



Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

MAY 21 2008

Dr. Theodore Heise
Vice President Regulatory Scientific Affairs
Cook Incorporated
750 North Daniels Way
Bloomington, IN 47404

Re: P070016
Zenith® TX2® Thoracic TAA Endovascular Graft with the H&LB One-Shot™
Introduction System
Filed: July 2, 2007
Amended: August 1, 6, and 23, October 1, and 2, 2007 and March 3, 2008
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) for the Zenith® TX2® Thoracic TAA Endovascular Graft with the H&LB One-Shot™ Introduction System. This device is indicated for the endovascular treatment of patients with aneurysms or ulcers of the descending thoracic aorta having vascular morphology suitable for endovascular repair, including:

- Adequate iliac/femoral access compatible with the required introduction systems,
- Non-aneurysmal aortic segments (fixation sites) proximal and distal to the aneurysm or ulcer:
 - with a length of at least 25 mm, and
 - with a diameter measured outer wall to outer wall of no greater than 38 mm and no less than 24 mm.

We are pleased to inform you that the PMA is approved. You may begin commercial distribution of the device in accordance with the conditions described below and in the "Conditions of Approval" (enclosed).

The sale, distribution, and use of this device are restricted to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Federal Food, Drug, and Cosmetic Act (the act) under the authority of section 515(d)(1)(B)(ii) of the act. FDA has also determined

that, to ensure the safe and effective use of the device, the device is further restricted within the meaning of section 520(e) under the authority of section 515(d)(1)(B)(ii), (1) insofar as the labeling specify the requirements that apply to the training of practitioners who may use the device as approved in this order and (2) insofar as the sale, distribution, and use must not violate sections 502(q) and (r) of the act.

In addition to the post-approval requirements outlined in the enclosure, you have agreed to the following conditions of approval:

1. You have agreed to provide a clinical update to physician users at least annually. At a minimum, this update will include, for your pivotal study cohort and your post-approval study cohort, a summary of the number of patients for whom data are available, with the rates of aneurysm rupture, secondary endovascular procedures, conversion to surgical repair, aneurysm-related mortality, major adverse events, endoleak, aneurysm enlargement, prosthesis migration, patency, misaligned deployment, aortic perforation and retrograde dissection. 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 supplements to your PMA.
2. In addition to the periodic report (often referred to as annual report) requirements outlined in the enclosure, you have agreed to provide the following data in a separate post-approval study report. You have agreed to perform a post-approval study for the Zenith® TX2® Thoracic TAA Endovascular Graft with the H&LB One-Shot™ Introduction System to evaluate the longer-term safety and effectiveness of the Zenith® TX2® Thoracic TAA Endovascular Graft through five years of implantation. The primary endpoint for this study is freedom from aneurysm-related mortality at 5 years. Aneurysm-related mortality is defined as:

Death from any cause occurring within 30 days of the initial procedure or a secondary intervention; or any death determined by the independent clinical events committee to be causally related to the initial implant procedure, secondary intervention, or rupture of the treated aneurysm.

This study is expected to include 273 patients, 160 endovascular patients from the original pivotal study cohort, as well as enrollment of an additional 125 patients at a minimum of 15 investigational sites. At 1 month, 12 months, and, at each annual visit, a contrast enhanced CT scan, chest x-ray, blood tests, pulses, ankle-brachial indices (ABIs), and a clinical examination will be conducted. All data will be entered into a database, analyzed, and submitted in post-approval reports to the FDA, and a final report will be submitted after completion of the follow-up and analysis. This follow-up plan will allow

an evaluation of aneurysm-related mortality, major adverse events, migration, patency, endoleaks, device integrity, aneurysm enlargement, aneurysm rupture, secondary endovascular procedures and conversion to open surgical repair over time. Upon completion of this post-approval study, you must provide a supplement with revised labeling that reflects the study findings.

