient contact is extremely limited.

Human Factors

The sponsor included a table identify how they have addressed FDA's Design Considerations for Devices Intended for Home Use Guidance Document on PDF pg. 21/698. This table mostly follows the various topics in the Guidance Document and identifies where and how they were evaluated. A majority of aspects were addressed under standards (e.g., 60601-1, 60601-1-2, and 60601-1-11).

The sponsor also provided a Usability and Human Factors Engineering Summary Report, TR-1011-034, in Attachment L, PDF Pg. 644/698. This document included background and historical testing, as well as Summative Testing.

The sponsor also provided a test report for IEC 62366, Medical Devices – Application of usability engineering to medical devices, Attachment M, PDF Pg. 673/698. This test report was completed by (b) (4) Testing was based on a review of Usability files provided by the sponsor and no new testing was performed by (b) (4)

Original Lead Reviewer Comment: The sponsor's Human Factors testing appears to be adequate. TR-1011-034 includes summative testing that includes objective user feedback and the users appear to be representative of actual patients. The IEC 62366 test report passed and the sponsor was found to be in compliance.

However, the sponsor's summary table on PDF Pg. 21/698, does not fully follow FDA's Home Use Guidance Document. As identified above, the sponsor's IEC 60601-1-2 test report did not use the recommended home use levels. This issue will be addressed in the review section above.

Risk Analysis:

The sponsor did not provide an overall risk analysis for the device or the I3 Electronics component. The sponsor only provided a software risk analysis.

Original Lead Reviewer Comment: The sponsor will be asked to provide a risk analysis that clearly identifies the risks related to the I3 Electronics and also identifies those risks impacted by the redesign. Please see Original Deficiency #9.

A001 MAJR Deficiency Response:

In response to Deficiency #9, the sponsor included an updated Risk Assessment in Attachment I.

A001 Lead Reviewer Comment: The sponsor included the FMEA specific to the I3 Electronics in Attachment I. This document was also updated following the design modifications for the EMC Testing and resubmitted as part of the Interactive Review.

The document appears to adequately identify and address the risks related to the device.

Software and Cybersecurity

The sponsor provided supporting software information and testing in Volumes II, III, and interactively via email. The sponsor stated that the primary purpose of the I3 patient application software is to control he user interface for the System. Specifically, this includes controlling the measurement process, provide options for I/O, control of the display, and storage and transmission of the data.

Original Lead Reviewer Comment: The software information was reviewed by Nathalie Yarkony, CDRH/ODE/DCD/CDDB and her review and comments can be found in Attachment A. The following table identifies her determination of the adequacy of the software sections.

Level of Concern: MODERATE		
	Adequate	**Deficient**
Software/Firmware Description:		X
Device Hazard Analysis:		X
Software Requirements Specifications:		X
Architecture Design Chart:	X	
Design Specifications:		X
Traceability Analysis/Matrix:		X
Development:		X
Verification & Validation Testing:		X
Revision level history:	X	
Unresolved anomalies:	X	

Her review did not include deficiencies, but I have drafted them based on her comments and included them in the deficiencies section below. Please see Original Deficiency #10.

A001 MAJR Deficiency Response:

In response to Deficiency #10.a., the sponsor provided a table comparing the programming language, OS, and OTS of each SW component. The sponsor also provided the individual Software Design Description Documents for each SW component.

In response to Deficiency #10.b., the sponsor provided responses to the various sub-deficiencies related to the hazard analysis.

In response to Deficiency #10.c., the sponsor provided responses to the various sub-deficiencies related to the software requirement specifications.

In response to Deficiency #10.d., the sponsor provided responses to the various sub-deficiencies related to the application specifications.

In response to Deficiency #10.e., the sponsor clarified that there is no difference between the distance specification between the home and hospital versions of the electronics.

In response to Deficiency #10.f., the sponsor stated the Handheld Requirements document has been updated to describe the colors used for the signal strength indicator.

In response to Deficiency #10.g., the sponsor provided a detailed assessment of the hardware platform, programming language, OS, and OTS. The sponsor also included a summary of the SW information following the layout of the FDA Guidance Document.

In response to Deficiency #10.h., the sponsor the Software Design Documents for each of the SW components.

