DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

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

January 14, 2015

Enteromedics, Inc.
Katherine Tweden, PhD
Vice President, Clinical & Regulatory
2800 Patton Road
Saint Paul, MN 55113

Re: P130019 - Maestro® Rechargeable System
Filed: June 24, 2013
Amended: August 16, 2013, September 13, 2013, November 27, 2013, July 17, 2014, August 8, 2014
Procode: PIM

Dear Dr. Katherine Tweden,

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 Maestro® Rechargeable System. This device is indicated for use in weight reduction in patients aged 18 years through adulthood who have a Body Mass Index (BMI) of 40 to 45 kg/m^2, or a BMI of 35 to 39.9 kg/m^2 with one or more obesity related co-morbid conditions, and have failed at least one supervised weight management program within the past five years. 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.

Expiration dating for this device has been established and approved at 18 months for the Model 2002 Neuroregulator and Model 1680 Torque Wrench, and 36 months for the Series 2200-47 Leads. This is to advise you that the protocols you used to establish this expiration dating are considered approved protocols 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" 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 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 reports (PAS). Two (2) copies, identified as either “ODE Lead PMA Post-Approval Study Report" or “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.

1. ODE Lead PMA Post-Approval Study Report - *Maestro Extended Follow-up of the Premarket Cohort (ReCharge Clinical Trial)*: The Office of Device Evaluation (ODE) will have the lead for this clinical study, which was initiated prior to device approval. The Extended Follow-Up Study is a multicenter, single-arm prospective, longitudinal study designed to gather long-term data on adverse events, weight loss, surgical revisions and explants, and change in obesity-related comorbidities. This study will continue to follow patients from the ReCharge pivotal study for 5 years post Maestro implantation. A total of 210 subjects are available for the extended follow-up study and will be invited to participate in the PAS. At 5 years, a minimum of 105 patients (50% of enrolled subjects) are expected to still be implanted with the device and attend the 5-year clinic visit. It is estimated that the remaining 105 patients will have been explanted prior to the 5-year visit and approximately 50% of the explanted patients will agree to provide additional follow-up data after explant.

   The primary safety objective is to show that the rate of SAEs related to the device, implant/revision procedure (including explant procedure), general surgical procedure, or therapy algorithm is lower than 25% at 5 years. The hypothesis test for the primary safety

objective will be evaluated using the Kaplan-Meier estimate of the 5-year SAE rate. The endpoint will be met if the estimate for the upper 95% log-log confidence limit is lower than 25% at 5 years. Assuming a 25% performance goal, 1-sided 0.05 type-I error rate, expected 5-year related SAE rate of 15%, and an 8% rate of censoring per year from implant/crossover, it was estimated that the objective would be powered at the 80% level.

Other study endpoints include: weight loss measured by %EWL and %TBL; change in obesity-related comorbidities (blood pressure, lipid levels, triglycerides, blood glucose, HbA1c and waist circumference); and 5-year rates of surgical revision, device explant, device explants specifically to undergo MRI, therapy-related AEs, and device (neuroregulator or lead) malfunction requiring a revision procedure; and AEs involving lead breakage/fracture, twisting/entanglement, replacement, lead erosion, and bowel/tissue obstruction.

2. OSB Lead PMA Post-Approval Study Report - *Maestro New Enrollment Study*: The Office of Surveillance and Biometrics (OSB) will have the lead for studies initiated after device approval. The New Enrollment Study is a prospective, 5-year, multicenter, single-arm study of the Maestro Rechargeable System. A total of 200 subjects will be enrolled at 15 centers (minimum of 10 centers) in the United States. The study will enroll a minimum of 40 subjects (20% of postmarket cohort) from minority racial and ethnic groups and also a minimum of 40 male subjects.

   The primary objective is to evaluate the long-term safety of Maestro in patients at least 18 years old who have a BMI of 40-45 kg/m2, or a BMI of 35-39.9 kg/m2 with 1 or more obesity related comorbidities and have failed at least 1 supervised weight management program in the past 5 years. Specifically, the study will assess the rate of SAEs related to the device, implant/revision procedure (including explant procedure), general surgical procedure, or therapy at 5 years. Other study endpoints include: weight loss measured by %TBL and %EWL; change in obesity-related comorbidities (blood pressure, waist circumference and the number, type and dose of medications for treatment of diabetes, hypertension and dyslipidemia); surgical revision, surgical explant, device explants specifically to undergo MRI, therapy-related AEs, and device (neuroregulator or lead) malfunction requiring a revision procedure; and AEs involving lead breakage/fracture, twisting/entanglement, replacement, lead erosion, and bowel/tissue obstruction. In addition physician training objectives include evaluation of surgical revision rates and implant procedure times by physician and site.

   At 5 years, a minimum of 120 patients (60% of 200 enrolled subjects) are expected to still be implanted with the device and attend the 5-year clinic visit. It is estimated that the remaining 80 patients will have been explanted prior to the 5-year visit and approximately 50% of the explanted patients will agree to provide additional follow-up data after explant.

   The primary safety objective is to demonstrate that the rate of SAEs related to the device,

implant/revision procedure (including explant procedure), general surgical procedure, or therapy is statistically lower than 25% at 5 years. The endpoint will be met if the estimate for the upper 95% log-log confidence limit is lower than 25% at 5 years. Assuming a 25% performance goal, one-sided 0.025 type-I error rate, expected 5-year related SAE rate of 15%, and an 8% rate of explant/dropout per year, it was estimated that the primary safety objective would have at least 90% power with 200 enrolled subjects.

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.

Within 30 days of your receipt of this letter, you must submit a PMA supplement that includes complete protocols of your 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. If there are multiple protocols being finalized after PMA approval, please submit each protocol as a separate PMA supplement.

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.

FDA would like to remind you that you are asked to submit separate PAS Progress Reports every six months during the first two years of the study and annually thereafter. The reports should clearly be identified as Post-Approval Study Report. Two copies for each study, identified as either “ODE Lead PMA Post-Approval Study Report" or “OSB Lead PMA Post-Approval Study Report” in accordance with how the study is identified above 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" (www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070974.htm#2).

Before making any change affecting the safety or effectiveness of the 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" (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 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 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 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 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 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 Elizabeth Katz at (301) 796-2495.

Sincerely yours,

William H. Maisel -S

William H. Maisel, MD, MPH
Director, Office of Device Evaluation (Acting)
Deputy Center Director for Center for Devices and Radiological Health