DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
466 Fernandez Juncos Ave. San Juan, PR 00901-3223 (787)-474-9500 Fax:(787) 729-6809 Industry Information: www.fda.gov/oc/industry	12/10/2009 - 03/10/2010* FEI NUMBER 3004369318

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Manuel A. Santiago, Vice President Medtronic Puerto Rico Operations Company

FIRM NAME	STREET ADDRESS
Medtronic Puerto Rico Operations Company	Road 31 Km 24ceiba Norte Industrial Par
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Juncos, PR 00777	Device manufacturer

This document lists observations made by the FDA representative(s) during the inspection of your facility. They are inspectional observations, and do not represent a final Agency determination regarding your compliance. If you have an objection regarding an observation, or have implemented, or plan to implement, corrective action in response to an observation, you may discuss the objection or action with the FDA representative(s) during the inspection or submit this information to FDA at the address above. If you have any questions, please contact FDA at the phone number and address above.

The observations noted in this Form FDA-483 are not an exhaustive listing of objectionable conditions. Under the law, your firm is responsible for conducting internal self-audits to identify and correct any and all violations of the quality system requirements.

DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

OBSERVATION 1

Complaints representing events that are MDR reportable were not promptly reviewed, evaluated, and investigated by a designated individual.

Specifically, CRDM division has not reported the following MDR reportable events as required.

Complaint Number	Product (Model)	Clinical Observation reported	Alert date	Returned product analysis findings
(b) (4)	P1501DR (EnRythm)	Explanted due to battery premature depletion	02/11/09	No anomalies found
(b) (4)	P1501DR (EnRythm)	Product replaced during surgery. Physician noticed noise and oversense after connecting leads at the OR once the device was placed in the patient body. Physician suspected device malfunction. Lead returned with blood residues.	02/04/09	Blood/Body fluids residues. Grommet damage with cause unknown.
(b) (4)	P1501DR (EnRythm)	Once implanted (IPG and leads) noise on the atrial and ventricular channels was obsereved. Blood observed in the IPG header block.	02/12/09	Blood noted in the header block. Grommet damage with cause unknown.
(b) (4)	P1501DR	During implant the physician	04/15/09	Grommet

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EMPLOYEE(S) SIGNATURE
Marilyn Santiago, Investigator
Rafael Gonzalez Pizarro, Investigator

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	(EnRythm)	found that it was impossible to connect leads to the Implantable Pulse Generator (IPG).		damage with cause unknown.

The firm failed to file MDRs as applicable for Complaints # (b) (4) (b) (4) and (b) (4) In all of these events a device was placed in the patients body during surgery and prior to completing the surgical process the Physician tested the device detecting that the product being implanted was apparently malfunctioning.

Concerning Complaint # (b) (4) the firm failed to review all past allegations of battery premature depletion to file the applicable MDRs after confirming that battery premature depletion was in fact a product malfunction that was related to a reduction in product longevity and that increases the risk of product explantation (03/2009 CAPA (b) was generated). Other MDRs for similar complaints were filed late, after the CAPA was initiated. Examples are Complaint (b) (4) with alert date 02/05/09 and MDR filing date 02/11/2010; and Complaint (b) (4) with alert date 02/13/09 and MDR filing date 02/11/2010.

OBSERVATION 2

Not all of the actions needed to correct and prevent the recurrence of nonconforming product and other quality problems have been identified.

Specifically, high risk priority CAPA investigation records have been held opened for a long period of time without written justification. For instance:

CAPA #*[1]	Product impacted	CAPA Creation date	Investigation start date	Investigation Completion date	Current CAPA status	Time opened*[2]
PR# (b) Multibeam Connector defects	Implantable Pulse Generators (CRDM)	04/04/2008	05/05/2008	02/01/2010*[3]	Opened	704 days
PR # (b) (CAPA (b) EnRythm Battery Voltage Issues	Implantable Pulse Generators, Implantable Cardiac Monitors and Cardiac Resynchronization Therapy devices	03/02/2009	03/16/2009	N/A	Opened: Investigation phase in Progress	371 days

*[1] Out of a sample of 15 CAPAs evaluated
*[2] Calculated up to March 09, 2010.

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*3 Date as shown in CAPA record; however, firm's management indicated that this investigation still in progress.