In response to Deficiency #10.i., the sponsor stated that the Software Development Environment information is included in Section 2, Life Cycle Development Plan, for each of the Software Requirement Specification documents for the SW components.

In response to Deficiency #10.j., the sponsor clarified the qualifications of the software tester, clarified that one of the test devices was powered off during testing, and included the missing raw data used in the analysis.

In response to Deficiency #10.k., the sponsor stated that all manual and automatic steps for set-up were successfully performed. The sponsor clarified which Test IDs covered these tests and also those for potential mismatch.

A001 Lead Reviewer Comment: Nathalie Yarkony reviewed the sponsor's responses to the deficiencies I drafted based on the issues identified in her original consulting review memo. Tali's review of the sponsor's responses can be found in Attachment A. She identified 5 follow-up deficiencies that were communicated to the sponsor on 6/22/15. These additional deficiencies were related to clarifying/updating the sponsor's documentation to fully reflect their A001 response.

The sponsor provided the additional clarification requested by Tali, with the exception of #4. After an interactive teleconference with the sponsor regarding #4, it appears that the information was present in the submission albeit in a non-ideal format. Therefore, the sponsor did not need to include this information.

Tali provided a brief email for the review of the additional interactive information because it was mostly ensuring the missing information was included. She found the additional information appeared to be adequate.

I concur with Tali's assessment of the sponsor's SW responses. All SW deficiency responses appear to be adequate.

Labeling

The sponsor provided a revised Patient Guide, System Guide, and Website Guide that incorporates the changes to the I3 Patient Electronics. The sponsor also provided redlined versions via email and hardcopy CD to facilitate an easier review.

Original Lead Reviewer Comment: *The changes made to the Guides appear to be limited only to updating the information on the patient electronics, new pictures, and revised connection/updating/setup instructions based on the changes to the I3 (handheld).*

CONSULTS

CON1424729: Software – Nathalie Yarkony CDRH/ODE/DCD/CDDB
CON152577: EMC and Wireless – Seth Seidman CDRH/OSEL/DBP (curbside)

INTERACTIVE REVIEW

December 30, 2014:	Received email with clarification on the software changes and corresponding testing. Also received Labeling version with the changes highlighted.
January 7, 2015:	FDA requested additional clarification regarding software documentation and requested that all referenced/needed materials be provided.
January 12, 2015:	FDA received additional software documents from CardioMEMS.
June 19, 2015:	Teleconference to discuss EMC Test Report failures.
June 22, 2015:	FDA emailed the sponsor with additional interactive SW deficiencies.
July 3, 2015:	FDA received new EMC Test report.

DEFICIENCIES

Note: All Deficiencies from the MAJR Letter appear to be adequately resolved.

1. You provided an Electromagnetic Compatibility Test Report to demonstrate compliance to IEC 60601-1-2: 2007, Edition 3, in Volume 001, Attachment E, PDF Pg. 243/698. FDA has identified the following issues with this test report that require resolution.

    a. It is unclear from the description of the unit under test whether or not the device configuration included the additional GSM cellular modem and WiFi dongle. Please clarify whether these components were present for the EMC testing. If these components were not included in the testing, please provide a revised test report that includes evaluation of the I3 Electronics with the GSM cellular modem and WiFi dongle installed. Alternatively, you may provide a rationale for not performing the testing with these components installed.

    b. The results for the Conducted RF Electromagnetic Immunity Test stated the results were out of specification in the exclusion band (b) (4) While this may be acceptable from an operational perspective, the test report did not identify how the device performed during this failure and if there was any effect on safety. Please provide an additional discussion regarding the device status, especially with regards to safety, during this failure.

