



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

April 28, 2017

Medtronic, Inc.  
Christopher Collins  
Principal Specialist, Regulatory Affairs  
3576 Unocal Pl  
Santa Rosa, California 95403

Re: P160043

Trade/Device Name: Resolute Onyx Zotarolimus-Eluting Coronary Stent System  
Filed: September 27, 2016  
Amended: January 26, 2017  
Product Code: NIQ

Dear Christopher Collins:

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 Onyx 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 5.0 mm. We are pleased to inform you that the PMA is approved. You may continue commercial distribution of the device upon receipt of this letter.

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 24 months at 25°C. This is to advise you that the protocol you used to establish this expiration dating is considered an approved protocol for the purpose of extending the expiration dating as provided by 21 CFR 814.39(a)(7).

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. 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 PMA 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.

You have agreed to provide the following non-clinical information in a separate report, annually:

Long-term and accelerated drug stability studies will be completed on three production-scale batches of the approved finished product (according to the formal stability protocol) through the expiration dating period. All products included in these studies will be manufactured according to the US in-process inspection for coating weight tolerance. A minimum of one batch per year should be placed into the long-term stability program.

In addition to the Annual Report requirements, you must provide the following data in post-approval study (PAS) reports for each PAS listed below. Separate PAS Progress Reports must be submitted for each study annually, unless otherwise specified by FDA. Two (2) copies of each report, identified at an "ODE 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 RESOLUTE ONYX Core (2.25mm-4.00mm) Clinical Study. The Office of Device Evaluation (ODE) will have the lead for this clinical study, which was initiated prior to device approval. The RESOLUTE ONYX Core (2.25mm-4.00mm) Clinical Study (G1401078/S001) is an open-label, single-arm, multi-center study which enrolled 75 patients and was designed to assess the safety and effectiveness of the Resolute Onyx Zotarolimus Eluting Coronary Stent System (Core Sizes) through 3 years post-index procedure. The primary endpoint is in-stent late lumen loss (LLL) at 8 months. You must collect and report clinical outcomes

to FDA through 3 years post-procedure on patients enrolled in the RESOLUTE ONYX Core (2.25mm-4.00mm) Clinical Study.

2. ODE Lead PMA Post-Approval Study – RESOLUTE ONYX Post-Approval Study (PAS). The Office of Device Evaluation (ODE) will have the lead for this clinical study, which was initiated prior to device approval under G140178/S008. The RESOLUTE ONYX PAS is a single arm, non-investigational, open-label multi-center study intended to evaluate the safety and effectiveness of the Resolute Onyx Zotarolimus Eluting Coronary Stent Systems in a real world, more-comers population. The study will enroll 510 study subjects: 410 study subjects will be enrolled in the Main Study cohort (2.00-4.00mm) and 100 subjects will be enrolled in an Extra-Large (XLV) sub-study (4.50-5.00mm) cohort. The study will be conducted in up to 25 US sites (representing at least 50% of total enrollment) and up to 5 OUS sites (maximum of 50 study subjects in the Main Study cohort and 49 subjects in the in XLV sub-study cohort). The primary endpoint for all study subjects enrolled in the RESOLUTE ONYX PAS is Target Lesion Failure (TLF) at 12 months, defined as Cardiac Death, Target Vessel Myocardial Infarction or Target Lesion Revascularization. The Main Study cohort will have a performance goal (PG) of 13.2%. The XLV sub-study cohort does not have a formal hypothesis but descriptive statistics will be provided. You must collect and report clinical outcomes to FDA through 3 years post-procedure on patients enrolled in the RESOLUTE ONYX PAS.

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.

Be advised that protocol information, interim and final results will be published on the Post Approval Study Webpage <http://www.fda.gov/devicepostapproval>.

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 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. 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" (<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 <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 <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 <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 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 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 Nicole Goodsell at 240-402-6600 or [Nicole.Goodsell@fda.hhs.gov](mailto:Nicole.Goodsell@fda.hhs.gov).

Sincerely,

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