DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION
CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

Division of Cardiovascular Devices
Pacing, Defibrillator & Leads Branch

DATE: March 14, 2011

TO: The Record

THRU: [redacted]
Chief, PDLB/DCD/ODE/CDRH

Initials Date

FROM: [redacted]

SUBJECT: P010015/S84/A01 to A04 and P890003/S189/A01 to A04
Consulta CRT-P C4TR01 and Syncra CRT-P C2TR01 Implantable Pulse Generator with Cardiac Resynchronization, Software Model 9995 (version 7.3), CareLink Monitor Model 2490G, and Model 2491 DDMA

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BACKGROUND

The 180-day PMA/S (subject file) was submitted by Medtronic (the company) dated March 30, 2010, requesting the approval for the above referenced devices, and an PMA/S Amendment 01 was submitted with additional manufacture information.

The summary of the past regulatory history is provided by the company from page 1-20 to page 1-24 located in the original PMA/S, it contains the background information for the subject file. The final approval of the subject file has to be reflected the consistency of the past FDA regulatory decisions.

FDA issued the first letter (dated, August 3, 2010) to the company with the deficiencies, the company provided the responses, and it is documented as the PMA/S Amendment 02 (dated, August 20, 2010) to the subject file.

Based on the information in the PMA/S Amendment 2, FDA issued the second deficiency letter (dated, October 14, 2010), to the company. The company submitted the PMA/S Amendment 03 (dated, November 3, 2010), and requested a face to face meeting with FDA.

The meeting was conducted on November 8, 2010, to address the 'unsolved' deficiencies of the subject file. The November 8, 2010, meeting min. is filed as part of the subject file based on the FDA policy.

The company submitted the PMA/S Amendment 4 (dated, December 8, 2010)) to address the remainder issues of the subject file.

FDA issued the third letter (dated, December 21, 2010), which is the approvable pending the on going GMP issues to be resolved.

The company received the clearance from the CDRH/OC for the GMP, and the CDRH/ODE/DCD/PDLB received the notification from CDEH/OC on March 9, 2011. Therefore, the approval of the subject file is recommended.

INDICATIONS FOR USE

NOTE: The company claims, "the indications for use" are unaffected by the purposed changes in this PMA/S, and are as follows:

For the Consulta CRT-P system:

The Consulta CRT-P system is indicated for NYHA Functional Class III and IV patients who remain symptomatic despite stable, optimal medical therapy, and have a left ventricular ejection fraction ≤ 35% and a prolonged QRS duration.

Rate adaptive pacing is provided for those patients developing a bradycardia indication who might benefit from increased pacing rates concurrent with increases in activity.

Dual chamber and atrial tracking modes are indicated for patients who may benefit from maintenance of AV synchrony.

Antitachycardia pacing (ATP) is indicated for termination of atrial tachyarrhythmias in patients with one or more of the above pacing indications.

Atrial rhythm management features such as Atrial Rate Stabilization (ARS) and Post Mode Switch Overdrive Pacing (PMOP) are indicated for the suppression of atrial tachyarrhythmias in patients with atrial septal lead placement and one or more of the above pacing indications

For the Syncra CRT-P system:

The Syncra CRT-P system is indicated for NYHA Functional Class III and IV patients who remain symptomatic despite stable, optimal medical therapy, and have a left ventricular ejection fraction ≤ 35% and a prolonged QRS duration.

Rate adaptive pacing is provided for those patients developing a bradycardia indication who might benefit from increased pacing rates concurrent with increases in activity.

Dual chamber and atrial tracking modes are indicated for patients who may benefit from maintenance of AV synchrony.

Device Descriptions

The Consulta CRT-P and Syncra CRT-P devices are multi-programmable, cardiac resynchronization therapy implantable pulse generators. The Consulta CRT-P C4TR01 system provided biventricular pacing for cardiac resynchronization therapy, monitors and regulates a patient's heart rate by providing dual chamber rate-responsive bradycardia pacing, atrial therapies and diagnostics.

The Syncra CRT-P C2TR01 system provides biventricular pacing for cardiac resynchronization therapy, monitors and regulates a patient's heart rate by providing dual chamber rate-responsive bradycardia pacing, and diagnostics.

The Consulta CRT-P and Syncra CRT-P devices contain the same firmware and use the same software application. The Consulta CRT-P device represents the most complex mechanical configuration and has the most extensive feature set. The Syncra CRT-P is similar to Consulta CRT-P with features "flexed off" in manufacturing.

THE SUMMARY FOR THE CONSULT and LEAD REVIEWERS

[redacted], *CDRH/OC/DOEB/CREB*, conducted the consult review with respect to the CDRH/OC issues, the manufacture and QSR information. The consult review memo. dated July 6, 2010, requested the additional information based on the original PMA/S submittal.

