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 13, 2015

Ms. Jennifer Bolton
Regulatory Fellow
Boston Scientific Corporation
One Scimed Place
Maple Grove, MN 55311-1566

Re: P130013
WATCHMAN LAA Closure Technology
Filed: May 14, 2013
Procode: NGV

Dear Ms. Bolton:

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 WATCHMAN LAA Closure Technology. This device is indicated to reduce the risk of thromboembolism from the left atrial appendage (LAA) in patients with non-valvular atrial fibrillation who:

- Are at increased risk for stroke and systemic embolism based on $CHADS_2$ or CHA_2DS_2-VASc scores and are recommended for anticoagulation therapy;
- Are deemed by their physicians to be suitable for warfarin; and
- Have an appropriate rationale to seek a non-pharmacologic alternative to warfarin, taking into account the safety and effectiveness of the device compared to warfarin.

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 3 years.

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. 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 study (PAS) reports for each PAS listed below. Two (2) copies of each report, identified as an “ODE Lead PMA Post-Approval Study Report" or “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.

1. ODE Lead PMA Post-Approval Study – ***Continued Follow-up of IDE Cohorts***: The Office of Device Evaluation (ODE) will have the lead for this clinical study, which was initiated prior to device approval. This study should be conducted per revision 06 of the CAP protocol, revision 02 of the PREVAIL protocol, and version AF of the CAP2 protocol. The study will consist of all IDE patients from PREVAIL, CAP, and CAP2 who are currently enrolled and alive.

The study objective is to characterize the safety and effectiveness of the WATCHMAN LAA Closure Technology annually through 5 years post-procedure. For continued follow-up of patients from CAP, the safety and effectiveness endpoints are listed in the protocol as follows: The primary effectiveness endpoint is the successful treatment of the patient without stroke (including ischemic or hemorrhagic), systemic embolism, and cardiovascular or unexplained death. The primary safety endpoint is treatment of the patient without the occurrence of life-threatening events as determined by the Clinical Events Committee, which would include events such as device embolization requiring retrieval, bleeding events such as pericardial effusion requiring drainage, cranial bleeding events due to any source, gastrointestinal bleeds requiring transfusion and any bleeding related to the device or procedure that necessitates an operation.

For continued follow-up of patients from PREVAIL and CAP2, the primary endpoints are listed in the protocol as follows: The first primary endpoint is the occurrence of the composite of stroke (including ischemic or hemorrhagic), systemic embolism, and cardiovascular or unexplained death. The second primary endpoint is the occurrence of ischemic stroke or systemic embolism, excluding the first 7 days post randomization. Additional outcomes which should be reported include complete LAA closure rate, effective LAA closure rate, warfarin discontinuation rate, warfarin or other oral anticoagulation resumption rate and reasons, and information regarding device thrombus (including event rate, treatment, and any associated adverse events).

All available patients in CAP will be followed semi-annually through 5 years. All available patients in PREVAIL and CAP2 will be followed at post-enrollment intervals of 45 days, 6 months, 12 months, semi-annually through 3 years, and thereafter annually through 5 years.

FDA would like to remind you that you are asked to submit separate PAS progress reports every four months for the "Continued Follow-up of IDE Cohorts" study.

2. OSB Lead PMA Post-Approval Study – ***WATCHMAN New Enrollment Study***: You have agreed to a study outlined on March 6, 2015 (email), which will assess whether the rates of safety and effectiveness during the early commercialization of the WATCHMAN device in the United States are consistent with the premarket findings. This will be a prospective, single-arm study comprised of 1,000 participants implanted with the WATCHMAN device and consented to two years of clinical follow-up. You have also agreed to link the data to Centers for Medicare and Medicaid Services (CMS) database for long-term surveillance (annually from years three through five years post-implant).

   Each of the following three primary endpoints must be met separately per the pre-specified performance goals in order to declare study success, where the upper bound of the 95% confidence interval for the event rates for the first, second, and third primary endpoints must be lower than 9.6%, 6.6% and 2.66%, respectively. The first primary endpoint is the occurrence of the composite of stroke (including ischemic or hemorrhagic), systemic embolism, and cardiovascular or unexplained death at 24 months from the time of enrollment. The second primary endpoint is the occurrence of ischemic stroke or systemic embolism at 24 months from the time of enrollment. The third primary endpoint is the

occurrence of one of the following events between the time of implant and within seven days of the procedure or by hospital discharge, whichever is later: all-cause death, ischemic stroke, systemic embolism, or device or procedure-related events requiring open cardiac surgery or major endovascular intervention such as pseudoaneurysm repair, AV fistula repair, or other major endovascular repair. Percutaneous catheter drainage of pericardial effusions, snaring of an embolized device, thrombin injection to treat femoral pseudoaneurysm, and nonsurgical treatments of access site complications will not be included in the assessment of the third primary endpoint, but the rates of these events should be calculated. Secondary endpoints include the following to be collected in the prospective cohort study: (1) implant success rate, procedural safety, and effective closure of the orifice of the left atrial appendage; and (2) CMS claims-identified occurrence of all stroke (including ischemic or hemorrhagic).

Should the left atrial appendage closure (LAAC) National Cardiovascular Device Registry (NCDR) be used for post-approval data collection, pre-procedure, peri-procedure, post-procedure, discharge, 45-day, 12-month, and 24-month follow-up will be nested within the NCDR registry with linkage of the data to CMS claims as described above.

Within 30 days of your receipt of this letter, you must submit a PMA supplement that includes a complete protocol of your nested post-approval study and a complete plan for the *New Enrollment Study* described above. Your PMA supplements 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.

FDA would like to remind you that you are asked to submit separate PAS progress reports every four months for the first two years and annually thereafter for "WATCHMAN New Enrollment Study."

3. OSB Lead PMA Post-Approval Surveillance – ***WATCHMAN Novel Surveillance***: In addition to the condition outlined above, you are required to support and actively participate as a stakeholder in the left atrial appendage closure (LAAC) National Cardiovascular Device Registry (NCDR) registry and undertake such activities to ensure that surveillance occurs through 12 months post-implant within the registry for the WATCHMAN LAAC in at least 1,000 serially implanted patients not participating in the *New Enrollment Study*. You have also agreed to link the data to Centers for Medicare and Medicaid Services (CMS) database for long-term surveillance (annually through five years post-implant).

   This surveillance should monitor registry collected data (including: implant success rate, procedural safety, effective closure of the orifice of the left atrial appendage, and stroke [including ischemic or hemorrhagic] through one- year post-implant] and CMS claims identified occurrence of all stroke (including ischemic or hemorrhagic).

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

includes a complete plan for the *Novel Surveillance* described above. Your PMA supplements should be clearly labeled as an "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.

FDA would like to remind you that you are asked to submit separate PAS progress reports every six months for the first two years and annually thereafter for "WATCHMAN Novel Surveillance."

Each PAS progress report should clearly be identified as a 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.

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. 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).

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
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If you have any questions concerning this approval order, please contact Rachel Neubrander, Ph.D. at 240-402-5086.

Sincerely yours,

William H. Maisel -S

William H. Maisel, MD, MPH
Director (Acting)
Office of Device Evaluation
Deputy Center Director for Science
Center for Devices and Radiological Health