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

NOV 20 2012

Ms. Maritza Celaya
Sr. Director, Regulatory Affairs
HeartWare, Inc.
14000 NW 57th Court
Miami Lakes, FL 33014

Re: P100047
HeartWare® Ventricular Assist System
Filed: December 28, 2010
Amended: March 21, March 25, May 3, and October 11, 2011
Procode: DSQ

Dear Ms. Celaya:

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 HeartWare® Ventricular Assist System (VAS). This device is indicated for use as a bridge to cardiac transplantation in patients who are at risk of death from refractory end-stage left ventricular heart failure. The HeartWare® VAS is designed for in-hospital and out-of-hospital settings, including transportation via fixed wing aircraft or helicopter. 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 25 months for the Implant Kit, Accessories and Surgical Tools of the system and 12 months for the Controller and Battery Pack. 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 provide the following data in post-approval study reports (PAS).

1. *Newly Enrolled (HW-PAS-01):* The study must be conducted as per protocol dated September 20, 2012 (Ver. 1.0) submitted via email. The study will consist of prospective enrollment of patients newly implanted with the HeartWare VAS and who may also be concurrently enrolled in the INTERMACS Registry. At least 1200 patients (600 HeartWare and 600 FDA approved VADS other than HeartWare) patients from at least12 non-IDE sites in the US will be followed annually according to standard of care through 24 months post implant.

   The primary endpoints will be success (alive, transplant, or recovery) at 180 days. Secondary endpoints will consist of:
   - Overall survival on device
   - Re-hospitalizations
   - INTERMACS adverse events
   - Quality of Life measures (as measured by the EuroQol EQ-5D-5L and
   - KCCQ)
   - Functional Status (as measured by the 6 minute walk and / or VO2 max)
   - Post-stroke QOL, Functional and Neurocognitive assessments

   If the propensity score between the HeartWare Group and the Control group is balanced (C-statistic <0.60) or somewhat balanced (C statistic ≥0.60), the study objective will be to demonstrate non-inferiority to the control device within a 10% margin for the primary endpoint of success, which is estimated to be 90%. If the propensity score between the treatment groups is not balanced (one or more strata <5 subjects per treatment group), the objective will be to demonstrate non-inferiority to an objective performance goal of 80%. Subgroup analyses must be conducted by gender and race. For all study patients with an INTERMACS neurologic dysfunction event, there must be a blinded 3rd party imputation

of a modified Rankin Scale Score (mRS) using the INTERMACS data from baseline and 3-6 month interval post-stroke.

2. *Training Program (HeartWare-PAS-02):* The study must be conducted as per protocol dated September 20, 2012 (Ver. 1.0) submitted via email. This study will consist of all centers that implant a commercial HeartWare System in the New Cohort Post Approval Study described in Protocol HW-PAS-01. At least 600 HeartWare patients from at least12 non-IDE sites in the US will be followed annually according to standard of care through 24 months post implant. All non-IDE centers will be trained according to HeartWare's educational and training program. The training will consist of four parts to provide adequate training prior to use of the device, during initial implants, and in follow-up and continuing education: (a) Surgical training, (b) On-site staff training, (c) Initial implant support and (d) Continuing education and support.

   The study must display and compare HW-PAS-1 outcomes (including survival) across sites and between patient cohorts of the IDE (at least 10 implants) vs. non IDE sites. Subgroup analyses must be conducted by gender and race. The objective will also be to assess the effectiveness of the training program by:
   - describing overall site compliance with the approved labeling by assessing the patient baseline characteristics
   - summarizing key clinical parameters including cardiac index, mean arterial pressure (MAP), flow, international normalized ratio (INR), and anti-thrombotic drug therapy
   - Summarize any adverse events including:
     - Bleeding
     - Neurologic events
     - Thromboembolism
     - Infection
     - Arrhythmias
     - Device malfunctions
     - Device exchanges
     - Hypertension

3. *Continued Follow-Up (HW-PAS-03):* The study must be conducted as per protocol dated September 20, 2012 (Ver. 1.0) submitted via email. This study will consist of the continued follow-up of patients who participated in the HeartWare Trials under IDE G070199. The 50 surviving candidates should be approached for re-consent and followed annually according to standard of care through 60 months post-implant.

