DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

SEP 6 2005

Ric Ruedy
Director, Regulatory Affairs
Abbott Vascular Devices
400 Saginaw Drive
Redwood City, CA 94063

Re: P040038
Xact® Carotid Stent System (model numbers 82095-01, 82093-01, 82089-01, 82099-01, 82094-01, 82092-01, 82088-01, 82098-01, 82091-01, 82087-01, 82097-01, 82090-01, 82086-01, 82096-01)
Filed: September 3, 2004
Amended: October 12, December 14, December 20, and December 27 2004; January 10, February 2, March 23, May 5, June 27, and September 2, 2005
Procode: NIM

Dear Mr. Ruedy:

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 Xact® Carotid Stent System. The Xact® Carotid Stent System, used in conjunction with the Abbott Vascular Devices embolic protection system, is indicated for the improvement of the lumen diameter of carotid arteries in patients considered at high risk for adverse events from carotid endarterectomy who require percutaneous carotid angioplasty and stenting for occlusive artery disease and meet the criteria outlined below:

1. Patients with carotid artery stenosis (≥ 50% for symptomatic patients by ultrasound or angiography or ≥ 80% for asymptomatic patients by ultrasound or angiography), located between the origin of the common carotid artery and the intra-cranial segment of the internal carotid artery; and

2. Patients must have a reference vessel diameter ranging between 4.8 mm and 9.1 mm at the target lesion.

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 postapproval requirements outlined in the enclosure, you have agreed to provide the following data in a postapproval report:

1. You have agreed to conduct the following studies and to report on these studies every 6 months following PMA approval until completion of the studies:

   a. You have agreed to perform a long-term follow-up study on at least 305 patients. The goals of this follow-up study are to evaluate the longer-term safety and effectiveness of the Xact Carotid Stent System and Emboshield® Embolic Protection System through three years of implantation. At each annual visit, a clinical examination, a carotid duplex ultrasound, and a neurological exam (NIHSS) will be conducted. Clinical data will be recorded on the corresponding case report forms (CRFs). Diagnostic studies on patients in this cohort will continue to be evaluated by the core laboratory. All data will be monitored, entered into a database, analyzed and submitted in reports to the FDA and a final report will be submitted after completion of the follow-up and analysis. This follow-up proposal will allow an evaluation of adverse events, neurological events, and percent stenosis.

   b. You have agreed to conduct a post-approval study(ies) that includes at least 1500 sequentially enrolled patients from up to 150 geographically disbursed sites. This study will follow all 1500 patients for 30 days, and 500 patients out to 12 months. The post-approval study will enroll patients from high, moderate and low volume centers and treated by physicians that represent Group 1, 2, and 3 training. Imaging data, that is, follow-up ultrasound or angiographic assessments, when performed, will be reviewed by a core laboratory. Stroke scale assessments will be conducted in addition to the proposed independent neurological assessments.

      The endpoint for the 1500 patients enrolled will be a 30-day composite death, stroke and myocardial infarction (MI). A pre-operative, discharge and 30-day independent neurological assessment for all patients and assessment of all device related adverse events will be conducted.

For the 500 patients with 12 month follow-up, the endpoints will be a composite of stroke, death and MI at 30 days and ipsilateral stroke at 12 months.

A subset of this post-approval study patient cohort may be used to obtain the long-term follow-up data specified in condition #1(a).

In addition to this information, the reports for this study will also include enrollment information (i.e., number of patients enrolled per site); a line listing summarizing information captured in the case report forms; and data summaries, analyses, and interpretation from the enrolled subjects.

Please note that if subsequent data analyses identify areas of significant off-label use, you should submit an IDE to conduct an appropriate study(ies) to evaluate the off-label use.

The post-approval study protocol(s) should be submitted as PMA supplements within 45 days of the date of this letter.

2. In your interim and annual PMA reports, be advised that the following information from your post-approval study should be included:

   a. Reports of adverse events reported to Abbott or a designated party by practitioners and user facilities as described below:

      i. For adverse events that are reported to FDA in accordance with the MDR Regulation (21 CFR Part 803) since the last post-approval report, a tabulation of the MDR report number and a short description/tabulation of event and outcome. Be advised that when reporting adverse events under MDR, you will need to note that the device was the carotid stent under Section D2 (generic name) of the report form.

      ii. For adverse events that are deemed not MDR-reportable, summary information of the events and outcomes. These events would include all events of device malfunction, even if no adverse clinical event was associated with the malfunction.

      iii. Summary analyses and summary interpretations of both anticipated and unanticipated adverse events.

3. In the event that primary endpoint rates or device related events observed in the post-approval study are higher than anticipated, you have agreed to apply the stopping rule detailed in your post-approval protocol.

4. You have agreed to implement a training program, as outlined in the PMA. Your reports of the post-approval study will include evaluations of the adequacy of this program based on 30 day death, stroke, and MI rates for the study as a whole and at each center. Should modifications be necessary to the training program, you will describe and justify each modification.

5. You have agreed to provide a clinical update to physician users at least annually until the last patients in your long-term follow-up study and post-approval studies have reached their final endpoint. The information contained in this update will be provided to the FDA via the PMA Annual Report. At a minimum, this update will include for your long-term study cohort a summary of the number of patients for whom data are available, with composite death, stroke, and MI rate at 30 days, and ipsilateral stroke at 31 days to 365 days, and annually to 5 years, and rates for freedom from target lesion revascularization, stent thrombosis, and device or procedure-related events. This update will also include a summary of the number of patients for whom data are available, with the rate of composite death, stroke, and MI and other device related adverse events at 30 days. For the patients followed out to 12 months, this update will include a summary of the number of patients for whom data are available, with rates of death, stroke, and MI at 30 days, and ipsilateral stroke at 31 days to 365 days. Stent fractures from any source are to be described. Additional relevant information from commercial experience within and outside of the US will also be included.

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

If you have any questions concerning this approval order, please contact Dr. Kenneth Cavanaugh at (301) 443-8517, extension 170.

Sincerely yours,

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

Enclosure

Last Modified: 1-31-02

# 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(e) 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

Copies of the MDR Regulation (FOD # 336&1336) and FDA publications entitled "An Overview of the Medical Device Reporting Regulation" (FOD # 509) and "Medical Device Reporting for Manufacturers" (FOD #987) are available on the CDRH WWW Home Page. They are also available through CDRH's Fact-On-Demand (F-O-D) at 800-899-0381. Written requests for information can be made by sending a facsimile to CDRH's Division of Small Manufacturers International and Consumer Assistance (DSMICA) at 301-443-8818.