December 31, 2018

William Cook Europe ApS
℅ Scott Williams
Director, Regulatory Science
Cook Incorporated
750 Daniels Way
PO Box 489
Bloomington, Indiana 47402

Re: P180001
Trade/Device Name: Zenith® Dissection Endovascular System
Product Code: MIH
Filed: January 30, 2018
Amended: April 30, 2018, October 1, 2018

Dear Scott Williams:

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 Zenith Dissection Endovascular System. The Zenith Dissection Endovascular System (Zenith TX2 Dissection Endovascular Graft with Pro-Form and Zenith Dissection Endovascular Stent) is indicated for the endovascular treatment of patients with Type B aortic dissection. The Zenith TX2 Dissection Endovascular Graft with Pro-Form is intended to seal the entry tear(s) and to exclude aneurysms associated with chronic dissections. The Zenith Dissection Endovascular Stent is intended to be used as a distal component to provide support to delaminated segments of non-aneurysmal aorta with dissection distal to a Zenith TX2 Dissection Endovascular Graft with Pro-Form. The system is indicated for use in patients having suitable vascular anatomy for endovascular repair, including:

- Adequate iliac/femoral access compatible with the required introduction systems
- For the Zenith TX2 Dissection Endovascular Graft with Pro-Form:
  - Non-dissected/aneurysmal aortic segments (fixation sites) distal to the left common carotid artery and proximal to the entry tear with a length of at least 20 mm,
  - Non-dissected/aneurysmal aortic segments (fixation sites) distal to the left common carotid artery and proximal to the entry tear with a diameter (measured outer-wall to outer-wall) of no greater than 38 mm and no less than 20 mm, and
- For the Zenith Dissection Endovascular Stent:
  - Diameter at non-aneurysmal intended implant site for the stent (measured outer-wall to outer-wall) of no greater than 38 mm (true lumen) and no less than 20 mm (total aortic diameter).

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. Although this letter refers to your

product as a device, please be aware that some approved products may instead be combination products. The Premarket Approval Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm identifies combination product submissions.

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 3 years.

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. 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.

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 a Clinical Update to physician users at least annually. At a minimum, this update will include, for your Zenith Dissection Endovascular System clinical studies, a summary of the number of patients for whom data are available, with a summary of false lumen characteristics (i.e., diameter change, patency, and source of persistent flow), dissection-related deaths, aortic ruptures, aortic enlargements, extension of the dissection, major adverse events (i.e., paraparesis, paraplegia, new ischemia), losses of device integrity, and additional dissection-related interventions, including the reasons for the interventions. A summary of any explant analysis findings is to be included. Additional relevant information from commercial experience within and outside of the U.S. is also to be included. The clinical update for physician users and the information supporting the updates must be provided in the Annual Report.

In addition to providing information regarding your dissection study in your clinical updates to physician users, you agreed to report any significant observations from the post approval study described below of the use of the Zenith Dissection Endovascular System to repair Type B dissections in the descending thoracic aorta.

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. Each report, identified as a "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. *Continued Follow-up of the Zenith Dissection Endovascular System Pivotal Study:* This is a prospective, consecutively enrolling, single-arm, multi-center study that consists of continued follow-up of all available subjects from the Zenith Dissection Endovascular System pivotal study. A total of 73 subjects were enrolled in the study and remaining subjects will be followed for 5 years. Secondary endpoints through 5 years will include false lumen characteristics (i.e., diameter change, patency, and source of persistent flow), dissection-related deaths, aortic ruptures, aortic enlargements, extension of the dissection, major adverse events (i.e., paraparesis, paraplegia, new ischemia), losses of device integrity, and additional dissection-related interventions, including the reasons for the interventions. No formal hypothesis testing will be performed for the longer-term follow-up.

2. *SVS VQI Post market Surveillance:* You also agree to support and actively participate as a stakeholder in the Society for Vascular Surgery Patient Safety Organization governed Vascular Quality Initiative and undertake such activities to ensure that surveillance occurs for the Zenith Dissection Endovascular System when used to repair Type B dissections in the descending thoracic aorta in 120 patients with acute dissections (using the complete Zenith Dissection Endovascular System) and 60 patients with chronic dissections (using any component of the Zenith Dissection Endovascular System).
This surveillance should monitor false lumen characteristics and freedom from dissection-related mortality, additional dissection-related intervention, dissection treatment success, the individual elements of the composite endpoint dissection treatment success, all-cause mortality, endovascular device penetration of the aortic wall, loss of device integrity, device technical success at the time of the procedure, and device procedural success. The reports will include data at the following timepoints: pre-operative, 30-day, 1-year, and yearly thereafter through 5 years.

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).

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. Combination Products may also be subject to UDI requirements (see 21 CFR 801.30). For more information on these requirements, please see the UDI website, http://www.fda.gov/udi.

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 for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products, 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 and on combination product postmarketing safety reporting is available at (see https://www.fda.gov/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm).

In accordance with the recall requirements specified in 21 CFR 806.10 for devices or the postmarketing safety reporting requirements (21 CFR 4, Subpart B) for combination products, 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 a copy 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, 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
Document Control Center - WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

If you have any questions concerning this approval order, please contact Stacy Monza at 301-796-2783 or Stacy.Monza@fda.hhs.gov.

Sincerely,

Nicole G. Ibrahim -S

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