   The primary safety endpoint of the study is a composite of transplant, explant, and death. This will include transplant date, reason for explant, and cause of death through 60 months.

   Other observational endpoints will be collected and analyzed in the study:
   - Overall survival
   - Re-hospitalizations

- Incidence of INTERMACS adverse events and unanticipated adverse device effects
- Incidence of all device failures and device malfunctions
- Quality of Life improvement (KCCQ and EuroQol EQ-5D-5L)
- Functional status improvement (NYHA and 6-minute walk)

Please note 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 under the PAS Program you are required to submit separate PAS Progress Reports for each PAS every six months during the first two years of the study and annually thereafter. The reports for each PAS 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

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 Anchal Kaushiva at 301-796-6330.

Sincerely yours,

Bram D. Zuckerman

Digitally signed by Bram D. Zuckerman
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, cn=Bram D. Zuckerman, 0.9.2342.19200300.100.1.1=1300079955
Date: 2012.11.19 16:32:17 -05'00'

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

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Medical Device Tracking Order

NOV 29 2012

Ms. Maritza Celaya
Sr. Director, Regulatory Affairs
HeartWare, Inc.
14000 NW 57th Court
Miami Lakes, FL 33014

Re: P100047
HeartWare Ventricular Assist System (DSQ)

Dear Ms. Celaya:

You are notified by this letter of your obligation to adopt a method of tracking for the device referenced above, as authorized by section 519(g) of the Federal Food, Drug, and Cosmetic Act (the Act), 21 U.S.C. § 360i(g). The implementation of section 519(g) of the Act requires the Food and Drug Administration (FDA) to issue an order to manufacturers when FDA determines that a person who manufactures and distributes a device meets the relevant statutory requirements and that tracking is required to protect the public health. This order is effective immediately.

Section 519(g) of the Act states that FDA, "may by order require a manufacturer to adopt a method of tracking a class II or class III device—

(A) the failure of which would be reasonably likely to have serious adverse health consequences; or

(B) which is—

(i) intended to be implanted in the human body for more than one year, or

(ii) a life sustaining or life supporting device used outside a device user facility."

As you know, the corresponding medical device tracking regulations, found in Title 21 Code of Federal Regulations (CFR) Part 821, are intended to ensure that tracked devices can be traced from the device manufacturing facility to the person for whom the device is intended when patient notification (under section 518(a) of the Act, 21 U.S.C. § 360h(a)) or device recall (under section 518(e) of the Act, 21 U.S.C. § 360h(e)) actions are ordered by the agency. The device tracking requirements for exemptions and variances, system and content requirements of tracking, the obligations of persons other than device manufacturers, records and inspection requirements, confidentiality, and record retention requirements, which were published in the Federal Register on August 16, 1993, remain in effect. (21 CFR sections 821.2, 821.25, 821.30, 821.50, 821.55 and 821.60, copy enclosed)

This order to adopt a tracking method does not change your obligations concerning other FDA regulations affecting your device. FDA published in the Federal Register on February 28, 2002, an amendment to the final rule to revise the scope of the regulation and add certain patient confidentiality requirements and non-substantive changes to remove outdated references and simplify terminology. (67 FR 6943) If you need specific guidance, please contact Ann Ferriter, in the Office of Compliance, FDA Center for Devices and Radiological Health, at (301) 796-5686. Other general information on your responsibilities under the Act, or more specific information, such as non-binding guidance on medical device tracking (copy enclosed), may be obtained from the Division of Small Manufacturers, International, and Consumer Assistance at its toll-free number (800) 638-2041, or at the internet address www.fda.gov/cdrh.

Sincerely yours,

Jan B. Welch for

Steven Silverman
Director
Office of Compliance
Center for Devices and
Radiological Health

Enclosures