

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

January 17, 2014

Ms. Mansi Gala Principal Specialist, Regulatory Affairs Medtronic CoreValve LLC 3576 Unocal Place Santa Rosa, CA 95403

Re: P130021

McS-P4-23-AOA (23 mm; CoreValveTM EvolutTM), McS-P3-26-AOA (26 mm), McS-P3-29-AOA (29 mm), and McS-P3-31-AOA (31 mm); Delivery Catheter System (DCS), Models DCS-C4-18FR and DCS-C4-18FR-23; and Compression Loading System (CLS),

Model CLS-3000-18FR Filed: July 25, 2013

Amended: October 4, 2013 and November 29, 2013

Procode: NPT

Dear Ms. Gala:

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 Medtronic CoreValve™ System. This device is indicated for relief of aortic stenosis in patients with symptomatic heart disease due to severe native calcific aortic stenosis (aortic valve area ≤ 0.8 cm², a mean aortic valve gradient of > 40 mmHg, or a peak aortic-jet velocity of > 4.0 m/s) and with native aortic annulus diameters between 18 and 29 mm who are judged by a heart team, including a cardiac surgeon, to be at extreme risk or inoperable for open surgical therapy (predicted risk of operative mortality and/or serious irreversible morbidity ≥50% at 30 days). 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 one year. 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 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 three post-approval studies (PAS) as described below:

1. PAS 1 Continued follow-up of the IDE pivotal cohort (extreme risk patients): This study should be conducted per protocol in PAS 1 Addendum (Version 1) to Medtronic CoreValve U.S. Pivotal Trial (Extreme Risk Patients) Clinical Investigational Plan (Version 12) as submitted to FDA by email on December 13, 2013. The study will consist of all IDE patients currently enrolled and alive who received the Medtronic CoreValve® System (MCS).

The objective of this PAS is to characterize the clinical outcomes at year 2 and annually through 5 years post-procedure. The safety and effectiveness endpoints listed in the protocol include major adverse cardiovascular and cerebrovascular events (MACCE), change in functional status and quality of life, conduction disturbance requiring permanent pacemaker implantation, echocardiographic assessment, and valve dysfunction. All available patients in the IDE study (656 ilio-femoral and non-iliofemoral and 63 roll-in patients) in all sites (41) will be followed annually through 5 years.

2. PAS 2 Continued follow-up of continued access protocol (CAP) cohort (extreme risk patients): This study should be conducted per PAS 2 Addendum (Version 1) to Medtronic CoreValve Continued Access Study Clinical Investigational Plan (Version 5) as submitted to FDA by email on December 13, 2013. The study will consist of all CAP patients currently enrolled and alive who received the Medtronic CoreValve® System

(MCS).

The objective of this PAS is to characterize the clinical outcomes at year 2 and annually through 5 years post-procedure. The safety and effectiveness endpoints as listed in the protocol include major adverse cardiovascular and cerebrovascular events (MACCE), change in functional status and quality of life, conduction disturbance requiring permanent pacemaker implantation, echocardiographic assessment, and valve dysfunction. All available patients in the CoreValve® Continued Access Study (approximately 1640 extreme risk patients, including both ilio-femoral and non-ilio-femoral implant access) in all sites (45) will be followed-up at 1 month, 6 months, and annually to 5 years post implant.

3. *PAS 3 New enrollment (extreme risk patients):* This study should be conducted per study protocol dated January 4, 2014, Version 0.4 as submitted to the FDA by email. This study will be a prospective non-randomized registry study using STS/ACC TVT Registry (TVT-R) housed jointly by the American College of Cardiology and Society for Thoracic Surgeons.

The primary safety objective is to characterize the composite safety endpoint at 30 days and 12 months, as per TVT-R definition: all-cause mortality, all stroke, life-threatening (or disabling) bleeding, acute kidney injury-stage 3 (including renal replacement therapy), peri-procedural myocardial infarction, and repeat procedure for valve-related dysfunction (surgical or interventional therapy). The secondary safety endpoints will be the individual components of the composite safety endpoint listed above per the TVT-R definition at 30 days and 12 months.

Device success (intra-procedure) is measured per TVT-R definition.

Additional safety/effectiveness objectives are to evaluate: (1) the neurological, vascular and quality of life outcomes at 30 days and 12 months, (2) the learning curves at 30 days, and (3) long term survival and safety annually through 5 years post-implant.