    c. You have tested your device to the test levels of IEC 60601-1-2:2007 for equipment intended for use in hospitals. The default immunity test levels specified by IEC 60601-1-2:2007 are appropriate for the general hospital environment but might not be appropriate for environments outside the hospital. IEC 60601-1-2:2007 states that "When the expected electromagnetic characteristics of the INTENDED USE environment justify

higher IMMUNITY TEST LEVELS, these higher IMMUNITY TEST LEVELS shall take precedence." Since your device is also intended for home use, it should be verified for use in this environment to ensure adequate safety and performance of the device. Please determine the characteristics of the intended use environments for your device and assure the device functions safety within these parameters. You can determine the reasonably foreseeable maximum levels of electromagnetic phenomena in your intended use environments (e.g. through study of published literature or environmental measurements). Alternatively, the Agency generally finds testing to the following immunity tests levels acceptable for the home environment:

i. ESD: ± 8 kV contact discharge, ± 15 kV air discharge

ii. Power frequency magnetic fields: 30 A/m at 50 Hz or 60 Hz

iii. Conducted RF: 3 V r.m.s outside industrial, scientific, and medical (ISM) and amateur radio bands between 0.15 MHz and 80 MHz, 6 V r.m.s. in ISM and amateur radio bands between 0.15 MHz and 80 MHz.

iv. Radiated RF: 10 V/m, 80 MHz to 2.6 GHz"

d. The table provided in the EMC Test Report on PDF Pg. 293/698 identifies the various Emissions Test, Compliance Level, and EM Environment Guidance. This table identifies that the Compliance Level for Harmonic Emissions and Flicker are Class A. Additionally, there is a comment at the bottom of the table that states "The i3 Pressure Monitoring System is suitable for use in all establishments, **other than** domestic, and those directly connected to the public low-voltage power supply network that supplies buildings used for domestic purposes. Both of these statements indicate the I3 Electronics are not suitable for their given environment. Please provide a detailed explanation of why you believe that the Class A compliance level and statement against domestic use are acceptable given that the I3 is intended to be used in a patient's home.

e. The three (3) Guides (Patient, System, and Website) included the required labeling information per IEC 60601-1-2. However, this information does not appear to reflect the actual testing and results. As identified in the deficiency above, the EMC Test Report indicates Class A compliance while your Guides indicate Class B compliance. Please revise your Guides to ensure that the EMC information is reflective of the actual test results.

2. Please specifically address exposure to known sources of Electromagnetic Interference (EMI) with medical devices such as Magnetic Resonance Imaging (MRI), computerized axial tomography (CT), diathermy, Radio Frequency Identification (RFID), and electromagnetic security systems such as metal detectors. If it is foreseeable that the device system device could be exposed to any of these types of RF sources you should assess and provide adequate mitigation, which can include performing testing, to assure safety and effectiveness. In general, the present published consensus standards do not adequately address these potential threats.

3. You provided information addressing FDA's Radio Frequency Wireless Technology in Medical Devices Guidance Document in Attachment F. This information included rationale for not conducting wireless coexistence testing, which included not having other devices in the same operating frequency bands, that two units are not anticipated to be used at the same time in the same vicinity, and that the labeling includes warnings against using multiple devices in the same vicinity. This rationale is insufficient to justify not performing coexistence testing. FDA is concerned that you have not evaluated the potential impact of other devices operating in the neighboring frequency bands (Amateur Radio and FCC Restricted) and that you have not fully

characterized the devices ability to coexist with other devices. Furthermore, the warning in the labeling is insufficient as it does not identify the necessary separation distance to ensure safe and effective performance on the I3 and CardioMEMS System. FDA is concerned with potential scenarios in which multiple patients may live in close proximity (i.e., apartment buildings) or using multiple devices in a clinic setting (i.e., multiple devices in multiple exam rooms). Therefore, please provide additional testing that evaluates the effects of the neighboring frequency bands on the I3 and provide wireless coexistence testing that demonstrates the acceptable separation distance of multiple I3 devices.

4. The information in Attachment F references a Pacemaker/ICD compatibility test report, TR-1000-11, which did not appear to be included in the submission. Please provide this test report as this information is necessary to ensure safe performance of the device and other life-saving medical therapies that a patient may require.

5. The 60601-1-2 EMC Test Report identified that Emissions testing was not performed. Instead, you have provided Emissions Test Reports in Attachments C and D that evaluate compliance to non-recognized standards from the FCC and European bodies. Additionally, no justification or rationale was provided discussing why these other standards are acceptable when demonstrating that the Emissions of the I3 system are acceptable. Therefore, please provide a revised 60601-1-2 Test Report that includes completed Emissions testing or provide a detailed explanation that compares the test procedures, acceptance criteria, and results of the FCC and other testing to the FDA recognized IEC 60601-1-2.