The company provided additional manufacture information in the PMA/S Amendment 01.

Another CDRH/OC consult request was generated for the responses from the company, and the CDRH/OC provided another consult review memo. dated July 13, 2010, as the final review for the manufacture information in this PMA/S. Based on the final review memo., CDRH/OC accepts all the manufacture information without any concern for the safety and effectiveness of the subject PMA/S, except the on going GMP issues. All the CDRH/OC consult reviews were placed in the file for the documentation of this file.

[redacted], *CDRH/ODE/DCD/PDLB*, conducted the clinical consult review for the clinical information in this file. The clinical review addressed the enhanced device features with respect to the patient safety. The final clinical consult review memo., dated July 2, 2010, recommended the approval of the subject PMA/S. The clinical review was placed in the file for the documentation.

[redacted], *CDRH/OSEL/DESE*, conducted the software/firmware review for the original PMA/S, and the consult review memo., dated June 22, 2010, requests additional information from the company. The company provided the additional information in the

PMA/S Amendment 2 to address those concerns (deficiencies). Another consult request was generated for the company's responses (PMA/S Amendment 2 dated September 3, 2010).

Based on the information in the PMA/S Amendment 2, FDA has additional concerns with respect to the firmware/software, and the deficiencies were generated as part of the second deficiency letter to the company.

The company submitted the PMA/S Amendment 3 (dated November 3, 2010) to address FDA concerns, and a meeting was conducted on November 8, 2010, in conjunction with the concerns in the second FDA letter. Both the meeting and the PMA/S Amendment 3 are related to the following concerns. Those are: the relationship among the RAMware, ROMware, firmware, and its configure method as part of the manufacture process. This also includes the separation between the design vs. manufacture process. The final consult review dated November 22, 2010, indicates all the above issues were addressed satisfactorily. All the consult reviews were placed in the file for the documentation.

[redacted] *CDRH/OSEL/DESE*, conducted the EMC/EMI review for the original PMA/S file. The consult review memo. (dated: July 6, 2010) requests the additional information, and the company provided the responses as part of the PMA/S Amendment 2.

Another consult review memo. dated September 15, 2010, was generated based on the information in the PMA/S Amendment 2. Three out four original issues are resolved, and additional information is required for one issue. The deficiency was generated as part of the second FDA letter to the company.

The company provided the responses as part of the PMA/S Amendment 3, and the 3rd consult review was conducted, dated December 2, 2010, and the company did not fully addressed the issue, therefore, another deficiency was generated in the FDA letter dated December 3, 2010.

The company provided the responses to the deficiency as the PMA/S Amendment 4. Based on the information in PMA/S Amendment 4, the deficiency is full addressed by the company. Therefore, all the EMI/EMC issues associated to this file are closed, and it is acceptable.

[redacted], *CDRH/ODE/DCD* conducted the animal study consult review. The final animal study consult review memo. dated July 14, 2010, pointing out the results of the past FDA regulatory decisions. In addition, clearly stated the final recommendation of the subject file should be based on the (human studies) clinical consult review, and it should not be based on the results of the animal study in the subject file. The lead reviewer agrees with the final recommendation of the animal study consult review. In addition, based on the clinical review of the subject file (please refer to the above), the FDA clinician recommended the approval of this file.

[redacted], *CDRH/ODE/DCD*, conducted the full review of this PMA/S. After completed the review of the information in the PMA/S, and the comments from the above consult reviewers, the following is the additional review summary:

> The company claims that, based on the past FDA actions, the subject file contains a few minor modifications with respect to the features of the device. However, it is the reviewer point of view that, after mixing various device features from various devices

into one, it raised the fundamental issue, the system integration process. Since the subject file is based on the existed (FDA approved) hardware platform (Consulta CRT-D), therefore, the hardware qualifications were approved by the FDA in the past. That is why, a number of the firmware issues were raised during the review process. It is reviewer's point of view that, the 'system integration' for the subject file should be based on the firmware to be integrated as part of this existed (Consulta CRT-D) platform.

In addition, the company provided the results of the animal study to justify the device features such as the sensing, etc. from various implantable devices are working well within the hardware platform (Consulta CRT-D). However, the animal study itself does not demonstrate the above due to the way it is designed. Therefore, the lead reviewer has to go back to the clinical and technical review of the subject device.

With the above, that is why an internal (FDA) post market performance search was requested/generated for the Consulta CRT-D (FDA approved) device. To make sure the post market performances of the hardware platform of the implantable device does not have any major safety issue. The internal FDA data search of the post market performance for the Consulta CRT-D is based on, from mud-2008 to end of 2009.

