December 22, 2017

Medtronic, Inc.
Barbara Chiponis
Distinguished Regulatory Affairs Advisor
8200 Coral Sea Street NE
Mail Stop MVS11
Mounds View, Minnesota 55112

Re: P140032
Trade/Device Name: Implantable System for Remodulin®
Filed: December 29, 2014
Amended: January 7, 2015, March 17, 2015, November 2, 2015, December 7, 2015, December 14, 2015, May 26, 2016, June 30, 2016, August 16, 2016, October 11, 2016, November 4, 2016, April 6, 2017
Product Code: LKK

Dear Barbara Chiponis:

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) for the Medtronic Implantable System for Remodulin®. The Implantable System for Remodulin® is indicated for adult patients with Class I, II and III pulmonary arterial hypertension (PAH) receiving intravenous delivery of Remodulin. Physicians prescribing this system for use with Remodulin must be familiar with the indications, contraindications, warnings, precautions, adverse events, and dosage and administration information described in the Remodulin drug labeling. The Model 8551 Refill Kit is intended for use in refilling the Medtronic implantable programmable infusion pumps with the exception of Medtronic MiniMed infusion pumps. We are pleased to inform you that the PMA is approved. You may begin commercial distribution of the device in accordance with the conditions of approval described below.

The sale and distribution of this device 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 device is 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 device. FDA has determined that these restrictions on sale and distribution are necessary to provide reasonable assurance of the safety and effectiveness of the device. Your device is therefore a restricted device 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. The sale and distribution of this device are further restricted to the conditions prescribed, recommended or suggested in the approved drug labeling for Remodulin. Your device is therefore a restricted device 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 this device has been established and approved at 24 months for the Model 8201 catheter and 90 days for the Catheter Patency Kit (Model 8450PAH).

Continued approval of the 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" 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. This is a reminder that as of September 24, 2014, class III devices are subject to certain provisions of the final UDI rule. These provisions include the requirement to provide a UDI on the device label and packages (21 CFR 801.20), format dates on the device label in accordance with 21 CFR 801.18, and submit data to the Global Unique Device Identification Database (GUDID) (21 CFR 830 Subpart E). Additionally, 21 CFR 814.84 (b)(4) requires PMA annual reports submitted after September 24, 2014, to identify each device identifier currently in use for the subject device, and the device identifiers for devices that have been discontinued since the previous periodic report. It is not necessary to identify any device identifier discontinued prior to December 23, 2013. For more information on these requirements, please see the UDI website, http://www.fda.gov/udi.

In addition to the above, and in order to provide continued reasonable assurance of the safety and effectiveness of the PMA device, 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 device.

You have agreed to provide the following non-clinical information in a report which may be followed by a PMA supplement where applicable.

1. Within 6 months of PMA approval, you must submit a report that contains a pump failure analysis of the root cause of internal pump tube kinking and leaking. In addition, within 12 months of PMA approval, you must implement effective mitigations to address this mechanism of device malfunction and submit the required documentation (e.g. PMA supplement).

2. Beginning at the time of market release, you have agreed to validate the initial training program (new system implant, follow-up and when to perform the catheter patency check) for the Medtronic Implantable System for Remodulin (ISR) utilizing the to-be-marketed user interface and training materials per a protocol that includes, but is not limited to, the following items:

    a. The user groups will include naïve users (i.e., users with no previous experience on the Medtronic Implantable System for Remodulin) from each of the following specified user groups:

        i. healthcare professionals involved in implanting the device
        ii. healthcare professionals involved in maintaining, programming, or refilling the device

b. Tasks to be included are critical tasks unique to ISR in the listed use scenarios. Tasks unique to ISR do not include those performed in the marketed SynchroMed II pump or as standard medical practice.

   i. pump preparation
   ii. therapy initiation
   iii. follow-up
   iv. surgical use
   v. dose accuracy checks
   vi. pump refill
   vii. when to perform the catheter patency check

c. The critical tasks will include all tasks that, if performed incorrectly, would or could cause serious harm to the patient or user, where harm is defined to include compromised medical care. The protocol will include a complete list of tasks for each scenario, and will designate which are critical tasks. Identification of critical tasks will include evaluation of incorrectly performed tasks that may result in dosing error or infection.

