April 27, 2018

MEDTRONIC Inc.
% Nicole Stanchina
Sr. Regulatory Affairs Manager
Medtronic Neuromodulation
7000 Central Ave., N.E. MS RCW235
Minneapolis, Minnesota 55432

Re: P960009/S219
Trade/Device Name: Medtronic DBS Therapy For Epilepsy
Filed: February 24, 2015
Amended: 6/27/2017
Product Code: MBX

Dear Nicole Stanchina:

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 the Medtronic DBS Therapy for expanding the indications to include Epilepsy. Bilateral stimulation of the anterior nucleus of the thalamus (ANT) using the Medtronic DBS System for epilepsy is indicated as an adjunctive therapy for reducing the frequency of seizures in individuals 18 years of age or older diagnosed with epilepsy characterized by partial-onset seizures, with or without secondary generalization, that are refractory to three or more antiepileptic medications. The Medtronic DBS System for Epilepsy has demonstrated safety and effectiveness in patients who averaged six or more seizures per month over the three most recent months prior to implant of the DBS system (with no more than 30 days between seizures). The Medtronic DBS System for Epilepsy has not been evaluated in patients with less frequent seizures.

We are pleased to inform you that the PMA supplement 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.

Expiration dating for this device is the same as for the approved devices in P960009/S052. Expiration dating for the Medtronic DBS System for Epilepsy has been established and approved at 18 months for the INS and 4 years for the extensions and the leads. 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 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.

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 "OSB 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.

OSB Lead PMA Post-Approval Study – Medtronic DBS for Epilepsy New Enrollment PAS. The Office of Surveillance and Biometrics (OSB) will have the lead for this study. You agreed to a study outline, via email on 8/19/2015.

This study will be a prospective single-arm study design. The purpose of the study is to evaluate clinical outcomes of safety and effectiveness in subjects treated with the DBS device + current medical management (CMM) following an initial period of 3 months of CMM only. Subjects will then be clinically eligible for the DBS device + CMM. Those meeting implant criteria will undergo DBS implant +CMM. Study subjects will be followed for three years.

A total of 216 subjects will be enrolled in the study in order to ensure that at least 140 subjects will be implanted with the DBS device and at least 112 subjects will have data through 3 years of follow-up.

The primary effectiveness objective will be to demonstrate a median percentage reduction in seizures of at least 40% from pre-implant to post-implant in subjects treated with the DBS system through 36 months. The primary safety objective will be to demonstrate that there is not a 20% worsening in seizures over time in subjects treated with the DBS system beginning at 6 to 12 months post-implant and extending long term (three years).

Secondary safety and effectiveness endpoints will also be evaluated. Secondary effectiveness objectives will be to demonstrate that the total seizure rate during CMM is reduced after 12 subsequent months of DBS+CMM, that the disabling seizure rate during CMM is reduced after 12 subsequent months of DBS and CMM, and that the rate of seizures originating in the temporal lobe during CMM is reduced after 12 subsequent months of DBS+CMM. A secondary safety objective will be evaluation of the Sudden Unanticipated Death from Epilepsy (SUDEP) rate at 3 years.

Additional study endpoints will be evaluated to characterize the following: Any serious adverse events, adverse events related to device implant and stimulation, device deficiencies, post-implant effects through the 6-month post-implant follow-up visit, lead explants and revisions, adverse events of depression, suicidality, memory impairment, and seizures in the CMM and DBS+CMM phases, SUDEP rate in the CMM and DBS+CMM phases, neuropsychological outcomes related to memory impairment, depression, suicidality, and 3 year long-term DBS+CMM effectiveness (seizure frequency, responder rate, disabling seizures, frequency by seizure type, most severe seizure, seizure-related injuries, seizure freedom). Also, the effect of DBS+CMM will be evaluated in subject subgroups including various seizure onset zones (temporal lobe, frontal lobe, diffuse or multifocal, parietal, occipital and other), previous VNS, previous resection, number of previous AEDs, and subjects aged 18-21. DBS stimulation parameters used over time, antiepileptic medication changes, quality of life over time and subject programmer use will also be assessed. Additionally, the effectiveness of physician training programs (duration/number of acute events following stimulation initiation, lead re-operation rate) will be evaluated.

PAS reporting will occur every six-months for the first two years of the PAS and then yearly thereafter.

Please be advised within 30 days of your receipt of this letter, you must submit a PMA supplement that includes the complete protocol of your post approval study. Your PMA supplement 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. If there are multiple protocols being finalized after PMA approval, please submit each protocol as a separate 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.

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).

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 Erin Keegan at 240-402-6534 or Erin.Keegan@fda.hhs.gov.

Sincerely,

Carlos L. Pena -S

Carlos L. Peña, PhD, MS
Director
Division of Neurological
and Physical Medicine Devices
Office of Device Evaluation
Center for Devices and Radiological Health