February 29, 2024

Boston Scientific Corporation
Danielle Lippmann
Senior Regulatory Affairs Manager
One Scimed Place
Maple Grove, Minnesota 55311-1566

Re: P230035
Trade/Device Name: AGENT™ Paclitaxel-Coated Balloon Catheter
Product Code: OOB
Filed: October 5, 2023
Amended: December 4, 2023

Dear Danielle Lippmann:

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 AGENT™ Paclitaxel-Coated Balloon Catheter. The AGENT™ Paclitaxel-Coated Balloon Catheter is intended to be used after appropriate vessel preparation in adult patients undergoing percutaneous coronary intervention (PCI) in coronary arteries 2.0 mm to 4.0 mm in diameter and lesions up to 26 mm in length for the purpose of improving myocardial perfusion when treating in-stent restenosis (ISR). Based upon the information submitted, the PMA is approved. You may begin commercial distribution of the device in accordance with the conditions of approval described below. Although this letter refers to your product as a device, please be aware that some approved products may instead be combination products. The Premarket Approval Database available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm identifies combination product submissions.

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). 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 all other applicable requirements, including those governing the manufacture, distribution, and marketing of devices.

Expiration dating for this device has been established and approved at 24 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. 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 must 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 PMA device, under 21 CFR 814.82(a)(9), 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.

You have agreed to provide the following non-clinical information in a separate report, annually, which may be followed by a PMA supplement where applicable.

1. Long-term drug stability studies will be completed on three total finished product batches representing the commercial process each year, evaluating one lot of the largest-longest device size, one lot of an intermediate size, and one lot of the shortest-smallest device size manufactured during that time period. All batches for these studies will be stored at Long Term Conditions of 25°C ± 2°C/60% RH ± 5%, per ICH Q1A(R2). Testing for all studies will occur at 0, 6, 12, 18, and 24 months, per detailed instruction in document 97105846. Be advised that failure to comply with any post-approval requirement, including test protocol, sampling size, sampling plan, and acceptance criteria, constitutes grounds for FDA withdrawal of approval of the PMA in accordance with 21 CFR 814.82(c) and 814.46(a)(2).

2. As you have proposed in your November 21, 2023 interactive response for the CMC module, further process development studies will be completed to support the current coating process, specifications, and process capability, which should be evaluated using all finished product testing. For the additional requested studies, in order to ensure that the commercial manufacturing process is capable of consistently delivering quality product across all proposed operating conditions, product should be manufactured at the extremes of solution concentration and full lot release testing should be provided to support these process parameters. If these parameters are not supported based on the added testing, you should further tighten your in-process specification. The full validation protocols, acceptance criteria, study outcomes, and supportive development and qualification studies should be submitted in a future PMA report. If any changes to your coating process are warranted (e.g., in process coating specification), then you should submit a PMA supplement to request this change.

Be advised that failure to comply with any post-approval requirement, as described, constitutes grounds for FDA withdrawal of approval of the PMA in accordance with 21 CFR 814.82(c) and 21 CFR 814.46(a)(2).

In addition to the Annual Report requirements, you must provide the following data in post-approval study (PAS) reports for each PAS listed below.

3. *AGENT Post-Approval Surveillance Analysis:* This surveillance will be carried out to assess the real-world safety and effectiveness of the AGENT Paclitaxel-Coated Balloon Catheter (AGENT DCB), including in patient populations underrepresented in the AGENT IDE pivotal trial (i.e., women and underrepresented racial and ethnic groups). It will involve all consecutive patients treated within the first 2 years following device approval who are entered into the American College of Cardiology (ACC) CathPCI Registry®, including approximately 30,000 patients through discharge and 10,000 patients through 2 years. Data from the CathPCI Registry will be linked to data from the Centers for Medicare and Medicaid Services (CMS) database to obtain data through 2 years. Endpoints include in-hospital

adverse events, and all-cause death, myocardial infarction, and revascularization through 2 years. Comparative outcomes in women and underrepresented racial and ethnic groups with in-stent restenosis will be specifically evaluated.

4. *The AGENT IDE Continued Follow-Up Study:* This study will evaluate the long-term safety and effectiveness of the AGENT DCB in 600 subjects from the premarket study (The AGENT IDE Study). The AGENT IDE Study was designed as a global, multicenter, single blind, randomized (2:1 AGENT DCB to POBA) trial. Subjects will be followed annually through 5 years post-procedure, and all efforts must be made to minimize the amount of missing long-term data (a minimum of 75% of subjects should be evaluable for the primary endpoint at 3 years, and a minimum of 90% of subjects should have a documented mortality status at 5 years).

