



FEB 17 2012

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

Ms. Sarah Sheppard
Senior Manager, Regulatory Affairs
Medtronic Vascular, Inc.
3576 Unocal Place
Santa Rosa, CA 95403

Re: P110013
Resolute MicroTrac Zotarolimus-Eluting Coronary Stent System and Resolute Integrity
Zotarolimus-Eluting Coronary Stent System
Filed: April 1, 2011
Amended: May 20, June 22, August 19, September 19, October 14, November 14, 15, and
21, December 19 and 23, 2011; January 5, 11, 13, 17, 18, 19, 23, 24, 26, 27, 30, and 31,
February 1, 9, and 10, 2012
Procode: NIQ

Dear Ms. Sheppard:

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 Resolute MicroTrac and the Resolute Integrity Zotarolimus-Eluting Coronary Stent Systems. These devices are indicated for improving coronary luminal diameters in patients, including those with diabetes mellitus, with symptomatic ischemic heart disease due to de novo lesions of length ≤ 27 mm in native coronary arteries with reference vessel diameters of 2.25 mm to 4.2 mm. We are pleased to inform you that the PMA is approved. You may begin commercial distribution of the devices 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 18 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 provide the following data in post-approval study reports (PAS). Two copies, identified as "PMA Post-Approval Study Report" and bearing the applicable PMA reference number, should be submitted to the address below.

1. *Resolute Integrity Post-Approval Study*: The study must be conducted as per approved protocol IP126, Rev 1A, dated February 8, 2012 (P110013/A024). The study will consist of a prospective, multi-center, non-randomized, single-arm, open-label study of newly enrolled US patients treated with the Resolute Integrity Zotarolimus-Eluting Coronary Stent System.

The primary study objective is to assess the safety and effectiveness of the Resolute Integrity stent for the treatment of *de novo* lesions in native coronary arteries with a reference vessel diameter of 2.25 mm to 4.2 mm. The primary endpoint for this trial is the composite of cardiac death and target vessel myocardial infarction (MI) at 12 months post-procedure.

The secondary endpoints assessed at hospital discharge, 30 days, 6 months, 12 months and 24 months post-procedure will include a composite of major adverse cardiac events (MACE), target lesion failure, target vessel failure, cardiac death, and target vessel MI. Clinical secondary endpoints are to include death, MI, target lesion revascularization, target vessel revascularization, stent thrombosis, stroke, and dual antiplatelet therapy compliance.

The study population will consist of adult patients with *de novo* lesions in native coronary arteries treated with the device per labeling followed up to 2 years post-procedure.

A total of 230 patients must be enrolled to ensure that at least 200 patients will be evaluable at 12 months (95% confidence interval = 0.5%, 5.0%). This assumes that the 12-month risk of the composite cardiac death and target vessel myocardial infarction endpoint is 2.0% (as observed in the Resolute-US pre-approval trial) and a lost to follow up rate of 10% per year.

Please be advised that the results from this 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.

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

2. *Continued Follow-up of the Premarket and OUS Cohort:* In addition to the post-approval study enrolling new US patients as outlined above, you must continue follow-up of patients in the Global RESOLUTE Clinical Trial program through 5 years post-procedure, with the exception of patients enrolled in the RESOLUTE International study, which you should continue to follow through 3 years post-procedure. You must collect clinical outcomes as outlined in the respective investigational plans submitted in G070165, analyzing and reporting on these findings as agreed upon in the Statistical Analysis Plan (P110013/A010). FDA would like to remind you that for this study you are required to submit PAS Progress Reports annually until study completion. The reports should clearly be identified as Post-Approval Study Report. Two copies, identified as "PMA Post-Approval Study Report" and bearing the applicable PMA reference number, should be submitted to the address below.

When appropriate, or as requested by FDA, you should submit a PMA supplement requesting to update the Instructions for Use (IFU) with information obtained from these studies.

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 Endeavor Zotarolimus Eluting Coronary Stent System (P060033). As the duration of dual antiplatelet therapy is also relevant for the Resolute MicroTrac and Resolute Integrity Zotarolimus Eluting Coronary Stent Systems, you must fulfill your commitment to the condition of PMA approval for P060033. When appropriate or as requested by FDA, you should submit PMA supplements to the Resolute MicroTrac and Resolute Integrity PMA (P110013) requesting approval to update your IFU to include the data collected in the DAPT trial. If you do not fulfill the condition of approval for P060033, 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 Resolute MicroTrac and Resolute Integrity Zotarolimus Eluting Coronary Stent Systems and subsequently submit PMA supplements to this PMA requesting approval to include these data in an update to the IFU.

You have agreed to provide the following data as part of a future supplement or report (as defined below):

4. Within 16 months of PMA approval, you should submit a PMA supplement that includes a report of your post-approval study evaluating the suitability of implementing an elution specification criterion of mean $\pm 10\%$. The report should include the summary and discussion of the entire elution data collected from the currently available batches and all additional batches manufactured within the first year after the product's approval. The study's objective should be to target an elution acceptance criterion of mean $\pm 10\%$ for the 1, 6, 24, and 48 hours timepoints and greater than 80% for the 72 hours timepoint, with data collected based on L1/L2/L3, as appropriate. If the results from this analysis indicate that the $\pm 10\%$ acceptance criteria cannot be implemented when the same elution specifications are used for all stents independently of their design, an analysis of the applicability of a $\pm 10\%$ elution acceptance criteria by stent design should be performed. Based on the results of this study, you must either revise elution specification criterion to mean $\pm 10\%$, or provide a scientifically valid explanation for why the revised elution specification cannot be implemented.
5. Within 12 months of PMA approval, you should submit a PMA supplement requesting approval to tighten the in-process coating weight specifications.
6. Within 12 months of PMA approval, you should submit a PMA supplement with details of your investigation into the process losses observed during manufacturing. The supplement should include a detailed explanation of the cause of all process losses, and of your investigations to mitigate these losses. This supplement should also request approval to change the current overage to 3% or less, or demonstrate that the identified losses are unavoidable in order to maintain an overage higher than 3%. A progress report on your efforts to address this issue should be submitted within 6 months of PMA approval.
7. As soon as the data are available, but no later than 18 months following PMA approval, you should submit a nonclinical postapproval report with the results of particulate testing on real-time aged samples of the Resolute MicroTrac and Resolute Integrity on the modified MicroTrac delivery system to confirm the specifications and shelf life established based on results from testing of accelerated aged samples. If the results from testing of real-time aged samples do not confirm the prior results, you should submit a PMA supplement requesting to modify the shelf life accordingly, to establish tighter release specifications for particulates, or both.

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.

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.

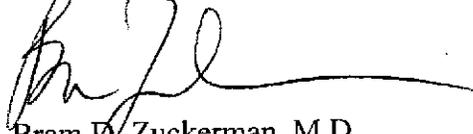
All required documents should be submitted in triplicate, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing. One of those three copies may be an electronic copy (eCopy), in an electronic format that FDA can process, review and archive (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
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

If you have any questions concerning this approval order, please contact Kimberly Peters at (301) 796-6350.

Sincerely yours,



Bram D. Zuckerman, M.D.

Director

Division of Cardiovascular Devices

Office of Device Evaluation

Center for Devices and Radiological Health