Based on the post market performance (Consulta CRT-D), a number of the deficiencies were generated in various FDA letters to the company. The company has responded to all the FDA deficiencies fully and acceptable.

In addition, the company modified the labeling with respect to the device longevity such as, the insertion of the pop-up window for the wireless ECG, etc.

THE DELTAIL FOR THE CONSULT and LEAD REVIEWS

PRECLINICAL/BENCH

ANIMAL STUDIES: ([redacted] **)**

[redacted] conducted the animal study consult review. The consult review memo. dated July 14, 2010, is part of this file.

The animal study consult review memo. indicates, the animal study in the subject file can NOT demonstrate the safety and effectiveness of the subject device, however, it is [redacted] point of view that, this PMA/S file can be approved as long as the clinical and branch testing are acceptable. In addition, it appears, Medtronic may not be conducting a quality animal study for the subject animal study. However, Medtronic claiming, FDA has approved the 'similar' animal study protocol is the past.

EMC/EMI: ([redacted] **)**

1. It is not clear that the performance of the LECG function was assessed during EMC testing. If you did perform this testing, please indicate

where in your submission it can be found. If you did not do so, please perform this testing and submit the results.

The company responses: The company claims, the pass for the test cases, EDVT Reports P2_V_331 and P2_V333 in page 2-418. However, the company did not provide the test reports for the above referenced test cases P2_V_331, and P2_V_333.

The Review Summary: It is important to review the full and completed test reports for this issue, to determine the test method (how it is tested) is acceptable for the leadless ECG feature under the EMC/EMI environment.

Additional information was required as part of the second FDA letter to the company. The company provided the full and completed test report as part of the PMA/S Amendment 3. The deficiency stated in the FDA letter dated December 3, 2010 as: *Deficiency #10 of the FDA letter dated August 3, 2010, asked you about assessment of the LECG function during EMC testing. You replied that EMC testing was performed during EDVT to verify the Leadless ECG (LECG or EzECG) function and rejection of known common mode and 50/60 Hz signals, and to verify acceptable LECG channel noise in the presence of telemetry. You referred to PMA-S pages 2-418, EzECG Amplifier Operation, EDVT Report P2_V_331, and EzECG: Surround Idle Channel Noise in presence of downlink, EDVT Report P2_V_333. We were able to find PMA-S page 2-418, and there was a single line stating the name of the test and "Pass". We were not able to find EDVT Report P2_V_331 or EDVT Report P2_V_333. We asked you in a letter dated 14 October 2010 to submit theses reports or indicate were in a submission they could be found.*

Based on the PMA/S Amendment 3, dated 02 November 2010, you submitted test summaries and test descriptions for the EDVT reports listed above. This was an acceptable response to our request for these reports. However, upon studying these reports, we found that other than a 50/60 Hz rejection test and verification of immunity of the inductive telemetry head, there is no description of EMC testing of the Leadless ECG function, and the documents do not provide evidence of assessment of the LECG function during EMC testing. While the inductive telemetry was active during the tests described in order to read the signals measured by the LECG amplifiers, RF telemetry was not active, there was no RF exposure source, and these tests do not appear to have been performed during EMC testing. Therefore, please explain how EMC testing of the LECG function can be considered acceptable or submit the results of EMC testing of the LECG function, including compatibility with RF telemetry.

The company responses: The company claims, the provided the rationale to justify EMC testing of the LECG, is based on the active of the telemetry. In addition, the test reports were provided as well. .

The Review Summary: Based on the information is the PMA/S Amendment 4,

this is acceptable.

2. The OptiVol feature uses an impedance measurement to monitor fluid in the chest cavity. Such impedance measurements have been found in the past to be susceptible to quasi-static electric fields. Please evaluate the immunity of the OptiVol feature to quasi-static electric fields or explain why such a test is not necessary. A quasi-static test method appears in (7)(ii)(f) of FDA draft guidance "Excerpts Related to EMI from November 1993 Anesthesiology and Respiratory Devices Branch, Division of Cardiovascular, Respiratory, and Neurological Devices" http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM081280.pdf

   The company responses: The company provided the rational of the above issue.

   The Review Summary: It is acceptable, and this issue is resolved.

3. During the review of Conducted Interference test data, you found that devices in unipolar test mode had atrial inhibition documented as observations during the test. Issue ISS-0000591 was created to track the issue analysis and closure. An investigational experiment at the lab was not able to repeat the same atrial inhibition behavior. After discussion with the test operator, it could not be confirmed that unipolar mode was actually programmed on the test device. Therefore, a full retest in unipolar programmed mode was conducted. Devices showed no indication of atrial inhibition, and this is conformant device behavior. Based on this evidence, the issue ISS-0000591 was closed.

