DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Room –WO66-G609
Silver Spring, MD 20993-0002

APR - 4 2012

Jenny Andersen
Senior Principal Regulatory Affairs Specialist
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8200 Coral Sea Street
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Re: P010031 / S232
Concerto CRT-D Model C154DWK
Consulta CRT-D Model D224TRK
Maximo II CRT-D Model D284TRK
Concerto II CRT-D Model D274TRK
Protecta CRT-D Model D334TRG
Protecta CRT-D Model D334TRM
Protecta XT CRT-D Model D314TRG
Protecta XT CRT-D Model D314TRM
Consulta CRT-D Model D204TRM
Maximo II CRT-D Model D264TRM
Filed: January 24, 2011
Amended: July 13, 2011; October 12, 2011; March 8, 2012
Procode: NIK

Dear Ms. Andersen:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) supplement for a modification to the indications for use as follows.

For the Concerto CRT-D Model C154DWK, Consulta CRT-D Model D224TRK, Concerto II CRT-D Model D274TRK, Protecta CRT-D Model D334TRG, Protecta CRT-D Model D334TRM, Protecta XT CRT-D Model D314TRG, Protecta XT CRT-D Model D314TRM, and Consulta CRT-D Model D204TRM Cardiac Resynchronization Therapy Defibrillators (CRT-Ds) the indications for use are:

> The [name of device] CRT-D system is indicated for ventricular antitachycardia pacing and ventricular defibrillation for automated treatment of life threatening ventricular arrhythmias and for providing cardiac resynchronization therapy in heart failure patients who remain

symptomatic despite optimal medical therapy, and meet any of the following classifications:

- New York Heart Association (NYHA) Functional Class III or IV and who have a left ventricular ejection fraction ≤ 35% and a prolonged QRS duration.
- Left bundle branch block (LBBB) with a QRS duration ≥ 130 ms, left ventricular ejection fraction ≤ 30%, and NYHA Functional Class II.

The system is also indicated for use in patients with atrial tachyarrhythmias, or those patients who are at significant risk for developing atrial tachyarrhythmias.

Atrial rhythm management features such as Atrial Rate Stabilization (ARS), Atrial Preference Pacing (APP), and Post Mode Switch Overdrive (PMOP) are indicated for the suppression of atrial tachyarrhythmias in implantable cardioverter defibrillator (ICD)-indicated patients with atrial septal lead placement and an ICD indication.

For the Maximo II CRT-D Model D284TRK and Maximo II CRT-D Model D264TRM Cardiac Resynchronization Therapy Defibrillators (CRT-Ds) the indications for use are:

The Maximo II CRT-D system is indicated for ventricular antitachycardia pacing and ventricular defibrillation for automated treatment of life threatening ventricular arrhythmias and for providing cardiac resynchronization therapy in heart failure patients who remain symptomatic despite optimal medical therapy, and meet any of the following classifications:

- New York Heart Association (NYHA) Functional Class III or IV and who have a left ventricular ejection fraction ≤ 35% and a prolonged QRS duration.
- Left bundle branch block (LBBB) with a QRS duration ≥ 130 ms, left ventricular ejection fraction ≤ 30%, and NYHA Functional Class II.

We are pleased to inform you that the PMA supplement is approved. You may begin commercial distribution of the devices as modified in accordance with the conditions of approval described below.

The sale and distribution of these devices are restricted to prescription use in accordance with 21 CFR 801.109 and under section 515(d)(1)(B)(ii) of the Federal Food, Drug, and Cosmetic Act (the act). The devices are further restricted under section 515(d)(1)(B)(ii) of the act insofar as the labeling must specify the specific training or experience practitioners need in order to use the devices. FDA has determined that these restrictions on sale and distribution are necessary to provide reasonable assurance of the safety and effectiveness of the devices. Your devices are therefore restricted devices subject to the requirements in sections 502(q) and (r) of the act, in addition to the many other FDA requirements governing the manufacture, distribution, and marketing of devices.

Expiration dating for these devices have been established and approved at one year. This is to advise you that the protocol you used to establish this expiration dating is considered an approved protocol for the purpose of extending the expiration dating as provided by 21 CFR 814.39(a)(7).

Continued approval of this PMA is contingent upon the submission of periodic reports, required under 21 CFR 814.84, at intervals of one year (unless otherwise specified) from the date of approval of the original PMA. Two copies of this report, identified as "Annual Report" (please use this title even if the specified interval is more frequent than one year) and bearing the applicable PMA reference number, should be submitted to the address below. The Annual Report should indicate the beginning and ending date of the period covered by the report and should include the information required by 21 CFR 814.84.