6. You provided a Design Verification Test Report, TR-1011-012, in Attachment G, PDF Pg. 333/698. This document included a high level summary of your design verification activities for the I3 that evaluated important parameters in different use scenarios. While the test parameters and scenarios appear to be appropriate, you did not provide the actual results that are listed as Appendices to TR-1011-012. Please provide these missing Appendices for review.

7. Design Verification Test Report, TR-1011-012, includes an evaluation of the I3's locking capability and the user interface during various scenarios including final test, new patient data file, and initial implant. A single device was used during all test scenarios. Based on the information included in the test report, it is unclear how you have evaluated the I3's ability to ensure it is interacting with the correct implanted sensor in a situation where multiple implants may be present. FDA is concerned that the device may not be able to differentiate between two patients who share a bed. Your System Guide states that "all sensors have a unique calibration", but it is unclear if this is an inherent characteristic of each individual sensor or a programed calibration value. It is also unclear based on the set-up information, if the individual sensor identifies itself to the I3. The labeling information refers to the user inputting the serial number of the sensor and inserting a thumb drive with device information. Please provide a detailed explanation that explains how the I3 is able to interact with a desired implanted sensor when multiple sensors may be present. This explanation should include clear test documentation and results.

8. You provided a test report for IEC 60601-1-11, Requirements for medical electrical equipment and medical electrical systems used in the home healthcare environment, in Attachment H, PDF Pg. 362/698. While the test report indicates that all tests passed and that the I3 is in compliance with the standard, FDA has identified the following two issues that require resolution:

    a. PDF Pg. 381/698, Clause 12, indicates that the Emissions are Class B per (b) (4) [redacted] However, as previously identified, you did not conduct Emissions testing per IEC 60601-1-2. It is unclear where the determination was made that the Emissions met Class B levels. Please clarify how the test report concluded Class B when the IEC 60601-1-2 Test Report did not evaluate emissions.

b. The test data for 10.1.2, Mechanical Strength for Non-Transit-Operable ME Equipment, indicated that the device "passed". However, there was a comment that indicated the unit did not initially function and required (b) (4) . Additionally, modifications were made to a component that resulted in a "(b) (4) that was deemed acceptable. However, there was no indication that the testing was repeated. Please provide a detailed explanation of the test failure, fix, if the test was repeated and the results, and a justification for not performing the testing if it was not repeated. Also, please provide a detailed explanation for why you did not redo the ANSI/AAMI 60601-1 Electrical Safety and IEC 60601-1-2 EMC Testing after modifying the device.

9. Your submission did not appear to include a Risk Analysis for the overall device, including information specific to the I3 component and its redesign. Please provide this missing information for review.

10. You provided software information according to FDA's Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices in Volumes 002 and 003 and interactively via email. FDA has reviewed this information and identified the following issues that require resolution:

    a. Your submission did not include a specific document addressing the software description. FDA found information related to the software description in the narrative summary in Volume 001 and in Attachment R. While a portion of this information was found to be adequate, FDA was unable to locate information describing the programming language, operating system (if applicable), and the use of Off-The-Shelf software (if applicable) for each component of the software. This information is necessary for FDA to fully understand your device software and capabilities. For example, you identify the processor for the handheld is PIC, which can be programmed using Assembly or C. However, this information could not be found. Additionally, the description in Attachment R does not describe the website. Please provide this missing information and revise the information in Attachment R.

    b. A software hazard analysis was including in Volume 1, Attachment N, and in (b) (4) 12, which was provided via email. FDA has reviewed this information and identified the following issues that require resolution:

        i. Both documents refer to TR-1011-009, I3 FMEA, which did not appear to be included in the submission or via email. Please provide this missing document.

        ii. Both documents include a table that has columns with values that are not explained or may be explained in the missing FMEA report. Please explain the following column values: S, O, D, RPN and Risk Level, SW PFORM

    The following items are for (b) (4)

        iii. The following ID's should have labeling added as a control method in the risk table: 3, 6, 12.a, and 24.

        iv. Pg. 12 – ID 7: Please provide the verification test report TR-1011-013, which did not appear to be included in the submission or the email.

        v. Pg. 17 – ID 12: This ID states that the corrective measure for software accuracy was verified across a range of operating conditions. Please define these

conditions.

vi. Pg. 24 – ID 18: FDA assumes that the logon process includes a password. Please discuss the password mechanism and how you have ensured the password is strong enough to protect from unauthorized use.

vii. Pg. 25 – ID 19: Please revise the table and indicate the encryption method used.

viii. Pg. 28 – ID 24: Please revise your labeling to include measures the user should take when the battery fails or clearly state where this is addressed in the labeling.

