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

March 23, 2015

Abiomed, Inc.
% William Bolt
Sr Vice President
22 Cherry Hill Dr.
Danvers, Massachusetts 01923

Re: P140003
Trade/Device Name: Impella 2.5 System
Filed: March 20, 2014
Product Code: OZD

Dear Mr. Bolt:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its evaluation of your premarket approval application (PMA) for the Impella. This device is indicated for:

> *The Impella 2.5 System is a temporary (≤ 6 hours) ventricular support device indicated for use during high risk percutaneous coronary interventions (PCI) performed in elective or urgent, hemodynamically stable patients with severe coronary artery disease and depressed left ventricular ejection fraction, when a heart team, including a cardiac surgeon, has determined high risk PCI is the appropriate therapeutic option. Use of the Impella 2.5 in these patients may prevent hemodynamic instability which can result from repeat episodes of reversible myocardial ischemia that occur during planned temporary coronary occlusions and may reduce peri- and post-procedural adverse events.*

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 2 years (24 months). 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" (please use this title even if the specified interval is more frequent than one year) 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 reports for the conditions listed below. Two (2) copies of each report, identified as an "OSB Lead PMA Post-Approval Study Report" labeled in accordance with how the requirement is identified below and bearing the applicable PMA reference number, should be submitted to the address below.

> OSB Lead PMA Post-Approval Study –***New Enrollment Study***: You have agreed to a study outlined on March 16, 2015 (email), which will characterize the post market Impella 2.5 System outcomes at discharge and 90 days relative to a performance goal (PG) which is derived from the PROTECT II study, and will study the outcomes associated with the learning curve. This study will be a prospective, multicenter, single-arm study comprised of 369 participants from 70 US sites supported with the Impella 2.5

system and consented to one year of clinical follow-up. The inclusion and exclusion criteria for the study population will be the same as the PROTECT II population.

The primary endpoint for safety and effectiveness will be the 10-component major adverse event (MAE) rate at 90 days compared to the established PG. The 10 components are: 1) death, 2) stroke/transient ischemic attack (TIA), 3) myocardial infarction (MI), 4) repeat revascularization, 5) cardiac operation or thoracic or abdominal vascular operation or vascular operation for limb ischemia, 6) acute renal dysfunction, 7) cardiopulmonary resuscitation or ventricular arrhythmia requiring cardioversion, 8) increase in aortic insufficiency by more than one grade, 9) severe hypotension (defined as: systolic blood pressure or augmented diastolic pressure [whichever is greater] <90mmHg for ≥5 min requiring inotropic/pressor medications or intravenous fluid), and 10) failure to achieve angiographic success defined as residual stenosis <30% after stent implantation. This data will be collected at discharge, 90 days, and one year follow up. The established PG is 53%, which is the upper bound of 95% confidence interval of the 45% point estimated rate.

The secondary endpoints include: 1) individual outcomes for each of the 10 MAE components; 2) in-hospital effectiveness and safety endpoints consisting of the effectiveness of hemodynamic support assessed by maximal decrease of cardiac power output from baseline, creatinine clearance change from baseline 24 hours post percutaneous coronary interventions (PCI), device failure assessed as Impella flow <1L/min for more than 5 minutes at the performance level 5 or higher (out of 9), and rate of in-hospital major adverse events; 3) pre-specified subgroup analyses of each of the 10 MAE components, including assessment of the use of adjunctive atherectomy (with versus without), coronary anatomy (unprotected left main/last patent conduit versus 3-vessel disease), morbidity risk (Society of Thoracic Surgery (STS) risk <10 versus ≥10), and learning curve effect.

For the composite primary and all secondary individual MI endpoints, the following definitions should be used: 1) peri-procedural MI's (those detected within 72 hours of the procedure) should use a more contemporary definition of peri-procedural MI, i.e. using 8x upper limit of normal (ULN) increase in enzyme release; and 2) all other MI's after 72 hours should use the standard spontaneous MI definition in American Heart Association (AHA) guidelines (i.e. >99% ULN). The total number of MI's at any time interval would be the total of the above two. The individual rates of each MI (early peri-procedural and late spontaneous) is also recommended to be reported**.**

Additional endpoints include 1) procedural safety (composite at 30 days), death, stroke or TIA, need for vascular operation, peri-procedural MI (using >8x ULN), transfusion >2 units or documented hemolysis requiring transfusion >2 units, increase in aortic insufficiency >1 grade, and acute renal dysfunction; 2) procedure effectiveness (composite at 30 days), i.e. alive with none of the procedural hypotension requiring treatment, or failure to achieve angiographic success, or intra-procedural cardiopulmonary respiration or cardioversion; and 3) long-term effectiveness (composite at 90 days and 1 year), i.e. alive with improvement from baseline (pre-procedural) in

Canadian Cardiovascular Society angina score from 30 days to measurement time point and none of these (MI using standard spontaneous MI, repeat rehospitalization for unstable angina, or repeat revascularization (PCI or coronary artery bypass).

Be advised that the failure to conduct any such study in compliance with the good clinical laboratory practices in 21 CFR part 58 (for a non-clinical study that is 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 (for a clinical study involving human subjects) may be grounds for FDA withdrawal of approval of the PMA. 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. FDA would like to remind you that you are asked to submit PAS Progress Reports every six months during first two years, and annually thereafter.

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" 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 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 Catherine P. Wentz at 301-796-6339 or Catherine.Wentz@fda.hhs.gov.

Sincerely yours,

Bram D. Zuckerman -S

Bram D. Zuckerman, M.D.
Director
Division of Cardiovascular Devices
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