3. You have also agreed to perform an evaluation to better understand the overall outcomes in females and non-Caucasians undergoing endovascular aneurysm repair (EVAR) with the Zenith® TX2® Thoracic TAA Endovascular Graft with the H&LB One-Shot™ Introduction System. This evaluation will include a subset evaluation of the females and non-Caucasians enrolled in the post-approval study described in item 2 above, as well as a summary of the current literature research results of females and non-Caucasians having undergone EVAR. This evaluation is to include descriptive statistics to summarize literature-derived outcomes in patients with the EVAR therapy, literature-derived Zenith® TX2® Thoracic TAA Endovascular Graft with the H&LB One-Shot™ Introduction System-specific outcomes, and post-approval study outcomes in female and non-Caucasians populations. Findings of this evaluation must be provided with each regular post-approval study report update until the completion of the post-approval study described in item 2 above.
4. You have agreed to implement a training program, as outlined in the PMA, which includes a subset analysis to examine the skills of new practitioners in the use of the Zenith® TX2® Thoracic TAA Endovascular Graft with the H&LB One-Shot™ Introduction System. This evaluation will include a subset of the 160 patients enrolled in the post-approval study described in item 2 above. You will evaluate a 30-day composite device effectiveness measure of freedom from any one of the following events in up to 5 patients from each site: technical failure; loss of patency (by core lab analysis); rupture; secondary intervention; conversion; stent fracture (by core lab analysis); Type I or III endoleak (by core lab analysis); or migration. Findings of this evaluation must be provided with the post-approval study report updates.

Within 30 days of your receipt of this letter, you must submit a PMA supplement that includes a complete protocol of your post-approval study to incorporate the collection and reporting of the information described in items 3 and 4 above. Your PMA supplement should be submitted in triplicate to the address below and reference the PMA number above to facilitate processing.

Expiration dating for this device has been established and approved at 3 years.

CDRH does not evaluate information related to contract liability warranties, however you should be aware that any such warranty statements must be truthful, accurate, and not misleading, and must be consistent with applicable Federal and State laws.

CDRH will notify the public of its decision to approve your PMA by making available 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/cdrh/pmapage.html>. Written requests for this information can also be made to the Dockets Management Branch, (HFA-305), Food and Drug Administration, 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 requesting an opportunity for administrative review, either through a hearing or review by an independent advisory committee, under section 515(g) of the Federal Food, Drug, and Cosmetic Act (the act).

Failure to comply with any postapproval requirement constitutes a ground for withdrawal of approval of a PMA. Commercial distribution of a device that is not in compliance with these conditions is a violation of the act.

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. The labeling will not routinely be reviewed by FDA staff when PMA applicants include with their submission of the final printed labeling 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.

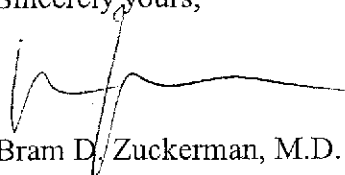
All required documents should be submitted in triplicate, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

PMA Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Blvd.
Rockville, Maryland 20850

Page 5 – Dr. Theodore Heise

If you have any questions concerning this approval order, please contact Dorothy Abel at (240) 276-4169.

Sincerely yours,

A handwritten signature in black ink, appearing to read 'Bram D. Zuckerman', with a long horizontal flourish extending to the right.

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

Enclosure

CONDITIONS OF APPROVAL

PREMARKET APPROVAL APPLICATION (PMA) SUPPLEMENT. Before making any change affecting the safety or effectiveness of the device, submit a PMA supplement for review and approval by FDA unless the change is of a type for which a "Special PMA Supplement-Changes Being Effected" is permitted under 21 CFR 814.39(d) or an alternate submission is permitted in accordance with 21 CFR 814.39(c) or (f). A PMA supplement or alternate submission shall comply with applicable requirements under 21 CFR 814.39 of the final rule for Premarket Approval of Medical Devices.

All situations that require a PMA supplement cannot be briefly summarized; therefore, please consult the PMA regulation for further guidance. The guidance provided below is only for several key instances.

A PMA supplement must be submitted when unanticipated adverse effects, increases in the incidence of anticipated adverse effects, or device failures necessitate a labeling, manufacturing, or device modification.

A PMA supplement must be submitted if the device is to be modified and the modified device should be subjected to animal or laboratory or clinical testing designed to determine if the modified device remains safe and effective.

