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

June 7, 2017

Berlin Heart Inc.
Dudley Rajapaksa
Vice President, Regulatory Affairs/Quality/Technical service
200 Valleywood Rd Suite B100
The Woodlands, Texas 77380

Re: P160035
Trade/Device Name: EXCOR Pediatric Ventricular Assist Device

Dear Dudley Rajapaksa:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) completed its review of your premarket approval application (PMA) and issued an approval order on June 6, 2017. We inadvertently made an error in the post approval surveillance condition of approval. The revised post approval surveillance condition of approval is below.

> **OSB Lead PMA Post-Approval Surveillance – Berlin Heart Novel Surveillance:** You are required to provide data to FDA from a registry which captures all-comers (pediatric age range only, <22 years of age) utilizing the Berlin Heart EXCOR (BHE) device as a bridge to cardiac transplant and ensure that surveillance occurs for the BHE over the next five (5) years.
>
> Surveillance through this registry will monitor the following: procedural safety and implant success, adverse events while on BHE device, anticoagulation therapy used while on BHE device, duration of device use, device malfunction or failure, and patient outcomes (survival to transplant, survival to cardiac recovery, death, or patient transfer to different device). Adverse events monitored include but are not limited to: stroke (hemorrhagic or ischemic), transient ischemic attacks, infection, thromboembolism, pump thrombosis requiring pump exchange, major bleeding, new or worsening right heart failure, hepatic dysfunction, new or worsening kidney failure, new or worsening arrhythmias. Device safety issues or malfunctions should also be monitored and reported.
>
> As part of this surveillance you will perform an analysis of a primary endpoint. The primary endpoint is the occurrence of stroke (including ischemic or hemorrhagic) while on BHE support. A minimum of 62 individual enrollees into the registry will allow comparison to a pre-specified performance goal for stroke while on device of 30%. The upper bound of the 95% confidence interval for the registry observed stroke rate will be compared to this pre-specified performance goal. Furthermore, you will work with the

registry to also collect data regarding anticoagulation protocol to determine if differences exist in the safety and effectiveness of this device for populations on newer anticoagulation regimens.

Secondary endpoints include the rate per patient-month of thrombotic events including but not limited to transient ischemic attack, and pump thrombosis requiring pump exchange. Additional secondary endpoints include the rate of above-mentioned surveillance-captured adverse events per patient-month, and a summary of device effectiveness by proportion of subjects experiencing a successful outcome (defined as survival to recovery/successful weaning, survival to transplant, or survival on-BHE device and transplant eligible at 180 days)). Surveillance reports should be provided on a semi-annual basis for the first two years after PMA approval, and then annually thereafter.

Within 30 days of the receipt of this letter, you must submit a PMA supplement that includes a complete plan for the Novel Surveillance described above. Your PMA supplement should be clearly labeled 'OSB Lead PMA Post-Approval Surveillance Plan' as noted above and submitted in triplicate to the address below. Please reference the PMA number above to facilitate processing.

We hope that this error has not inconvenienced you. If you have any questions about this corrective action, please contact Nicole Milligan at 240-402-6630 or Nicole.Milligan@fda.hhs.gov.

Sincerely,

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

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June 6, 2017

Berlin Heart Inc.
Dudley Rajapaksa
Vice President, Regulatory Affairs/Quality/Technical service
200 Valleywood Rd Suite B100
The Woodlands, Texas 77380

Re: P160035
Trade/Device Name: EXCOR® Pediatric Ventricular Assist Device
Filed: August 23, 2016
Amended: January 23, 2017, March 1, 2017, March 8, 2017, and April 21, 2017
Product Code: DSQ

Dear Mr. Rajapaksa:

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 EXCOR® Pediatric Ventricular Assist Device (EXCOR Pediatric). This device is intended to provide mechanical circulatory support as a bridge to cardiac transplantation for pediatric patients. Pediatric candidates with severe isolated left ventricular or biventricular dysfunction who are candidates for cardiac transplant and require circulatory support may be treated using the EXCOR Pediatric. 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 4 years for the EXCOR Blood Pump and 3 years for the EXCOR cannula.

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 Surveillance – Berlin Heart Novel Surveillance: You are required to provide data to FDA from a registry which captures all-comers (pediatric age range only, <22 years of age) utilizing the Berlin Heart EXCOR (BHE) device as a bridge to cardiac transplant and ensure that surveillance occurs for the BHE over the next five (5) years.

Surveillance through this registry will monitor the following: procedural safety and implant success, adverse events while on BHE device, anticoagulation therapy used during procedure and while on original BHE device, duration of device use, device malfunction or failure, and patient outcomes (survival to transplant, survival to cardiac recovery, death, or patient transfer to different device). Adverse events monitored include but are not limited to: stroke (hemorrhagic or ischemic), transient ischemic attacks, infection, thromboembolism, pump thrombosis requiring pump exchange, major bleeding, new or worsening right heart failure, hepatic dysfunction, new or worsening kidney failure, new or worsening arrhythmias. Device safety issues or malfunctions should also be monitored and reported.

As part of this surveillance you will perform an analysis of a primary endpoint. The primary endpoint is the occurrence of stroke (including ischemic or hemorrhagic) while on BHE support.

A minimum of 62 individual enrollees into the registry will allow comparison to a pre-specified performance goal for stroke while on device of 30%. The upper bound of the 95% confidence interval for the registry observed stroke rate will be compared to this pre-specified performance goal. Furthermore, you will work with the registry to also collect data regarding anticoagulation protocol to determine if differences exist in the safety and effectiveness of this device for populations on newer anticoagulation regimens.

Secondary endpoints include the rate per patient-month of thrombotic events including but not limited to transient ischemic attack, and pump thrombosis requiring pump exchange. Additional secondary endpoints include the rate of above-mentioned surveillance-captured adverse events per patient-month, and a summary of device effectiveness by proportion of subjects experiencing a successful outcome (defined as survival to recovery/successful weaning, survival to transplant, or survival on-BHE device and transplant eligible at 180 days)). Surveillance reports should be provided on a semi-annual basis for the first two years after PMA approval, and then annually thereafter.

Within 30 days of the receipt of this letter, you must submit a PMA supplement that includes a complete plan for the Novel Surveillance described above. Your PMA supplement should be clearly labeled 'OSB Lead PMA Post-Approval Surveillance Plan' as noted above and submitted in triplicate to the address below. Please reference the PMA number above to facilitate processing.

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 "OSB 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
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If you have any questions concerning this approval order, please contact Nicole Milligan at 240-402-6630 or Nicole.Milligan@fda.hhs.gov.

Sincerely,

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