



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

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

FEB 22 2013

Re: P110013/S005  
Resolute Integrity Zotarolimus-Eluting Coronary Stent System  
Filed: July 17, 2012  
Amended: August 3 and December 5, 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) supplement for the Resolute Integrity Zotarolimus-Eluting Coronary Stent System. This device is 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  $\leq 35$  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 supplement is approved. You may begin commercial distribution of the device as modified 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 a separate post-approval study (PAS) report. Two (2) copies, identified as "PMA Post-Approval Study Report" and bearing the applicable PMA reference number, should be submitted to the address below. As a condition of approval, you have agreed to conduct the following post-approval studies as described below:

1. *Resolute Integrity Post-Approval Study*: You must incorporate the Resolute Integrity stent lengths 34 and 38mm (2.25 mm to 4.2 mm diameters) into the existing post-approval study required for P110013. As per investigational plan version 126 rev 1C, dated February 7, 2013 this is a prospective, open-label, multi-center post-approval study, consisting of consecutively newly enrolled US patients with a follow-up duration of at least 5 years. The primary endpoint will be a composite of cardiac death and target vessel myocardial infarction at 12 months. The secondary endpoints will be a composite of major adverse cardiac events (MACE), target lesion failure, target vessel failure, and cardiac death/target vessel MI at 5 years. Clinical secondary endpoints are to include death, MI, target lesion revascularization, target vessel revascularization, stent thrombosis, stroke, bleeding complications, and dual antiplatelet therapy compliance at 5 years. All endpoints should be evaluated separately for the following categories: (1) *de novo* lesion treated with stent lengths  $\leq 30$  mm in length (2.25 mm to 4.2 mm diameters) and (2) *de novo lesion* treated with stents 34 mm and 38 mm (2.25 mm to 4.2 mm diameters) as subset analyses. In addition to the original 230 patients required for enrollment in the post-approval study under P110013, you will enroll 56 more patients with a minimum of 20 patients enrolled in the 34 mm cohort and a minimum of 20 patients enrolled in the 38 mm cohort.

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, until study completion.

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 per protocol (P110013). 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 version dated February 8, 2013 (email).

FDA would like to remind you that for this study you are required to submit PAS Progress Reports annually until study completion.

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.

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>

3. Annual testing reports will be provided that evaluate drug stability. The Resolute Integrity stent sizes (34 and 38 mm) will be incorporated into your ongoing stability protocol to bracket the additional stent sizes to be marketed. Please identify this as a nonclinical post-approval report.

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](http://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](http://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](http://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](http://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 six 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 Matthew Trachtenberg at (301) 796-6332.

Sincerely yours,

**Bram D. Zuckerman**

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