   It is well-known that there can be variations in results of EMC testing due to random occasional alignment between the EMC test signal and the internal signals of the device. Please discuss the risk evaluation associated with atrial inhibition, explain the details of the "investigational experiment" that was performed, and explain if the test was repeated once or multiple times in an attempt to reproduce a potentially rare event. If once and if atrial inhibition is a significant risk, please repeat the test a number of times and submit the results.

   The company responses: The company provided the rationale of the above issue.

   The Review Summary: It is acceptable, and this issue is resolved.

4. During testing for immunity to helical and dynamic CT scans without R-wave injection, the device under test experienced atrial inhibition, atrial inhibition with ventricle tracking, as well as some total inhibition. All of these devices returned to the normal pacing operation within 3 pacing intervals after the CT scan. You determined that this performance of the device was acceptable. Please discuss the risk evaluation for these device

responses and explain why they are acceptable.

The company responses: The company provided the rational of the above issue.

The Review Summary: It is acceptable, and this issue is resolved.

HARDWARE/COMPONENT TESTING: ([redacted])

1. Based on the information in Vol. 2 for the [redacted] Multilayer Ceramic Capacitor (MCC), please provide the characterization test report for the [redacted]. The [redacted] characterization test report should be consistent with other MCCs which your company has provided to FDA for review in the past.

   The company responses: The company provided the characterization report for [redacted] MCC, and [redacted] is part of the [redacted] MCC family. In addition, based on the accelerated aging testing under the [redacted] test group, the subject MCC ([redacted]) can perform for a period of, [redacted] years at [redacted] C.

   The Review Summary: It is acceptable, and this issue is resolved.

2. Based on the information in Vol. 2 for the [redacted], you claim the [redacted] does not require qualification based on its similarity to the [redacted]. However, [redacted] is intended to correct five design violations in the [redacted] In addition, you have stated those five design violations were related to CAPA [redacted]; therefore, the qualification process/testing for [redacted] is required. Please provide the test report which demonstrates [redacted] is qualified and reliable to be used as a component for the implantable device.

   The company responses: The company provided the rationale for the modifications, from the [redacted] to [redacted].It is due to the CAPA [redacted] The increasing of the distances between the [redacted] and the [redacted] features, it will prevent the battery drainage. The modifications are the design lay-out only, and the design must meet the 'required' separating distance between the [redacted] and [redacted] features. With the 'new' lay-out for the [redacted] it corrected the 5 design violations in the [redacted]

   In addition, the separation distances between the [redacted] and [redacted] for the design lay-out is approved by FDA as part of the P990001/S30. The distance itself is validated in the P990001/S30, therefore, the testing for the [redacted] is not required.

   The Review Summary: It is acceptable, and this issue is resolved.

3. Based on the information in the qualification of the [redacted] ([redacted]), [redacted], you have claimed, since all three failures were not design-related electrical failures, therefore, the [redacted] meets the reliability target [redacted] per the qualification plan [redacted]. Based on above, you have totally excluded

those three failures as part of your estimated reliability rate for the [redacted]. Therefore, please identify the failure types for those three failures, and provide the reliability rate for [redacted] it should include the all failures.

The company responses: The company provided the explanation for justifying the three failures should not be accounted as part of the design failures, etc.

The Review Summary: The ODE reviewer is not fully agreeing with the company based on the responses from the company. HOWEVER, the subject device does not contain the [redacted]. The subject device is based on the [redacted] and the company made the claims that [redacted] contains the 'modifications' which is to correct the design issues in the [redacted] With above, it is ODE reviewer's opinion that, QA issues for the [redacted] should not be addressed in this file. Therefore, the response is acceptable for this PMA/S file, since the subject file DOES not contain [redacted]

4. Please confirm all the components in the subject implantable devices are in compliance with all the design rules without any exception. Otherwise, please provide the information to address the components that is not in compliance with the design rules.

***The company responses**: The company provided the design violations for the subject the device. Those are:*

[redacted]*: The company claims this design rule shall not be applied to the [redacted] the design rule is to prevent the [redacted], it can cause the [redacted]. The justification for the exception of this design rule for [redacted] is, the [redacted] for [redacted] has the same voltage potential, therefore, the required [redacted] should not be applied, it will not cause any [redacted].*

The Review: If the claim made by the company is completed, then I accept this exception for this case only.