A "Special PMA Supplement - Changes Being Effected" is limited to the labeling, quality control and manufacturing process changes specified under 21 CFR 814.39(d)(2). It allows for the addition of, but not the replacement of previously approved, quality control specifications and test methods. These changes may be implemented before FDA approval upon acknowledgment by FDA that the submission is being processed as a "Special PMA Supplement - Changes Being Effected." This procedure is not applicable to changes in device design, composition, specifications, circuitry, software or energy source.

Alternate submissions permitted under 21 CFR 814.39(e) apply to changes that otherwise require approval of a PMA supplement before implementation of the change and include the use of a 30-day PMA supplement or annual postapproval report (see below). FDA must have previously indicated in an advisory opinion to the affected industry or in correspondence with the applicant that the alternate submission is permitted for the change. Before such can occur, FDA and the PMA applicant(s) involved must agree upon any needed testing protocol, test results, reporting format, information to be reported, and the alternate submission to be used.

Alternate submissions permitted under 21 CFR 814.39(f) for manufacturing process changes include the use of a 30-day Notice. The manufacturer may distribute the device 30 days after the date on which the FDA receives the 30-day Notice, unless the FDA notifies the applicant within 30 days from receipt of the notice that the notice is not adequate.

POSTAPPROVAL REPORTS. Continued approval of this PMA is contingent upon the submission of postapproval reports required under 21 CFR 814.84 at intervals of 1 year from the date of approval of the original PMA. Postapproval reports for supplements approved under the original PMA, if applicable, are to be included in the next and subsequent annual reports for the original PMA unless specified otherwise in the approval order for the PMA supplement. Two copies identified as "Annual Report" and bearing the applicable PMA reference number are to be submitted to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850. The postapproval report shall indicate the beginning and ending date of the period covered by the report and shall include the following information required by 21 CFR 814.84:

1. Identification of changes described in 21 CFR 814.39(a) and changes required to be reported to FDA under 21 CFR 814.39(b).
2. Bibliography and summary of the following information not previously submitted as part of the PMA and that is known to or reasonably should be known to the applicant:
 - a. unpublished reports of data from any clinical investigations or nonclinical laboratory studies involving the device or related devices ("related" devices include devices which are the same or substantially similar to the applicant's device); and
 - b. reports in the scientific literature concerning the device.

If, after reviewing the bibliography and summary, FDA concludes that agency review of one or more of the above reports is required, the applicant shall submit two copies of each identified report when so notified by FDA.

ADVERSE REACTION AND DEVICE DEFECT REPORTING. As provided by 21 CFR 814.82(a)(9), FDA has determined that in order to provide continued reasonable assurance of the safety and effectiveness of the device, the applicant shall submit 3 copies of a written report identified, as applicable, as an "Adverse Reaction Report" or "Device Defect Report" to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850 within 10 days after the applicant receives or has knowledge of information concerning:

1. A mix-up of the device or its labeling with another article.
2. Any adverse reaction, side effect, injury, toxicity, or sensitivity reaction that is attributable to the device and:
 - a. has not been addressed by the device's labeling; or
 - b. has been addressed by the device's labeling but is occurring with unexpected severity or frequency.

3. Any significant chemical, physical or other change or deterioration in the device, or any failure of the device to meet the specifications established in the approved PMA that could not cause or contribute to death or serious injury but are not correctable by adjustments or other maintenance procedures described in the approved labeling. The report shall include a discussion of the applicant's assessment of the change, deterioration or failure and any proposed or implemented corrective action by the applicant. When such events are correctable by adjustments or other maintenance procedures described in the approved labeling, all such events known to the applicant shall be included in the Annual Report described under "Postapproval Reports" above unless specified otherwise in the conditions of approval to this PMA. This postapproval report shall appropriately categorize these events and include the number of reported and otherwise known instances of each category during the reporting period. Additional information regarding the events discussed above shall be submitted by the applicant when determined by FDA to be necessary to provide continued reasonable assurance of the safety and effectiveness of the device for its intended use.