- For both CAPA records mentioned in table above it was found that there was impacted product in the field. None of these CAPA Records provide written justification or management approval for the extensive time these CAPA records and their corresponding investigations have been held open.
- CAPA PR#(b) was generated after complaints were received for high impedance and/or no capture. Products affected include Adapta, Versa, Sensia and Enrythm Models. The observed failure mode is damaged/oversized Multi Beam Contacts (MBC) contact springs. Investigation concluded that the MBCs were misshapen during the manufacturing process. However, after a year and nine months of investigation the firm was unable to determine the root cause for the observed non-conformity.
- CAPA PR#(b) was generated after complaints were received reporting differences in battery voltage measurements and consequent explantation of the devices. The products impacted are EnRhythm IPGs models. Potential health impact was determined as premature explantation of the device. The firm initiated a field action during this inspection on 02/11/2010. This investigation still in progress.

OBSERVATION 3

Complaints involving the possible failure of a device to meet any of its specifications were not evaluated where necessary.

Specifically, your firm's process of evaluating adverse tendencies of products is inadequate because it is unable to establish adverse tendencies per individual product and not always the pertinent investigations are conducted.

- Investigations are made only when all the devices that are part of the same family together exceed the pre-calculated threshold for a specific defect or hazard. Meaning that if only one product within a family is having an adverse trend, but still it is not enough to exceed the established group threshold, you will not be able to detect that and you will not investigate.
- Complaints generated from literature (publications) as well as those related to old events are excluded from threshold signals investigations; meaning that when they are removed the signal disappears and consequently it is not investigated. No retrospective analysis is performed to evaluate the excluded old events within its corresponding time space.
- For example, your document(b) (4) Threshold Signal Investigation Report - Infection - Apr-08, version(b) related to CAPA #(b) (4) (b) (4)), shows that signals from years 2007 and 2008 related to infection were not investigated because when the literature complaints and old events complaints were removed the signal disappeared and with it the need of investigating. In this document it is shown that all Drug Delivery devices were trend together and then divided by therapy (e.g. non malignant pain) as shown in monitoring charts included. The information provided in your analysis of findings is not specific on how the complaints were distributed per single product.

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OBSERVATION 4

Records of complaint investigations do not include the results of the investigation.

Specifically, during inspection it was disclosed that your firm does not always document the results of investigations related to complaints. For instance:

- (b) (4) was generated on 03/05/2009 upon receipt of the allegation *"Rep reports patient at last refill the patient's pump still had all of the drug remaining; possible blockage in catheter access port. Device was replaced. Patient outcome not provided."* on 02/06/2009. Reason for return (RFR) assigned was *"Accuracy rate"*. Rationale for not implementing a corrective action as indicated in complaint record was *"Device Returned, no anomalies found"*. Findings description provided in complaint record for returned product analysis was *"NO ANOMALY FOUND – NORMAL DEVICE FUNCTION"*. Investigation final conclusion was *"Inconclusive because analysis did not support allegation"*. Nevertheless, photographs showing corrosion/residues at the pump head pins and gear wheel were found attached as part of this complete complaint file during review. No reference whatsoever was made to these photographs in the complaint record. During inspection it was disclosed that corrosion is not a normal finding and that it is in fact included as a root cause of failure and as a failure mode itself in the corresponding Design Failure Mode Analysis document. Furthermore, your firm completed an investigation on 02/24/2009 (b) (4)) as a result of CAPA (b) that recognizes corrosion/residues as an adverse event; but this investigation was not referenced in the complaint record.
- Moreover, Medtronic Neurological Analysis Summary Report dated 06/04/2009 for PCR 410372 forwarded to the complainant (Physician) containing a summary of the analyses findings states that **all internal components were functioning per specification and that motor wire connections were inspected and no anomalies were seen**. Therefore, the analysis report that was sent to the Physician reporting firm's findings was incomplete in that it makes no reference to the corrosion observed or the investigation previously performed by your firm.
- In addition, Medtronic Neurological Product Comment Report Analysis document, that summarizes all tests performed to the returned product, dated 12/14/2009, does not provide the results for the Catheter Access Port (CAP) test, this although the allegation also included the possibility of blockage in the CAP.
- It was found that for some complaints (PCRs) where the DHR review was completed, it was documented as part of an e-mail message (e.g. (b) (4)) that was printed and attached to the complaint file instead of using the required DHR Check Form (b) (4) as per standard operating procedures. Furthermore, the DHR check form (b) (4) is deficient in that it does not provide detail information on how the review was conducted and in what context or scope. Therefore, there is no written evidence to support that a thorough DHR review was performed to whether confirm or discard that the manufacturing process or either the materials, components or their suppliers could have been related to the allegations made in the complaint under investigation.

