April 9, 2018

Angel Medical Systems, Inc.
Kimberly Moore-Mora
Manager of Quality and Regulatory Affairs
788 Shrewsbury Avenue, Suite 2200
Tinton Falls, New Jersey 07724

Re: P150009
Trade/Device Name: AngelMed Guardian System
Filed: March 16, 2015
Amended: September 23, 2015; April 8, 2016; July 25, 2016; October 26, 2016; and May 5, 2017
Product Code: QBI

Dear Kimberly Moore-Mora:

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 AngelMed Guardian System. This device is an implantable cardiac monitor with patient alerting capability and an additional external alarm device. The device is indicated for use in patients who have had prior acute coronary syndrome (ACS) events and who remain at high risk for recurrent ACS events.

The Guardian System is indicated as an adjunct to patient recognized symptoms. The Guardian System detects potential ongoing ACS events, characterized by sustained ST segment changes, and alerts the patient to seek medical attention for those potential ACS events.

A Guardian System alert is a more accurate predictor of ACS events when compared to patient recognized symptoms alone and demonstrates a reduced rate over time of patient presentations without ACS events (false positives) when compared to patient recognized symptoms alone.

In the absence of symptoms, the Guardian System may identify asymptomatic ACS events and prompt the patient to seek medical attention.

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 12 months.

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 Study – AngelMed Guardian PAS.* The Office of Surveillance and Biometrics will have the lead for studies initiated after device approval. Per protocol synopsis dated 03/29/18 you agreed to conduct a post-approval study to assess diagnostic accuracy of the AngelMed Guardian System, and to evaluate the training programs for both physicians and patients.

You will conduct a prospective, non-randomized, single arm, event-based, multicenter trial. The purpose of the study is to assess: (1) the diagnostic accuracy of the device, (2) the compliance of the prescribing physician, (3) the experience of the implanting physician, (4) the experience of the emergency department physician and (5) the patient compliance for “Emergency” and “See Doctor” alerts.

A total of 500 subjects who have had prior acute coronary syndrome (ACS) events and who remain at high risk for recurrent ACS events will be enrolled in the AngelMed Guardian PAS, for the purpose of accruing 314 True Positive or False Positive acute coronary syndrome (ACS) events.

The diagnostic accuracy primary endpoint is composed of the positive predictive value (PPV) and False Positive Rate (FPR) of the AngelMed Guardian System associated with acute coronary syndrome events. The PPV for Alarms (with or without symptoms) will be compared to a performance goal of 20%. The FPR (with or without symptoms) will be compared to a performance goal of 0.328 false positive events per patient year.

Secondary endpoints include: (1) the frequency of ALARM-Only ACS events (i.e., Silent ACS events), which is defined as the device alarm only presented to the emergency room (ER) physicians and not showing any other symptoms or discomfort/pain , and (2) the symptom-to-door times, defined as time between device alarm and medical presentation. Both secondary endpoints will be analyzed descriptively (frequency, mean, median and percentage of pre-hospital arrivals as a function of time).

Study subject visits will occur at implant, 7-14 days post-implant, 6 and 12 months post-implant and every 6 months thereafter until study exit or study completion. The PAS will be completed once 314 PPV events are collected."

In addition, the adequacy of the training program for the prescribing physician, implanting physician, emergency department physician, and patients will be assessed. Descriptive statistics (the raw count, percentage of all subjects, rate and number of sites) for the following assessments will be provided:

1. instances where the device was prescribed and implanted for patients that do not meet the proper labeling criteria to qualify for a Guardian implantable medical device (IMD)
2. instances of system revisions, e.g. any system problem that requires an invasive corrective procedure to resolve, required within 6 months of implant
3. instances of "Emergency" alarm non-compliance, failure to report to the ER within 72 hours of the alarm
4. instances of "See Doctor" noncompliance, defined as both failure to present to the doctor within 2 weeks of the alarm or reporting to the ER instead of to the doctor in response to the alarm
5. instances of patient non-success to reconfirm ability to recognize and distinguish between "Emergency" and "See Doctor," defined by being able to report the proper actions to take for each and what to do when only symptoms occur in the absence of an alarm.
6. instances of percutaneous intervention (PCI) without at least one positive standard of care (SOC) test reported on a site-based and visit-based basis.

AngelMed Guardian interim PAS reports will be provided every six months, including study site/patient enrollment, demographics, visit compliance, deviations/deficiencies, number of endpoint events out of total required, and descriptive analytics for physician/patient training compliances. The PPV and FPR for the AngelMed Guardian System will be estimated at study completion and provided in the Final Report.

Post Approval Study reports should be provided on a semi-annual basis after PMA approval. Two copies identified as "AngelMed Guardian" and bearing the applicable PMA reference number should be submitted to the address below.

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 the description of the study protocol with analysis plan, interim (per agreed plan), 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
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 Stephen Browning at 240-402-5241 or Stephen.Browning@fda.hhs.gov.

Sincerely,

FDA William H. Maisel - S

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