[redacted] *The company claims this design rule shall not be applied to the [redacted] the design rule is to prevent the [redacted], it can cause the [redacted]. The justification for the exception of this design rule for [redacted] is, the [redacted] for [redacted] has the same voltage potential, therefore, the required [redacted] should not be applied, it will not cause any [redacted].*

The Review: If the claim made by the company is completed, then I accept this exception for this case only.

[redacted] *The company claims this design rule shall not be applied to the [redacted] the design rule is to prevent the [redacted], it can cause the [redacted]*

(b) (4) *The justification for the exception of this design rule for* (b) (4) *is, the* (b) (4) *for* (b) (4) *has the same voltage potential, therefore, the required* (b) (4) *should not be applied, it will not cause any* (b) (4) *.*

The Review: If the claim made by the company is completed, then I accept this exception for this case only.

(b) (4) *. The company claims this design rule shall not be accepted. It is company's point of view that the grid is off the alignment is acceptable.*

The Review: It the reviewer point of view that, if the company can accept the lower manufacture yield and/or met the manufacture quality standards, then the exception of this design rule is acceptable. Since the subject design rule affects the manufacture yield, and based on CDRH/OC's review that all the manufacture information are acceptable. Therefore, this issue is acceptable for this file.

(b) (4) *The company claims this design rule shall not be applied. The design rule requests the spacing between the* (b) (4) *to be* (b) (4) *uM for* (b) (4) *V. However, the company claims that, the voltage is* (b) (4) *V, so the* (b) (4) *uM spacing is not applicable.*

The Review: If the claim made by the company is completed, then I accept this exception for this case.

The following are the hybrid design violations (total : 6):

Number 1, Signal Integrity design rules: The company claims the signal and noise ratio may be affected, however, based on the branch test, P2_V_333,it passed the branch test.

The review: The specification allows a (b) (4) *% error margin. In addition, OSEL is requesting the full test report of the P2_V_333, please see the EMC/EMI consult review. In addition, this issue is part of the FDA second letter.*

The company provided the full and completed test report for P2_V_333 as part of the PMA/S Amendments 3 and 4.

The review: This item is closed based on the information the PMA/S Amendments.

Number 2 to 6, Manufacturability Rules: The company provided the five 'rule violations' for the manufacturability issues, and claiming all those violations are acceptable for the manufacture process.

<u>The Review:</u> CDRH/OC reviewed the manufacture information, and accepted all the manufacture and QSR information of the subject file. Based on the CDRH/OC final review memo. in the subject file, this issue is closed.

5. Based on the (b)(4) H battery information in Vol. 2 of this file, you have identified an issue which the internal battery resistance will increase over the time/charge, and it will impact the device longevity after the 3rd year of the implant. Your proposed solutions to resolve this battery issue are: Modify the ERI from (b)(4) V to (b)(4) V, and modify the EOL from (b)(4) V to (b)(4) V; Implement a coating to the surface of the cathode current collector to reduce the growth of the resistive film; Increase the battery internal resistance specifications, therefore, the test results can be classified as pass. In addition, you have claimed the (b)(4) H Battery testing is not required since the above solutions were implemented in the 26H battery. Based on above, please address the following:

    a. Please provide the test report which demonstrates the subject device can function correctly for a minimum of 90 days after ERI is set. This includes the leadless ECG is activated, three or more wireless remote telemetries between the implanted and external devices, and various pacing settings as you have listed in the battery modeling/longevity prediction. This test report should also address the reliability of the battery performances after ERI is set, specifically, the battery information in the submittal demonstrates the growth of the resistive film is not at a constant rate.

    <u>The company responses:</u> The company claims the subject of this item is TWO issues. Those are: (a). The battery will increase the impedance during the life of the battery; (b). The battery will increase the impedance started at (b)(4) V until EOL. In addition, the company provided the warning statements for the leadless ECG usage and turn-off the leadless ECG feature at the ERI; Modified the ERI setting, etc.

    <u>The review:</u> Since the company divided the increasing of the battery internal impedances into two unique issues. Therefore, based on the TWO issues by itself, it is acceptable. Specifically, the battery is continuously increasing the internal impedances during the life of the battery, this is correct for all the battery, but... In addition, FDA has approved the PMA/Ss that is related to the 'surprised' additional impedance increasing started at (b)(4) V. With above, the reviewer accepts the company responses due to nature of this issue, which is related to the past FDA decisions.

    b. Based on the information in Vol. 4, page 4-225, etc., please confirm the device longevity tables in the labeling are based on the 18 months shelf life, not 5. Otherwise, please modify your labeling to include the information in Table 4 on page 4-225, and clearly indicate the labeling for the device longevity tables are based on a 5 months shelf life, not 18.

