DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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

Dr. Theodore Heise
Vice President, Regulatory Scientific Affairs
Cook, Inc.
P.O. Box 489
Bloomington, IN 47402-0489

APR 11 2012

Re: P020018/S40
Zenith® Fenestrated AAA Endovascular Graft (with the adjunctive Zenith Alignment Stent)

Dear Dr. Heise:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) completed its evaluation of your premarket approval application (PMA)/Supplement and issued an approval order on April 4, 2012. We inadvertently made an error in the second condition of approval regarding the data to be provided in the post-approval study report. In our approval order we stated that technical success for the evaluation of your training program is defined as:

> Successfully completed procedure with endograft patency, preservation of all vessels targeted by fenestrations, and no Type I or **II** endoleaks at the time of deployment completion.

The appropriate definition for technical success is:

> Successfully completed procedure with endograft patency, preservation of all vessels targeted by fenestrations, and no Type I or **III** endoleaks at the time of deployment completion.

We hope that this error has not inconvenienced you. If you have any questions about this corrective action, please contact Dorothy Abel at (301) 796-6366.

Sincerely yours,

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

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APR – 4 2012

Re: P020018/S40
Zenith® Fenestrated AAA Endovascular Graft (with the adjunctive Zenith Alignment Stent)
Filed: October 7, 2011
Amended: December 22, 2011, and January 6, January 25, and March 20, 2012
Procode: MIH

Dear Dr. Heise:

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 Zenith Fenestrated AAA Endovascular Graft (with the adjunctive Zenith Alignment Stent). The Zenith Fenestrated AAA Endovascular Graft is indicated for the endovascular treatment of patients with abdominal aortic or aortoiliac aneurysms having morphology suitable for endovascular repair, including:

- Adequate iliac/femoral access compatible with required introduction systems
- Nonaneurysmal infrarenal aortic segment (neck) proximal to the aneurysms with:
  - Length ≥ 4 mm and unsuitable for a non-fenestrated graft
  - Diameter ≤ 31 mm and ≥ 19 mm
  - Angle < 45 degrees relative to long axis of aneurysm
  - Angle < 45 degrees relative to axis of suprarenal aorta
- Ipsilateral iliac artery fixation site > 30 mm in length and between 9 – 21 mm in diameter
- Contralateral iliac artery distal fixation site >30 mm in length and between 7 – 21 mm in diameter

The Zenith Alignment Stent is indicated for use as an adjunct to the Zenith Fenestrated AAA Endovascular Graft to secure positive alignment of fenestrations or scallops with the orifice of aortic branch vessels having diameters ranging from 3 to 8 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 3 years.

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.

You have agreed to provide the following information as part of the Annual Report:

1. You will provide a clinical update to physician users at least annually. At a minimum, this update will include, for your long-term post-approval study cohort, a summary of the number of patients for whom data are available, with the rates of technical success, treatment success, aneurysm-related mortality, aneurysm rupture, secondary endovascular procedures, conversion to surgical repair, complications, endoleak, aneurysm enlargement, prosthesis migration, and patency. Reports of losses of device integrity, reasons for conversion and causes of aneurysm-related death and rupture are to be described. A summary of any explant analysis findings are to be included. Additional relevant information from commercial experience within and outside of the US is also to be included. The clinical updates for physician users and the information supporting the updates must be provided in the Annual Report.

In addition to the Annual Report requirements, you must provide the following data in a separate post-approval study (PAS) report:.

1. *Long-term follow-up study:* The study must be conducted as per agreement reached on April 2, 2012. This prospective, observational, single-arm study will consist of continued follow-up of the premarket cohort, as well as newly enrolled subjects, and patients will be followed annually.

The primary endpoint of the study is aneurysm-related mortality at 5 years. Aneurysm-related mortality is defined as:

> Death from aneurysm rupture through 5 years; death from any cause occurring within 30 days of the initial procedure or a secondary intervention; or any death determined to be related to the aneurysm or its treatment.

Additional study endpoints will include rupture, conversion, morbidity, device integrity, device patency, changes in aneurysm size, endoleak, migration, and secondary interventions. In addition, the study will evaluate your training plan effectiveness as measured by the composite freedom from the following events at 30 days in up to the first 3 patients from each site: technical failure, loss of patency (by core lab analysis), rupture, secondary intervention, conversion, and Type I or III endoleak (by core lab analysis).

In order to evaluate the hypothesis for 5-year aneurysm related mortality 70 patients are needed to determine if the performance goal of 18% has been met. Allowing for 14% of patients who may withdraw or become lost to follow-up and 6 additional patients that refused to consent for long-term follow-up in the pre-approval study, the total PAS number of enrolled subjects will be 88. The study population will consist of patients enrolled in the premarket study and de novo patients. Information on clinical outcomes is expected to be collected annually through 5 years post-procedure on at least 80% of patients enrolled (excluding those discontinued due to death).

2. *Evaluation of training program:* The study must be conducted as per agreement reached on April 2, 2012. This prospective, observational, single-arm registry study will consist of the evaluation of de novo subjects who have been treated by physicians who completed your training program.

   The primary endpoint for this study is technical success. Technical success is defined as:

   > Successfully completed procedure with endograft patency, preservation of all vessels targeted by fenestrations, and no Type I or II endoleaks at the time of deployment completion.

   The study population will consist of the first patients (2 max) treated by at least 41 investigators who have completed the commercial training program.

   The rate of technical success in the registry will be statistically compared to a performance goal of 80%. The sample size for this study will be 82 subjects.

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.

FDA would like to remind you that for each of your PAS's, you are required to submit PAS Progress Reports every six months during the first two years and annually thereafter. The PAS Progress Reports should be submitted separately from the Annual Reports. 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

Within 30 days of your receipt of this letter, you must submit a PMA supplement that includes a complete protocol of your post-approval studies. 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. If there are multiple protocols being finalized after PMA approval, please submit each protocol as a separate PMA supplement.

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/PremarketSubmissions/ucm134508.htm; clinical and statistical data: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/ucm136377.htm)

U.S. Food and Drug Administration
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If you have any questions concerning this approval order, please contact Dorothy Abel at (301) 796-6366.

Sincerely yours,

Christy Foreman
Office Director
Office of Device Evaluation
Center for Devices and Radiological Health