The following item is for Attachment N:

ix. Please clarify the encryption method used for the flash drive / thumb drive. Additionally, use of removable media storage (i.e., flash drive) exposes the device to cyber-attacks. Please revise the hazard analysis to include this risk and provide mitigations for this risk.

c. The Software Requirements Specifications were submitted in different attachments for the various parts of the system. System Software Requirements, (b) (4) addressed the overall System requirements. This document is inadequate in that it does not address the following:

i. This document did not appear to indicate how many patients the device can handle, how this number was tested including RF testing for interference, and how the device differentiates between different implanted sensors. Please provide a detailed explanation addressing these missing items.

ii. Req. No 16 on pg. 8 does not define the maximum distance between the sensor and antenna needed to optimize coupling efficiency. Please provide this information and the test results that support this distance.

d. The Application Requirements provided in (b) (4) were reviewed and found to be inadequate in that it does not address the following:

i. Section 3.2 notes that there are no special memory constraints besides those imposed by (b) (4). The (b) should be revised to clearly include these constraints.

ii. Section 3.3.4 references the initial setup of a new sensor. It is unclear if this initial setup also applies to the hospital system, and if not, how the hospital system acquires the sensor serial number. Additionally, there did not appear to be any validation testing assessing the setup. Please provide a detailed explanation of the setup and validation testing support that setup.

iii. Requirement (b) (4) is related to the handheld software version. It is unclear how the handheld unit will be updated. Please provide an explanation of the software update process for the handheld and revise the requirement to include this process. Additionally, please also update this information in (b) (4) Requirement (b)

e. The (b) (4) were provided in Requirement (b) (4) states that the unit must be able to lock to an HF sensor at 6" distance in air from the antenna. It is unclear whether there is a difference in this distance between the home and hospital

environment. Please provide an explanation of the locking distance between the two versions.

f. The Handheld Requirements were provided in (b) (4). Requirement 4662 references signal strength bar color requirements, but does not reference or discuss the actual colors. Please revise this document to reference or directly state the color requirements.

g. All the software requirement specifications documents included in the submission and received interactively via email appear to be higher level documents. The specifications did not appear to fully explain the hardware, programming language, interface and performance and functional requirements as identified in FDA's Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices. Please review the items listed in the guidance and provide a summary of the revised requirements that have been modified based on a detailed review of the guidance.

h. FDA was unable to find information addressing the recommendation for Software Design Specification as described in FDA's software guidance document referenced above. Please provide information that includes the Software Design Specifications for the device.

i. FDA was unable to find information addressing the recommendation for Software Development Environment Description as described in FDA's software guidance document referenced above. Please provide information that describes the software development for the system, including a reference and discussion of each of the components.

j. You provided the System Software Test, (b) (4), in Attachment U of the submission. In the description for the test procedure, you stated that all testing was performed by an independent individual. However, you did not state whether or not the individual who performed the testing was qualified to do so. Additionally, please clarify how two devices with the same f0 that are operating in the same vicinity do not interrupt each other. Therefore, please clarify the qualifications of the individual who performed the tests, clarify how devices will not interrupt or interfere with each other, and provide the six (6) missing test Attachments referenced in the test report.

k. You provided the Application Protocol, (b) (4), in Attachment W of the submission. Test step (b) involves the initial setup of the sensor. It appears that you have only evaluated the manual identification of the sensor in the test protocol and that you have not evaluated the automatic (via communication interface) identification of the system. Additionally, it is unclear what will happen if the sensor ID is valid but does not match the patient. Please provide a test protocol and results for the automatic identification of the sensor by the I3 and include test results or discussion on how the I3 handles mismatches between the sensor and patient.