



NOV 22 2011

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Room -WO66-G609
Silver Spring, MD 20993-0002

Ms. Theresa A. Carlson
Senior Regulatory Affairs Specialist
Boston Scientific Corporation
One Scimed Place
Maple Grove, MN 55311

Re: P110010
PROMUS® Element™ Plus Everolimus-Eluting Platinum Chromium Coronary Stent System (Monorail™ and Over-The-Wire)
Filed: March 28, 2011
Amended: May 9, 2011, May 16, 2011, June 13, 2011, June 17, 2011, July 28, 2011, August 4, 2011, August 9, 2011, August 24, 2011
Procode: NIQ

Dear Ms. Carlson:

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 PROMUS Element Plus Everolimus-Eluting Platinum Chromium Coronary Stent System. This device is indicated for improving luminal diameter in patients with symptomatic heart disease due to de novo lesions in native coronary arteries ≥ 2.25 mm to ≤ 4.00 mm in diameter in lesions ≤ 28 mm in length.

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 twelve months.

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.

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 the following post-approval studies:

1. *Platinum Post-Approval Study*: You must conduct a prospective, open-label, multi-center post-approval study, consisting of 2,500 consecutively newly enrolled US patients, with at least 1,000 on-label patients. The data from at least 1,000 newly enrolled on-label patients will be pooled with data from 862 PROMUS PLATINUM WH and SV patients and 400 PE-PROVE patients, in order to provide a minimum of 2,100 on-label patients with 12 months of outcome data, which will provide at least 80% power to assess the primary endpoint of cardiac death or myocardial infarction (MI). Patients should be evaluated at the timepoints of 30 days, 180 days, and annually through 5-years post-procedure. These study cohorts will be used to assess the primary endpoint (cardiac death or MI at 12 months) and secondary endpoints (stent thrombosis at 5 years and rate of longitudinal stent deformation). In addition, to further elucidate the incidence and etiology of events related to longitudinal stent deformation, the protocol must include:
 - a. a specific definition for longitudinal stent deformation;
 - b. questions added to the baseline and procedure forms to capture procedural and anatomic factors, including, but not limited to, whether pre and post-dilatation was performed, whether IVUS was performed, whether other ancillary devices were used and if any resistance was noted during advancement or withdrawal of the ancillary device through a newly implanted stent, target lesion calcification, and tortuosity;
 - c. a specific question regarding longitudinal stent deformation as part of the device deficiency form as well as additional questions to be addressed by the operator if stent deformation occurs (e.g., the clinical circumstances of the event, the identification of any ancillary or adjunctive devices involved, palliative action taken, if any, and whether malapposition was present prior to stent deformation); and

- d. a requirement that angiograms from stent deformation cases be sent to a core laboratory for confirmation that stent deformation occurred, including full analysis of the film. The core laboratory definition for stent deformation will be finalized and included in the protocol as soon as possible, but no later than 60 days following PMA approval.

When appropriate, or as requested by FDA, you should submit a PMA supplement to P110010 requesting to update the DFU with the information obtained from this study.

2. *Continued Follow-up of Premarket Cohort:* In addition to the post-approval study enrolling new patients as outlined above, you must continue follow-up of the premarket cohorts, consisting of 1,646 patients (Workhorse RCT – 1,530; Small Vessel sub-trial – 94; Human Pharmacokinetics sub-trial – 22 participants). You must collect clinical outcomes through 5 years post-procedure on at least 80% of patients enrolled (excluding those discontinued due to death) in the PLATINUM clinical trials. This study will be conducted as per protocol submitted in G080202, and you must provide this follow-up data to the PMA as post-approval study reports.
3. The issue of the optimal duration of dual antiplatelet therapy following PCI with drug-eluting stents (DES) remains a critical question that is currently being studied in the DAPT trial. FDA acknowledges that you are participating in this trial to address a condition of approval for the TAXUS Liberté DES (P060008). Patients treated with the PROMUS DES (approved as XIENCE V/PROMUS P070015) are also included in this trial. As the duration of dual antiplatelet therapy is also relevant for the PROMUS Element Plus, you must fulfill your commitment to the condition of PMA approval for P060008. When appropriate or as requested by FDA, you should submit PMA supplements to the PROMUS Element Plus PMA (P110010) requesting approval to update your DFU to include the data collected in the overall DAPT trial. If you do not fulfill the condition of approval for P060008, you must conduct or participate in a separate clinical trial that will develop data to study the duration of dual antiplatelet therapy following implantation of the PROMUS Element Plus DES. When appropriate, or as requested by FDA, you should submit PMA supplements to this PMA requesting approval to include these data in a DFU update.

Within 30 days of your receipt of this letter, you must submit separate PMA supplements that include the complete protocol of each of your post-approval studies. Each of your PMA supplements 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. 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#2).

FDA would like to remind you that you are required to submit separate PAS Progress Reports for each PAS requirement:

- For post-approval study 1, “*Platinum Post-approval Study*,” you are required to submit a report every 3 months for the first year, then at 18-months, 24-months, and 5 years annually thereafter.
- For post-approval study 2, “*Continued Follow-up of Premarket Cohort*,” you are required to submit a report every 6 months during the first 2 years and 5 years annually thereafter.

Two copies for each PAS requirement, 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”

<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 triplicate, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing. One of those three copies may be an electronic copy (eCopy), in an electronic format that FDA can process, review and archive (general information:

<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/Pre-marketSubmissions/ucm134508.htm>; clinical and statistical data:

<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/Pre-marketSubmissions/ucm136377.htm>)

U.S. Food and Drug Administration
Center for Devices and Radiological Health
PMA Document Mail Center – WO66-G609
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If you have any questions concerning this approval order, please contact Erica Takai, PhD at (301) 796-6353 or erica.takai@fda.hhs.gov.

Sincerely yours,

A handwritten signature in black ink, appearing to read 'Bram D. Zuckerman', with a long horizontal line extending to the right.

Bram D. Zuckerman, M.D.
Director
Division of Cardiovascular Devices
Office of Device Evaluation
Center for Devices and Radiological Health