    *<u>The company responses:</u> The company corrected the labeling by using a **5** months shelf-life, not 18 months for the device longevity notes. Also, insert the information, which indicates that, if the shelf life is greater than 5*

months period, then the decrease of the device longevity can be up to 10.1%.

The review: Since the company modified and corrected the labeling, therefore, based on the FDA policy, this is acceptable.

c. Please include the remote leadless ECG feature as part of the device longevity calculation for your labeling.

The company responses: The company provided a pop up window for the warning statements in the programmer, which indicates ***the operation of the less ECG for 14 days will reduced the implantable device's longevity by 7 days, and asking the user to accept this condition****.*

The review: Since the company modified the original labeling information, and the user MUST accept the pop-up window, therefore, based on the FDA policy, ***this is acceptable, even the less ECG drains on the battery.***

d. Please provide the chemical reactions for the (b) (4) H battery.

The company responses: The company provided the chemical reactions for the battery. It is located in the PMA/S Amendment 2, page 1-95.

The review: Since the company provided the information, it is acceptable, therefore, this issue is closed.

e. Based on the report, "Consulta EDVT Assessment for (b) (4) (b) (4) Battery", it was recommended the subject device should perform the characterization testing to verify the POR feature. Please provide this characterization test report for review.

The company responses: The company provided the test reports for this issue.

The review: Since the company provided the information, it is acceptable, therefore, this issue is closed

6. You have claimed the Digital Sensing Processing (DSP) and other hardware were approved by FDA, therefore, it is acceptable to be used as part of the implantable device without performing the Electrical Design Verification Testing (EDVT) as you have indicated in Table 2-3 on age 2-274. However, based on the MDR search, it shows a high number of the MDR issues that is associated to sensing feature. In addition, FDA does not agree with you that the animal study can demonstrate the safety and effectiveness of the subject device. Therefore, the full and complete EDVT testing shall be required. In addition to the EDVT testing, please address, how and what additional steps that you have taking to assure the safety and effectiveness of the implantable device, since a number of the MDRs indicates the replacement of the implantable device was the solution for the correcting the sensing issues.

The company responses: *The company provided the information which point to other company' sensing performances, the product report for the past, etc. In addition, the company is claiming the sensing issues are within the expected performances.*

The review: This issue will be linked to the testing of the firmware/RAMware, since the digital sensing is part of firmware/RAMware codes.
This issue was stated to the company again as part of the FDA letter (dated October 14, 2010). The company submitted the additional information to address the DSP issue as part of the PMA/S Amendment 3, and present the 'summary' responses during the November 8, 2010 face to face meeting.

The review: *The company provided the information for the post market performance of the market approved devices that contains the DS; and the company opened a CAPA for the header of the implantable deices, which is one of the causes for the sensing issue. In addition, the company is claiming that, the number of the known MDRs that is related to the sensing issue is very low. This information provided by the company which demonstrates the very low percentage of the post market events that is related to the sensing issue. With above, the reviewer is recommending to close this issue for now, unless the future MDR shows otherwise.*

7. Please confirm the version of the OptiVol in the subject device is market approved.

   The company responses: The company claims the version of the OptiVol in the subject device is approved.

   The Review Summary: It is acceptable, and this issue is resolved.

SOFTWARE/FIRMWARE: ([redacted] **)**

The following is the review of the deficiencies stated in the FDA letter dated August 3, 2010.

1. Based on the two tables, 1-10 and 1-11 in Vol. 1 of the file, which describe new features of the Consulta and Sensa. Please explain how each of these features is supported by the firmware, with any modifications made to the requirements, specification, implementation, and testing of the firmware. If the firmware was not changed, please explain how modification of the firmware was avoided. We need this information to evaluate the safety and effectiveness of the firmware information in this submittal.

   The company responses: The company claims the version of the firmware and RAMware ARE NOT UNIQUELY corrected. In addition, the company claims ONE version firmware can be used by pacemaker, CRT-P, CRT-D, and ICD.

In addition, the company claims the firmware in the subject is approved by FDA without any modification for the subject file. All the 'enhanced/modified' features in the implantable devices (CRT-Ps) of the subject file were 'configured' as part of the manufacture process. Since the firmware was NOT modified, therefore, firmware testing will not be required. In addition, the company claims the enhanced and modified implantable features in the subject file are classified as the minor change, and the RAMware configured as part of the manufacture process, therefore, branch testing is NOT required.

The Review Summary: Based on the above, it raised additional questions/concerns. Those questions were generated in the second FDA letter to the company.

2. Based on the firmware information in Vol. 3 of the subject file, it appears the firmware version numbers are not uniquely correlated with the RAMware version numbers. Please provide the explanation for this. In addition, please provide the unique firmware version numbers for the last three unique RAMware versions and this must include the increment numbers for the RAMware.