The analyses will be descriptive and no statistical hypothesis testing will be performed. Comparisons of PAS3 to the Pivotal (PAS1) and CAP (PAS2) continued follow-up patients will be made in learning curves at 30 days and the survival rate annually out to 5 years as well as other components of the TVT-R safety composite adverse events.

A total of 5000 consecutive patients in TVT-R from all participating US sites will be enrolled. The data collection for this study (i.e. pre-procedure, peri-procedure, post-procedure, discharge, 30-day, and one-year follow-up) must be nested within TVT-R. The long-term follow-up (annually through 5 years post-implant) will be conducted through linkage of the TVT-R data to Centers for Medicare and Medicaid Services (CMS) claims data.

Within 30 days of your receipt of this letter, you must submit a PMA supplement that

includes a complete protocol for PAS3. Your PMA supplement 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.

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.

FDA would like to remind you that you are asked to submit separate PAS Progress Reports annually for PAS1 and PAS2, and every six months during the first two years and annually thereafter for PAS3. The reports should clearly be identified as Post-Approval Study Report. Two copies for each study, 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"

(www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070974 .htm#2.

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.

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 https://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

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.

committee. FDA may, for good cause, extend this 30-day filing period.

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 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 PMA Document Mail Center – WO66-G609 10903 New Hampshire Avenue Silver Spring, MD 20993-0002

If you have questions concerning this approval order, please contact Changfu Wu, Ph.D., at (301) 796-6086.

Sincerely yours,

for Bram D. Zuckerman, M.D.

Director

Division of Cardiovascular Devices

Office of Device Evaluation

Center for Devices and Radiological Health



Food and Drug Administration 10903 New Hampshire Avenue Silver Spring, MD 20993

Medical Device Tracking Order

1/21/14

MEDTRONIC INC. 3576 UNOCAL PLACE SANTA ROSA, CA 95403-1774 UNITED STATES

Re: P130021

AORTIC VALVE, PROSTHESIS, PERCUTANEOUSLY DELIVERED (NPT)

Dear Mansi Gala:

You are notified by this letter of your obligation to adopt a method of tracking for the device referenced above, as authorized by section 519(g) of the Federal Food, Drug, and Cosmetic Act (the Act), 21 U.S.C. § 360i(g). The implementation of section 519(g) of the Act requires the Food and Drug Administration (FDA) to issue an order to manufacturers when FDA determines that a person who manufactures and distributes a device meets the relevant statutory requirements and that tracking is required to protect the public health. This order is effective immediately.

Section 519(g) of the Act states that FDA, "may by order require a manufacturer to adopt a method of tracking a class II or class III device—

- (A) the failure of which would be reasonably likely to have serious adverse health consequences; or
- (B) which is—
 - (i) intended to be implanted in the human body for more than one year, or
 - (ii) a life sustaining or life supporting device used outside a device user facility."

The corresponding medical device tracking regulations, found in Title 21 Code of Federal Regulations (CFR) Part 821, are intended to ensure that tracked devices can be traced from the device manufacturing facility to the person for whom the device is intended when patient notification actions under section 518(a) of the Act, 21 U.S.C. § 360h(a), or device recall actions under section 518(e) of the Act, 21 U.S.C. § 360h(e), are ordered by the FDA. The device tracking requirements for exemptions and variances; system and content requirements of tracking; the obligations of persons other than device manufacturers; records and inspection requirements; and confidentiality requirements, which were published in the Federal Register on August 16, 1993, remain in effect. (21 CFR sections 821.2, 821.25, 821.30, 821.50, 821.55 and 821.60)

This order to adopt a tracking method does not change your firm's obligations concerning other FDA regulations affecting its device. FDA published in the Federal Register on February 28, 2002, an amendment to the final rule to revise the scope of the regulation and add certain patient confidentiality requirements and non-substantive changes to remove outdated references and simplify terminology. (67 FR 6943) If you need specific guidance, please contact Deb Yoder, in the Office of Compliance, FDA Center for Devices and Radiological Health, at (301) 796-6109. Other general information on your firm's responsibilities under the Act, or more specific information, such as non-binding guidance on medical device tracking (link provided), may be obtained from the Division of Small Manufacturers, International, and Consumer Assistance at its toll-free number, (800) 638-2041, or at the internet address www.fda.gov/cdrh.

Sincerely,

Steven Silverman

Director

Office of Compliance Center for Devices and Radiological Health

Enclosures/Links

Medical Device Tracking; Guidance for Industry and FDA Staff Federal Register Notice on Tracked Devices