   The primary endpoint is the Target Lesion Failure (TLF) rate, defined as any ischemia-driven revascularization of the target lesion (TLR), myocardial infarction (MI, Q-wave and non–Q-wave) related to the target vessel, or cardiac death. The MI events include the PPMI according to the SCAI MI definition and the spontaneous MI according to the 4th Universal MI definition.

   The endpoints to be assessed through 5 years post-procedure are rate of: (1) serious adverse events (SAE), (2) death (including cardiac, non-cardiac, and all-cause), (3) MI (Q-wave and non-Q-wave) rate (PPMI per the SCAI definition and spontaneous MI per 4th Universal Definition), (4) stent/vessel thrombosis rates, (5) target lesion failure (TLF) rate, (6) target lesion revascularization (TLR) rate, (7) target vessel revascularization (TVF) rate, and (8) changes in Quality of Life (as measured by changes in EQ-5D score; through 3 years only).

PAS Progress Reports must be submitted every six (6) months for the first year and annually thereafter, from the date of the PMA approval letter, unless otherwise specified by FDA. The Final PAS Report should be submitted no later than three (3) months after study completion (i.e., last subject's last follow-up date).

From the date of study protocol approval, you must meet the following timelines for the *AGENT Post-Approval Surveillance Analysis:*

- First subject enrolled within 6 months
- 20% of subjects enrolled within 12 months
- 50% of subjects enrolled within 18 months
- 100% of subjects enrolled within 24 months

In addition, you must submit separate periodic reports on the progress of the *AGENT Post-Approval Surveillance Analysis* as follows:

- PAS Progress Reports every six (6) months until subject enrollment has been completed, and annually thereafter, from the date of the PMA approval letter, unless otherwise specified by FDA.
- If any enrollment milestones are not met, you must begin submitting quarterly enrollment status reports every 3 months in addition to your periodic (6-month) PAS Progress Reports, until FDA notifies you otherwise.
- Submit the Final PAS Report three (3) months from study completion (i.e., last subject’s last follow-up date).

Each PAS report should be submitted to the address below identified as a "PMA Post-Approval Study Report" in accordance with how the study is identified above and bearing the applicable PMA reference number.

Be advised that failure to comply with any post-approval requirement, including initiation, enrollment, and completion requirements outlined above, constitutes grounds for FDA withdrawal of approval of the PMA in accordance with 21 CFR 814.82(c) and 814.46(a)(2).

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 accordance with 21 CFR 814.46(a)(3)-(4).

Be advised that protocol information, interim and final results will be published on the Post-Approval Studies Program Database Webpage, available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma_pas.cfm.

In addition, the results from any post approval study should be included in the labeling as these data become available. Under 21 CFR 814.39, 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 Premarket Approval Application Order" (https://www.fda.gov/media/71327/download).

This is a reminder that as of September 24, 2014, class III devices are subject to certain provisions of the final Unique Device Identification (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 Part 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. Combination Products may also be subject to UDI requirements (see 21 CFR 801.30). For more information on these requirements, please see the UDI website available at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-udi-system.

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. Additional information about changes that may require a PMA supplement are provided in the FDA guidance document entitled, "Modifications to Devices Subject to Premarket Approval (PMA) - The PMA Supplement Decision-Making Process" https://www.fda.gov/media/81431/download.

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a

change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production and process controls (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

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 for devices or post-marketing safety reporting (21 CFR Part 4, Subpart B) for combination products, 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 https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems and on combination product post-marketing safety reporting is available at https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products.

In accordance with the recall requirements specified in 21 CFR 806.10 for devices or the post-marketing safety reporting requirements (21 CFR Part 4, Subpart B) for combination products, 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 https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts/industry-guidance-recalls.

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 at https://www.fda.gov/medical-devices/device-approvals-denials-and-clearances/pma-approvals. 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 a copy 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, 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
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 Eleni Whatley at 301-796-6372 or Eleni.Whatley@fda.hhs.gov.

Sincerely,

Brian D. Pullin -S

for Bram Zuckerman, M.D.
Director
OHT2: Office of Cardiovascular Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health