The company responses: The company claims the version of the firmware and RAMware ARE NOT UNIQUELY corrected.

The Review Summary: It is NOT acceptable. Therefore, additional questions/concerns were generated as part of the second FDA letter.

The following is the review of the deficiencies stated in the FDA letter dated October 14, 2010

1. Based on your responses to the deficiencies #8 and #9, you have indicated the firmware and RAMware versions are not uniquely correlated. Please address the following:

    a. Please confirm the specific firmware version in the subject file is, Version 21.1 for the Consulta CRT-P C4TR01 and Syncra CRT-P C2TR01 Implantable Pulse Generators (the subject device). In addition, please confirm the firmware version 21.1 is specific configuration to an unique RAMware version for the subject device, or is it for multiple RAMware configurations? If the firmware version 21.1 contains multiple RAMware configurations, please provide the explanation.

    b. You have claimed the firmware version for the subject device was not changed, and the RAMware was modified for the enhancements of the device features in the subject device. Please provide the explanation to address your design process for achieving this. In addition, FDA may have additional questions in on this issue.

c. Please address, is the firmware ever changed or is the RAM ware always used as an overlay to the pre existing firmware when updating the device features?

d. Please provide the explanation to address, exactly how the RAMware and firmware come together to form the final embedded medical device software component that is loaded on the subject device.

e. Please provide the explanation to address, how the version of the embedded medical device software be tracked.

f. Please confirm the firmware and the RAMware designed and validated using appropriate 21 CFR 820.30 design controls.

g. Based on your claim, all the RAMware versions are configured as part of the manufacture process, not design process. FDA may not fully agree with you. Therefore, please explain your process, which portions of the change of these items (firmware, RAMware, and configuration) are considered a "design change" and which portions Medtronic's considers a manufacturing change. FDA may have additional question on this deficiency in the future.

h. What is Medtronic protocol for the "embedded software validation" of multitude of the various embedded device software configurations that are possible using the firmware, RAMware and configuration approach?

i. Based on your explanation that the firmware for Gen2 devices was intended to cover all models. Please explain how your firmware can provide guaranteed temporal determinism, if some of features are disabled, so that timing is not affected. In this question we want to know not that the feature is configured as intended, but that its timing has been verified by your development process. We need this information to evaluate the safety and effectiveness of these new devices.

j. Based on your response to the deficiency #8, with your explanation that the firmware for Gen2 devices was intended to cover all models. In your response, you state that the Gen2 family models all share the same collection of possible features. Please explain how your process has established that all selectable features are compatible and safe in every combination. We need this information to evaluate the safety and effectiveness of these new devices.

Since the RAMware and firmware are not uniquely related to each other, therefore, all the branch tests for the subject device shall be based on the final configured RAMware version for the appropriated verification and validation of the device performance. Please provide the full and completed branch tests based on the final configured RAMware version of the subject device. This includes, but not limited to, system tests, system integration tests, and device feature tests.

The company responses:

The company claiming, a key factor to the Gem2 design strategy was use of common components across the system. A common version of firmware, ROM Baseline 21.1 with RAMware Increment 3, is used for all 23 models within the Gen2 family of models. The Gen2 family of models includes 5 device types: CRT-P, IPG DR, CRT-D, ICD DR, and ICD VR.
Medtronic stated that all firmware (ROM code and RAMware) is developed and verified under the design control process. There are 23 Configuration Files (Device Memory Files), one for each model, that define the Flex Configuration Parameter Values (visibility of features to the clinician) and Shipping Parameter Values (specific to feature control: features "on" and "off"). Medtronic explained that the bulk of the code is in ROM. RAMware Increment 3 uses about (b) (4) *of RAM. The ROM, RAMware, and Configuration Files are all developed under the design control process, version controlled and then transferred to manufacturing.*

Medtronic clarified the integrated circuits: (b) (4), (b) (4), (b) (4) *and whether the* (b) (4) *products used these ICs. The* (b) (4) *IC is the microprocessor used across the Gen2 family of models. The D273 IC is used to control operation of distance telemetry in the Gen2 defibrillation products, but is not part of the Consulta and Syncra CRT-P products. The* (b) (4) *IC is the microprocessor used in the Adapta/Versa/Sensia product line.*

The company clarified the version of the RAMware and the ROMware. Medtronic stated the Baseline 21.1 ROM code was locked down, what was the date; RAMware Increment 3 was locked down and Medtronic responded 2008. Medtronic noted that all Gen 2 devices have Baseline 21.1 ROM code with RAMware Increment 3.