REPORTING UNDER THE MEDICAL DEVICE REPORTING (MDR) REGULATION.

The Medical Device Reporting (MDR) Regulation became effective on December 13, 1984. This regulation was replaced by the reporting requirements of the Safe Medical Devices Act of 1990 which became effective July 31, 1996 and requires that all manufacturers and importers of medical devices, including in vitro diagnostic devices, report to the FDA whenever they receive or otherwise become aware of information, from any source, that reasonably suggests that a device marketed by the manufacturer or importer:

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 or importer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

The same events subject to reporting under the MDR Regulation may also be subject to the above "Adverse Reaction and Device Defect Reporting" requirements in the "Conditions of Approval" for this PMA. FDA has determined that such duplicative reporting is unnecessary. Whenever an event involving a device is subject to reporting under both the MDR Regulation and the "Conditions of Approval" for a PMA, the manufacturer shall submit the appropriate reports required by the MDR Regulation within the time frames as identified in 21 CFR 803.10(c) using FDA Form 3500A, i.e., 30 days after becoming aware of a reportable death, serious injury, or malfunction as described in 21 CFR 803.50 and 21 CFR 803.52 and 5 days after becoming aware that a reportable MDR event requires remedial action to prevent an unreasonable risk of substantial harm to the public health. The manufacturer is responsible for submitting a baseline report on FDA Form 3417 for a device when the device model is first reported under 21 CFR 803.50. This baseline report is to include the PMA reference number. Any written report and its envelope is to be specifically identified, e.g., "Manufacturer Report," "5-Day Report," "Baseline Report," etc.

Any written report is to be submitted to:

Food and Drug Administration
Center for Devices and Radiological Health
Medical Device Reporting
PO Box 3002
Rockville, Maryland 20847-3002

Additional information on MDR is available at <http://www.fda.gov/cdrh/devadvice/351.html>



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Medical Device Tracking Order

Food and Drug Administration
Center for Devices and
Radiological Health
9200 Corporate Blvd
Rockville, MD 20850

Theodore Heise, PhD
Cook, Inc.
750 Daniels Way
P.O. Box 489
Bloomington, Indiana 47402

MAY 21 2008

RE: Endovascular graft (P070016)

Dear Dr. Heise:

You are notified by this letter of your obligation to adopt a method of tracking for the devices referenced above, as authorized by section 519(g) of the Federal Food, Drug, and Cosmetic Act, (the Act) as amended by section 211 of the Food and Drug Administration Modernization Act of 1997 (FDAMA). The implementation of section 519(g) of the Act, as amended, 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 tracking is required to protect the public health. This order is effective immediately.

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

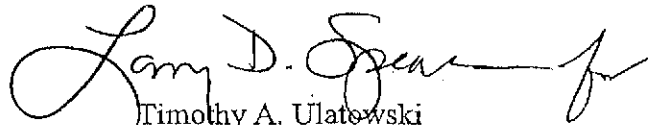
- (A) the failure of which would be reasonably likely to have serious adverse health consequences; or
- (B) which is—
 - (i) intended to be implanted in the human body for more than one year, or
 - (ii) a life sustaining or life supporting device used outside a device user facility."

As you know, 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 by whom the device is intended to be used when patient notification (under section 518(a) of the act) or device recall (under section 518(e) of the act) actions are ordered by the agency. The device tracking requirements for exemptions and variances, system and content requirements of tracking, the obligations of persons other than device manufacturers, such as distributors, records and inspection requirements, confidentiality, and record retention 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, copy enclosed.)

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This order to adopt a tracking method does not change your obligations concerning other existing FDA regulations affecting your 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 Chet Reynolds, in the Office of Compliance at (240) 276-0100. Other general information on your responsibilities under the Act, or more specific information, such as non-binding guidance on medical device tracking (copy enclosed), may be obtained from the Division of Small Manufacturers, International, and Consumer Assistance at its toll-free number (800) 638-2041 or (240) 276-3150, or at the internet address www.fda.gov/cdrh.

Sincerely yours,



Timothy A. Ulatowski
Director
Office of Compliance
Center for Devices and
Radiological Health

Enclosures