In addition to the above, and in order to provide continued reasonable assurance of the safety and effectiveness of the devices, the Annual Report must include, separately for each model number (if applicable), the number of devices sold and distributed during the reporting period, including those distributed to distributors. The distribution data will serve as a denominator and provide necessary context for FDA to ascertain the frequency and prevalence of adverse events, as FDA evaluates the continued safety and effectiveness of the devices.

In addition, because your devices are pacemakers, implantable cardioverter-defibrillators (ICD), or system leads, FDA has determined that the following additional information is necessary to provide continued reasonable assurance of the safety and effectiveness of the devices. In the Annual Report, provide the following information known by or reported to the applicant:

1. The number of pulse generators domestically implanted and the number of reported explants and deaths.

2. A breakdown of the reported deaths into pulse generator related and non-pulse generator related.

3. A breakdown of the reported explants into the number reported that were:

    a. For pacemakers and pulse generators: at end of battery life, the number that had complications not resolvable by programming, and, as applicable, the numbers that experienced other safety and effectiveness complications as ascertained by the user, applicant, or otherwise, or

    b. For leads: associated with mechanical failure, associated with clinical complications, and as applicable, the numbers that experienced other safety and effectiveness complications as ascertained by the user, applicant, or otherwise.

4. The number of pulse generators returned to the applicant for cause from domestic sources, with a breakdown into:

   a. For pacemakers and pulse generators: the number currently in analysis, the number operating properly, and the number at normal battery depletion and failed (with the failure mechanisms described).

   b. For leads: the number currently in analysis, the number operating properly, the number failed (with failure mechanisms described); broken down into groupings for full leads and partial leads.

5. A cumulative survival table for the pulse generators.

In addition to the Annual Report requirements, you have agreed to provide the following data in separate post-approval study reports. As a condition of approval, you have agreed to conduct two post-approval studies (PAS) as described below:

1. *REVERSE NCDR ICD Registry Study:* The study will consist of a newly enrolled prospective, observational study of US patients implanted with a Medtronic CRT-D device who meet the expanded indication identified American College of Cardiology (ACC) National Cardiovascular Data Registry (NCDR) Implantable Cardioverter Defibrillator (ICD) Registry.

   The primary study objective is to estimate the five-year survival probability for patients implanted with a Medtronic CRT-D device meeting the expanded indication criteria.

   Additional analyses will estimate the five-year survival probability by gender specific and QRS group.

   The study population will consist of adult patients treated with a Medtronic CRT-D device, meeting the expanded indication, who are identified through the ACC NCDR ICD Registry. Mortality through five years will be tracked for this cohort using the National Death Index. At least 1500 patients, with a minimum of 500 patients with a QRS < 150ms, will provide a two-sided confidence interval precision of 3% assuming a five-year survival probability of 75%.

2. *REVERSE Product Surveillance Registry:* The study will consist of a newly enrolled prospective, observational study of patients implanted with a Medtronic CRT-D device who meet the expanded indication with a QRS duration < 150ms enrolled into Medtronic's Product Surveillance Registry.

The co-objectives are:

- to estimate the 3-year survival probability of freedom from centrally adjudicated heart failure hospitalization or all-cause death for patients implanted with a Medtronic CRT-D device meeting the approved expanded indication criteria with a QRS duration < 150ms.

- to estimate the 3-year survival probability of freedom from centrally adjudicated heart failure event or all cause death for patients implanted with a Medtronic CRT-D device meeting the approved expanded indication criteria with a QRS duration < 150ms. Where a heart failure hospitalization event is defined as due to or associated with worsening heart failure with treatment either in-patient (hospitalization) or out-patient (emergency department, clinic, urgent care, etc.).

The study population will consist of adult patients treated with a Medtronic CRT-D device, meeting the expanded indication with a QRS duration < 150ms, enrolled into Medtronic's Product Surveillance Registry. Patients will be consented for follow-up through 5-years and actively followed approximately every 6 months from implant through a minimum of 3-years but potentially out to 5-years. Enrollment outside the US will be allowed but will be limited to no more than 40% of the total sample size. Assuming a three-year heart failure hospitalization or all-cause death proportion of 26.8%, a total of 500 patients will provide the ability to estimate the rate of patients with heart failure related hospitalization or all-cause death at 3 years with a 95% confidence interval within +/- 5%.

Please be advised that the results from these studies should be included in the labeling as these data become available. Any updated labeling must be submitted to FDA in the form of a PMA Supplement.