Medtronic explained the definition of Firmware, ROM, RAMware and Configuration files. Medtronic stated that firmware includes ROM code and RAMware. Specific to feature control configuration files mean features "On" vs "Off" and these files are not considered code. The configuration file values are loaded into RAM, but are fixed. The fixed values are data, not code.

Medtronic explained the how to validate the final configuration for address FDA OC commented that from a compliance standpoint it seemed as if Medtronic was reaching back into the manufacturing steps and changing parameters without validation of the firmware. FDA asked where RAMware changes get made. Where do you make enhancements, corrections, and patches? Medtronic responded that if other changes were necessary, Medtronic would release another RAMware Increment. Charge Timeout RAMware increment 4 for ICDs is an example. FDA stated that the use of RAMware for corrections is consistent with the industry. This issue is closed.

In addition to the above, FDA stated that it is important that the final ROM + RAMware code is tested as one and the models need to be fully tested. FDA asked for confirmation that RAMware does not exist independently of ROM. FDA OC perspective is that manufacturers tend to incorporate changes at manufacturing that are really design changes, potentially bypassing design controls. Medtronic needs to

make it clear that this isn't the case with RAMware and configuration files. Medtronic confirmed that changes to ROM code, RAMware and configuration files are considered design changes made under the design control process; and ROM code and RAMware are verified together. FDA OC asked Medtronic to confirm that the configuration is not varied per patient and that there are just 23 permutations – one for each model. FDA OSEL clarified that there are 23 permutations used, but many more are possible. Medtronic confirmed that both of these are correct. Through the explanations given during the meeting (11/8/2010), FDA indicated that they understood and that there were no further questions.

The following tabbe is provided to summarize firmware versus configuration.

		Location		Type		Installed at Manufacturing	Modified after Manufacturing
		ROM	RAM	Code	Data		
Firmware *(developed and verified under design control)*	**ROM code** (b) (4)	(b) (4)					
	RAMware (b) (4)						
Configuration *(developed and verified under design control)*	**Feature Visibility on Programmer** *(Flex Configuration Parameter Value)*						
	Features On/Off						
	HW Capability *- IPG or ICD, and 1, 2, or 3 chambers (Flex Configuration Parameter Value)*						

Medtronic explained that the firmware requirements, design, and code are model independent; firmware is designed to use the same Event Processing Flow (independent of model); and firmware verification strategy is model independent. There is model independence because the two aspects of the device configuration that affect the firmware are: 1) Features on or off (to FW, a feature programmed off by clinician is the same as a feature configured off); and 2) Hardware capability (IPG or ICD, and number of chambers). Firmware requirements define these aspects of the device configuration that affect the firmware. Therefore, FW verification achieves full requirements and code coverage. Firmware has been tested fully/completely for every device in the Gen2 family of models.

FDA Question (11/8/2010 meeting): Since the firmware is the same for each model and RAMware is able to overlay/correct ROM. How do you address "dead code"? CPU timing is affected by dead code.

Medtronic explained that firmware is fully verified; RAMware verification ensures the RAMware logic is correct, including any ROM code bypass; and timing analysis

is updated to account for RAMware. FDA asked if the analysis included RAMware. Medtronic confirmed that the timing analysis included the RAMware as well as ROM. Medtronic stated that the timing analysis submitted included Baseline 21.1 with RAMware Increment 3. Medtronic described what the worst case was: a combination of high event frequency, multiple timers expiring simultaneously, maximum number of features enabled, etc. FDA asked the % of bandwidth used. Medtronic responded that it depends on what metric you are interested in assessing: average CPU bandwidth is about (b) (4) *%, although continuous execution time can be* (b) (4) *ms or longer at some points. FDA asked what the value would be from a worst case stress situation – what is the maximum usage. Medtronic replied* (b) (4) *ms of CPU time (the exact numbers are provided in the timing analysis report).*

FDA Question (11/08/2010 meeting): *Is it possible to test the timing without the debugger? The debugger does not represent real-timing. Set the device to maximum load and test the device itself. The debugger only gives you an indication of timing.*

Medtronic explained Debugger tool provides op code level visibility and does not disrupt firmware timing in CPU simulator environment.

The review:

Based on the above information provided by the company, this deficiency is resolved, and it is acceptable.

CLINICAL DATA:

Based on the clinical consult review, no issue was raised for this PMA/S.

CONCLUSION

Based on the information in the file, the company has provided appropriate data to demonstrate the subject device is safe and effective.

RECOMMENDATION – I recommend that the supplement be **Approval.**

[redacted] _____
Date
Reviewer

[redacted] _____
Date
Chief, PDLB