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

May 28, 2014

Ty Cowart
Vice President, Regulatory Affairs
CardioMEMS, Inc.
387 Technology Circle NW, Suite 500
Atlanta, GA 30313

Re: P100045
CardioMEMS™ HF System
Filed: December 15, 2010
Amended: April 5, August 16, and August 25, 2011; May 21, 2013; July 31, 2013; and April 2, 2014
Procode: MOM

Dear Mr. Cowart:

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 CardioMEMS™ HF System, which includes the CM2000 implantable PA Sensor/Monitor and transvenous catheter delivery system, the CM1000 Patient Electronics System (GSM), the CM1010 Patient Electronics System (GSM), and CM3000 Hospital Electronics System. This device is indicated for wirelessly measuring and monitoring pulmonary artery (PA) pressure and heart rate in New York Heart Association (NYHA) Class III heart failure patients who have been hospitalized for heart failure in the previous year. The hemodynamic data are used by physicians for heart failure management and with the goal of reducing heart failure hospitalizations.

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 (implantable sensor/monitor and transvenous catheter delivery system) has been established and approved at two (2) years. 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" 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 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 conduct the two (2) post-approval studies described below and provide the following data in post-approval study reports (PAS). Two (2) copies, identified as "PMA Post-Approval Study Report" and bearing the applicable PMA reference number, should be submitted to the address below.

1. *Newly Enrolled Champion:* This study will be conducted as per protocol dated March 21, 2014, Version 1.0. The study will be a prospective, multi-center, open-label trial conducted in the United States to examine the safety and effectiveness of CardioMEMS™ HF System. The study populations will be adults (≥18 of age) with New York Heart Association (NYHA) Class III Heart Failure (HF) who have experienced a heart failure hospitalization within the past 12 months.

   The primary safety objectives are evaluate (1) if device/system-related complication (DSRC)-free proportion of subjects is at least 80% at 24 months, and (2) if the pressure sensor failure-free proportion of subjects is at least 90% at 24 months. DSRCs include adverse events related to the systems and is at least treated by invasive means or results in subject death or device explantation.

   The primary effectiveness objective is to demonstrate that there is not a worsening in heart failure (HF) hospitalization rate 1 year in the PAS compared to 1 year prior to enrollment (based on hospitalization records). Effectiveness will be examined overall, by community and academic hospitals for the training evaluation, and by the following subgroups: women vs. men, reduced ejection fraction (≤ 40%) vs. preserved ejection fraction (> 40%), ischemic vs. non-ischemic etiology, and with ICD/CRT-D vs. without ICD/CRT-D.

   Additional objectives will be to analyze 1-year mortality, compare the annualized HF hospitalization or death rate at 1 year in study to the HF hospitalization rate in the year prior to enrollment, and patient compliance.

Patients will be followed out to 2-years post implant with follow-up visits at 1 month and every 6 months. For the two-year primary safety endpoint of freedom from device-related complications, a total of 1,200 subjects will be enrolled, using an exact two-sided test for one-sample binomial proportions with alpha of 0.05, and attrition rate of 49.1%, a minimum of 663 evaluable subjects at 2 years are needed to provide greater than 90% power to detect a difference as small as 5% from the null proportion rate of 0.80 (i.e., objective performance criterion of 80%). Of the enrolled subjects, a total of 420 will be women to ensure a minimum of 206 evaluable women at 2 years to provide greater than 90% power to detect a difference as small as 0.06 from the null proportion rate of 0.90.

2. *Champion Substudy:* This will be a prospective, multi-center, open-label trial conducted in the United States to examine safety and compare the postmarket effectiveness of CardioMEMS™ HF System to premarket. The substudy patients will be all patients selected by independent committee from the PAS 1 (Main Cohort) who are optimally managed and are clinically similar to the Control group in CHAMPION based on pre-enrollment data.

   The primary safety objectives are evaluate (1) if device/system-related complication (DSRC)-free proportion of subjects is at least 80% at 24 months, and (2) if the pressure sensor failure-free proportion of subjects is at least 90% at 24 months. DSRCs include adverse events related to the systems and is at least treated by invasive means or results in subject death or device explantation.

   The primary effectiveness objective is to demonstrate that there is not a worsening in heart failure (HF) hospitalization rate 1 year in the PAS compared to the 1 year HF hospitalization rate in the premarket control group (Part 1). Effectiveness will be examined overall, by community and academic hospitals for the training evaluation, and by the following subgroups: women vs. men, reduced ejection fraction (≤ 40%) vs. preserved ejection fraction (> 40%), ischemic vs. non-ischemic etiology, and with ICD/CRT-D vs. without ICD/CRT-D.

   Patients will be followed out to 2-years post implant with follow-up visits at 1 month and every 6 months. Using an exact one-sample, 2-sided Poisson 95% confidence interval with alpha of 0.05, and a 2 year attrition rate of 49.1%, a minimum of 256 evaluable patients are required to achieve 90% power to show a difference between the estimated Treatment rate of 0.52 and the control rate of 0.75 for effectiveness.

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 (Champion Substudy). 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.

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. This information will include total number of enrolled subjects, follow-up rate, demographic information; safety and effectiveness results; mortality; serious adverse events; days alive outside of the hospital for heart failure; patient compliance; sensor performance; and medication changes in response to PA pressure.

FDA would like to remind you that you are asked to submit separate PAS Progress Reports for each study every six (6) months during the first two (2) years of the study and annually thereafter. The reports should clearly be identified as Post-Approval Study Report. Two (2) copies for each study, 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" (www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070974.htm#2).

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.

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 Mail Center – WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

If you have any questions concerning this approval order, please contact Bradley Quinn at (301) 796-5575.

Sincerely yours,

Christy L. Foreman -S

Christy Foreman
Director
Office of Device Evaluation
Center for Devices and Radiological Health