d. Acceptable validation of the training program will be based on the following

   i. An analysis of human factors validation test results with focus on any problems found during the testing. Problems are use errors and "close calls" on critical tasks observed by the test facilitators (observational data) and difficulties with use, including close calls, reported by the test participants (interview data).

   ii. For those use errors and problems that could result in serious harm, the test data should be analyzed to determine which part of the user interface was involved and how the user interaction could have resulted in the use error or problem.

   iii. An analysis of these data will describe any remaining residual use-related risk. Acceptability of this residual risk is then established based on a sound rationale that modifications to the user interface (including the device and the labeling) or the training program are unlikely to further reduce risk, are not practicable, and the remaining residual use-related risks are outweighed by the benefits derived from use of the device.

3. The following warning statements will be included in your labeling:

   a. During the pivotal clinical trial for the Implantable System for Remodulin, 10% of patients experienced pump failures after 4 years of use. At least 33% of these failures occurring after four years of use resulted in the device failing to deliver Remodulin without corresponding error alarm. The remaining percentage of reported malfunctions occurred with a motor stall alarm that was reported by the patient. Patients who cannot tolerate a sudden cessation of Remodulin therapy may not be appropriate candidates for the Implantable System for Remodulin.

b. Patients with hearing loss may not be able to hear pump error alarms coming from the implanted pump, which may cause delay in therapy if the patient does not hear the alarm and contact the physician in a timely manner.

In addition to the Annual Report requirements, you must provide the following data in post-approval study (PAS) reports for each PAS listed below. Separate PAS Progress Reports must be submitted for each study every six (6) months during the first two (2) years of the study and annually thereafter, unless otherwise specified by FDA. Two (2) copies of each report, identified as an "ODE Lead PMA Post-Approval Study Report" in accordance with how the study is identified below and bearing the applicable PMA reference number, should be submitted to the address below.

1. ODE Lead PMA Post-Approval Study: The Office of Device Evaluation (ODE) will have the lead for this clinical study. You must conduct a prospective, open-label, multi-center evaluation of the PMA-approved, commercially-distributed Implantable System for Remodulin® (ISR) consisting of at least 50 US patients that receive the ISR post-approval. The effort should assess the rate of catheter-related complications and pump failures through five years for the RIS as used according to the labeled indications for use. The evaluation of patients at each patient follow-up visit should require that clinicians perform a review of the pump logs in addition to a standard interrogation since a review of the logs will provide more complete information on pump stalls and alarms. When appropriate or as requested by FDA, you should submit PMA supplements requesting approval to update your Instructions for Use (IFU) to include follow-up data from these trials.

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.

Be advised that protocol information, interim and final results will be published on the Post Approval Study Webpage http://www.fda.gov/devicepostapproval.

In addition, the results from any post approval study 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. 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 a PMA supplement that includes a complete protocol of your post-approval study described above. Your PMA supplement should be clearly labeled as an "ODE Lead PMA Post-Approval Study Protocol" as noted above and submitted in triplicate to the address below. Please reference the PMA number above to facilitate processing. If there are multiple protocols being finalized after PMA approval, please submit each protocol as a separate PMA supplement.

Before making any change affecting the safety or effectiveness of the PMA device, 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" http://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 this device. 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 device or similar device 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 http://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 this device initiated by you to: (1) reduce a risk to health posed by the device; or (2) remedy a violation of the act caused by the device 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 http://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 http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/PMAApprovals/default.htm. Written requests for this information can also be made to the Food and Drug Administration, Dockets Management Branch, (HFA-305), 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 device, you must submit an amendment to this PMA submission with copies of all final labeling. Final 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 labeling is identical to the labeling approved in draft form. If the final 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 6 copies, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

U.S. Food and Drug Administration
Center for Devices and Radiological Health
PMA Document Control Center - WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

If you have any questions concerning this approval order, please contact CAPT Alan Stevens at 301-796-6294 or alan.stevens@fda.hhs.gov.

Sincerely,

Tina Kiang, Ph.D.
Acting Director
Division of Anesthesiology,
General Hospital, Respiratory,
Infection Control, and Dental Devices
Office of Device Evaluation
Center for Devices and Radiological Health