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OBSERVATION 5

Complaint handling procedures have not been defined to ensure that all complaints are processed in a uniform and timely manner.

Specifically, the firm fails to evaluate complaints in a timely and uniform manner.

- It was found during inspection that several tests required as part of firm's returned product analysis were performed late or not performed at all.
  - (b) (4) (EnRythm) was generated on 02/19/2009 based on the allegation that the device was pacing inappropriately (b) (4) ". The device was explanted and replaced. The investigation was completed by **May 15, 2009**; then 8 months later, on January 29 2010, without written justification, the firm reopened the investigation to conduct the Accelerometer and Long term monitoring tests. Your firm was unable to provide an explanation on why these tests were not performed previously.
  - (b) (4) (EnRythm) was generated based on the allegation of battery premature depletion; however it was not sent to Medtronic Energy and Components Center (MECC) for additional battery testing as it was done with other (b) Complaints with the same Reason For Return (RFR) code assigned (allegation) (e.g (b) (4) , EnRythm). Your firm was unable to provide an explanation for this lack of uniformity.
- Inconsistency was also observed related to the criteria or priority rationale used at the moment a complaint is notified to generate a complaint record and to further investigate a complaint. For instance, complaint (b) (4) was created in 2 days; in this case the physician was not reporting patient symptoms; however for complaints (b) (b) and (b) (4) , where patient symptoms related to hazards such as underdose and overdose were reported, took longer to the firm to generate the complaint record. The firm was unable to explain this inconsistency.

Complaint #	Product	Hazard	Alert Date	Days to creation
(b) (4)	Synchromed II	Refilling problems	12/01/2008	2
(b) (4)		Underdose	02/06/2009	27
(b) (4)		Overdose	12/09/2008	10

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OBSERVATION 6

Records of complaint investigations do not include the date the complaint was received.

Specifically, your firm does not document the complaint notification date in the complaint record. In addition, information such as complainant address, current status of investigations and justification for actions (e.g. held in progress an investigation for a long period of time) was not always documented in your complaint records. The following three complaint records out of a sample of 17 records evaluated were found with abovementioned insufficiencies:

Complaint No.	Business Sector*1	Product	Clinical Observation Reported	Missing Information
(b) (4)	CRDM	EnRythm	Battery Voltage Variations	Alert date; Complainant Information; Status of investigation task is shown "in progress" since 02/23/09, no written justification included.
(b) (4)	CRDM	EnRythm	Battery Premature depletion	Alert date; Complainant Information; Status of investigation task is shown "in progress" since 02/16/09, no written justification included.
(b) (4)	CRDM	EnRythm	Excessive stimulation when pacing the atrium	Alert date; Complainant Information

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Observation Annotations

Observation 3: Promised to correct.

Observation 4: Promised to correct.

*** DATES OF INSPECTION:**
12/10/2009(Thu), 12/11/2009(Fri), 12/14/2009(Mon), 12/15/2009(Tue), 12/16/2009(Wed), 12/17/2009(Thu), 12/18/2009(Fri), 12/21/2009(Mon), 12/22/2009(Tue), 01/13/2010(Wed), 01/14/2010(Thu), 01/15/2010(Fri), 01/20/2010(Wed), 01/21/2010(Thu), 01/22/2010(Fri), 01/25/2010(Mon), 01/26/2010(Tue), 02/01/2010(Mon), 02/05/2010(Fri), 02/08/2010(Mon), 02/09/2010(Tue), 02/10/2010(Wed), 02/11/2010(Thu), 02/12/2010(Fri), 02/17/2010(Wed), 02/19/2010(Fri), 02/23/2010(Tue), 02/24/2010(Wed), 02/25/2010(Thu), 03/05/2010(Fri), 03/10/2010(Wed)

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