Be advised that the failure to conduct any such study in compliance with the good clinical laboratory practices in 21 CFR part 58 (if a non-clinical study subject to part 58) or the institutional review board regulations in 21 CFR part 56 and the informed consent regulations in 21 CFR part 50 (if a clinical study involving human subjects) may be grounds for FDA withdrawal of approval of the PMA.

FDA would like to remind you that you are required to submit separate PAS Progress Reports for each requirement every six months during the first two years and annually thereafter. The reports should clearly be identified as Post-Approval Study Report. Two copies, identified as "PMA Post-Approval Study Report" and bearing the applicable PMA reference number, should be submitted to the address below. For more information on post-approval studies, see the FDA guidance document entitled, "Procedures for Handling Post-Approval Studies Imposed by PMA Order"
http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070974.htm

Within 30 days of your receipt of this letter, you must submit two (2) separate PMA supplements that include the complete protocols for your two (2) post-approval studies. Your PMA supplements should be clearly labeled as a "Post-Approval Study Protocol" and submitted in triplicate to the address below. Please reference the PMA number above to facilitate processing.

Before making any change affecting the safety or effectiveness of the devices, you must submit a PMA supplement or an alternate submission (30-day notice) in accordance with 21 CFR 814.39. All PMA supplements and alternate submissions (30-day notice) must comply with the applicable requirements in 21 CFR 814.39. For more information, please refer to the FDA guidance document entitled, "Modifications to Devices Subject to Premarket Approval (PMA) - The PMA Supplement Decision-Making Process" (www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089274.htm).

You are reminded that many FDA requirements govern the manufacture, distribution, and marketing of devices. For example, in accordance with the Medical Device Reporting (MDR) regulation, 21 CFR 803.50 and 21 CFR 803.52, you are required to report adverse events for these devices. Manufacturers of medical devices, including in vitro diagnostic devices, are required to report to FDA no later than 30 calendar days after the day they receive or otherwise becomes aware of information, from any source, that reasonably suggests that one of their marketed devices:

1. May have caused or contributed to a death or serious injury; or

2. Has malfunctioned and such devices or similar devices marketed by the manufacturer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

Additional information on MDR, including how, when, and where to report, is available at www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm.

In accordance with the recall requirements specified in 21 CFR 806.10, you are required to submit a written report to FDA of any correction or removal of these devices initiated by you to: (1) reduce a risk to health posed by the devices; or (2) remedy a violation of the act caused by the devices which may present a risk to health, with certain exceptions specified in 21 CFR 806.10(a)(2). Additional information on recalls is available at www.fda.gov/Safety/Recalls/IndustryGuidance/default.htm.

CDRH does not evaluate information related to contract liability warranties. We remind you; however, that device labeling must be truthful and not misleading. CDRH will notify the public of its decision to approve your PMA by making available, among other information, a summary of the safety and effectiveness data upon which the approval is based. The information can be found on the FDA CDRH Internet HomePage located at www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/PMAApprovals/default.htm. Written requests for this information can also be made to the

Dockets Management Branch, (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. The written request should include the PMA number or docket number. Within 30 days from the date that this information is placed on the Internet, any interested person may seek review of this decision by submitting a petition for review under section 515(g) of the act and requesting either a hearing or review by an independent advisory committee. FDA may, for good cause, extend this 30-day filing period.

Failure to comply with any post-approval requirement constitutes a ground for withdrawal of approval of a PMA. The introduction or delivery for introduction into interstate commerce of a device that is not in compliance with its conditions of approval is a violation of law.

You are reminded that, as soon as possible and before commercial distribution of your devices, you must submit an amendment to this PMA submission with copies of all approved labeling in final printed form. Final printed labeling that is identical to the labeling approved in draft form will not routinely be reviewed by FDA staff when accompanied by a cover letter stating that the final printed labeling is identical to the labeling approved in draft form. If the final printed labeling is not identical, any changes from the final draft labeling should be highlighted and explained in the amendment.

All required documents should be submitted in triplicate, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing. One of those three copies may be an electronic copy (eCopy), in an electronic format that FDA can process, review and archive (general information: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/ucm134508.htm; clinical and statistical data: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/ucm136377.htm)

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If you have any questions concerning this approval order, please contact Ken Skodacek at 301-796-6364.

Sincerely yours,

for Bram D. Zuckerman, M.D.
Director
Division of Cardiovascular Devices
Office of Device Evaluation
Center for Devices and Radiological Health