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

October 24, 2013

Joanna Develter
Director, Regulatory Affairs
Abbott Vascular
4045 Campbell Avenue
Menlo Park, CA 94025

Re: P100009
MitraClip Clip Delivery System (MitraClip CDS)
Filed: March 4, 2010
Amended: March 18, 30, April 12, 22, May 27, September 3, December 16, 2010, January 14, 26, March 10, April 25, May 23, June 2, 13, December 5, 7, 2011, August 28, October 23, 2012, March 28, May 6, July 22, 2013
Procode: NKM

Dear Ms. Develter:

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 MitraClip Clip Delivery System (MitraClip CDS). This device is indicated for the percutaneous reduction of significant symptomatic mitral regurgitation (MR $\geq$ 3+) due to primary abnormality of the mitral apparatus [degenerative MR] in patients who have been determined to be at prohibitive risk for mitral valve surgery by a heart team, which includes a cardiac surgeon experienced in mitral valve surgery and a cardiologist experienced in mitral valve disease, and in whom existing comorbidities would not preclude the expected benefit from reduction of the mitral regurgitation. 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. 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 two post-approval studies (PAS) as described below:

1. PAS 1 Device Registry (Prohibitive Risk DMR Serial Enrollment Patient Registry): You have agreed to a study outline on October 4, 2013 (email) to assess the long term safety and effectiveness in a broad patient population and to study how prohibitive risk is being interpreted in the real world use of the device to ensure the device is used in appropriate circumstances. The study will be a prospective observational cohort registry.

   Newly enrolled patients will be serially enrolled, from varying institutions, until a total of 2000 patients are enrolled or until the MitraClip PAS Analysis Cohort (PAS 2) enrollment is complete. Patients will be followed annually through 5 years. The safety endpoints will include NYHA Class, hospitalizations, stroke, and mortality through 1 year post implant. Annual follow-up data (e.g., death, stroke, surgical intervention, hospitalizations) from year 2 through year 5 post-implant will be obtained by linking to the Center for Medicare and Medicaid Services (CMS) database.

   If a patient goes on to mitral valve surgery within the first year, the following effectiveness endpoints should be collected: echo parameters at baseline and changes in left ventricular end-diastolic volume (LVEDV), in left ventricle internal diameter diastole (LVIDd), and in mitral regurgitation (MR) from baseline. Prohibitive risk status will be audited by a qualified central review committee through a random sampling of prohibitive risk patients according to a predefined schedule throughout the enrollment period.

   Should the Mitral Module of the National Transcatheter Aortic Valve Replacement (TVT) registry housed jointly by the American College of Cardiology and Society for Thoracic Surgeons be used, the data collection for this study (i.e. pre-procedure, peri-procedure, post-procedure, discharge, 30-day, and one-year follow-up) will be nested within this registry.

2. PAS 2 MitraClip Registry (Analysis Cohort): You have agreed to a study outline on October 4, 2013 (email) to characterize longer term (5 year) MitraClip device performance by defining a) long term safety and effectiveness, and b) patient and procedure characteristics that potentially lead to maximum benefit from MitraClip. This study will consist of a subset of patients enrolled in the Device Registry (PAS 1) who meet specific pre-defined entry criteria as determined by a heart team at baseline.

   The primary safety objective is to compare the adverse event (AE) rate at 30 days to a performance goal of 80%. The primary safety endpoints will include freedom from a composite of death and device-related complications including single leaflet device attachment (SLDA), device and/or component embolization, mitral valve stenosis resulting in mitral valve surgery, and any catastrophic device failure resulting in an AE. The secondary safety objective is to compare freedom from death at 1 year to a performance goal of 66%, and freedom from device-related complications through 1 year to a performance goal of 90%. Device related complications will include SLDA, device and/or component embolization, mitral valve stenosis resulting in mitral valve surgery, and any catastrophic device failure resulting in an AE.

   The primary effectiveness endpoint is to compare change in 6 minute walk test distance (6MWT) at 1 year to baseline. The secondary effectiveness endpoints will include changes of MR Severity, LVEDV and LVIDd, Kansas City Cardiomyopathy Questionnaire (KCCQ), and NYHA Functional Classes at 1 year to baseline. Echo parameters will be collected at 1 year. Primary and secondary effectiveness endpoints will also be reported based on MR at discharge or the last visit (whichever is later).

   Other endpoints which will be descriptively reported include baseline demographics and clinical characteristics, procedure time, device time, radiation exposure, time in catheterization laboratory (cath lab), short-term device success and procedure success, and long-term mortality heart failure (HF) hospitalization, stroke, and surgical intervention through 5 years.

   A minimum of 420 evaluable patients at 12-month post-implant will be followed through 5 years. There will be a minimum of 15 sites and maximum of 40 sites with no more than 10% of patients enrolled into PAS 2 per site. Active follow-up of patients will be performed through 1 year. Annual follow-up (e.g., death, stroke, surgical intervention, hospitalizations) from year 2 through year 5 post-implant will be obtained by the link to the CMS database established in PAS 1.

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.

Within 30 days of your receipt of this letter, you must submit a PMA supplement that includes

complete protocols of your post-approval studies. 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.

FDA would like to remind you that you are asked to submit separate PAS Progress Reports every six months during the first two years of the study and annually thereafter. The reports should clearly be identified as Post-Approval Study Report. Two 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).

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 Fernando Aguel at 301-796-6326.

Sincerely yours,

Christy L. Foreman -S

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