SUMMARY OF SAFETY AND EFFECTIVENESS DATA

1.0 GENERAL INFORMATION

Devices Generic Name:	Carotid Stent
Devices Trade Names:	Xact® Carotid Stent System
Applicant's Name and Address:	Abbott Vascular Devices 400 Saginaw Drive Redwood City, California 94063 USA On behalf of: MedNova Ltd. IDA Enterprise Park Tuam Road Galway Ireland
PMA Number:	P040038
Date of Panel Recommendation:	None
Date of Notice of Approval to the Applicant:	September 6, 2005

2.0 INDICATIONS FOR USE

The Xact® Carotid Stent System (hereafter referred to as Xact®), 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:

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

3.0 CONTRAINDICATIONS

Contraindications associated with angioplasty must be considered when using the Xact® device. These include, but are not limited to:

- Patients in whom anticoagulant and/or antiplatelet therapy is contraindicated.
- Patients with severe vascular tortuosity or anatomy that would preclude the safe introduction of the Guiding catheter/ Introducer Sheath BareWire™, Delivery Catheter, Filtration Element, and/or Retrieval Catheter.
- Patients with a known hypersensitivity to nickel-titanium.
- Patients with uncorrected bleeding disorders.
- Lesions in the ostium of the common carotid artery.

4.0 WARNINGS AND PRECAUTIONS

***Warnings* and *Precautions* can be found in the Instructions for Use for the Xact® Carotid Stent System.**

5.0 DEVICE DESCRIPTION

Xact® Device Description

The Xact® Carotid Stent System is comprised of a delivery system designed to deliver a pre-loaded Xact® stent to the carotid vasculature.

The 6F (5.7Fr OD) sheath compatible Xact® Stent Delivery System is tracked over a Filter Delivery Wire. The radiopacity of the stent enables fluoroscopic monitoring and assists in achieving accurate stent placement and precise lesion length matching. Xact® stent deployment is achieved by rotation of the delivery system handle in a clockwise direction.

The Xact® stent is a self–expanding Nitinol (nickel-titanium alloy) stent with properties of superelasticity and shape memory. Upon deployment at body temperature, the stent recovers to its pre-formed shape. The Xact® stent is provided in two configurations, tapered and straight, to accommodate the appropriate carotid anatomy. The Xact® Carotid Stent System is available in the configurations outlined in Table 1.

Table 1: Xact® Product Range

Product Code	Unconstrained Stent Diameter	Stent Length	Configuration
RX			
82095-01	7 mm	20 mm	Straight
82093-01	8 mm	20 mm	Straight
82089-01	9 mm	20 mm	Straight
82099-01	10 mm	20 mm	Straight
82094-01	7 mm	30 mm	Straight
82092-01	8 mm	30 mm	Straight
82088-01	9 mm	30 mm	Straight
82098-01	10 mm	30 mm	Straight
82091-01	8-6 mm	30 mm	Tapered
82087-01	9-7 mm	30 mm	Tapered
82097-01	10-8 mm	30 mm	Tapered
82090-01	8-6 mm	40 mm	Tapered
82086-01	9-7 mm	40 mm	Tapered
82096-01	10-8 mm	40 mm	Tapered

6.0 ALTERNATIVE PRACTICES AND PROCEDURES

Alternative practices and procedures for treatment of atherosclerotic disease of the carotid arteries currently includes other stent and embolic protection systems for which there is an approved PMA, carotid endarterectomy, medical therapy, or a combination of both surgical and pharmaceutical intervention. The primary treatment used to prevent stroke in patients with Carotid Artery Disease (CAD) is surgical removal of the plaque by means of an endarterectomy. Medical therapy includes antiplatelet and/or anticoagulant medicine (aspirin, clopidogrel or ticlopidine) as well as pharmaceutical treatment for hypertension and hyperlipidemia. Stroke risk factor reduction is recommended through lifestyle modifications such as cessation of smoking and changes to diet and alcohol usage.

7.0 MARKETING HISTORY

The Xact® Carotid Stent System was CE marked in April 2003. It is marketed for the treatment of CAD in the following countries: Australia, Austria, Belgium, Cyprus, Czech Republic, Denmark, Egypt, Estonia, Finland, France, Germany, Greece, Hong Kong, Hungary, Ireland, India, Italy, Latvia, Lebanon, Lithuania, Luxembourg, Malaysia, Malta, Netherlands, Norway, Portugal, Poland, Saudi Arabia, Singapore, Slovak Republic, Slovenia, South Africa, Slovenia, Spain, Sweden, Switzerland, Turkey, and the United Kingdom.

The Xact® Carotid Stent System has not been withdrawn from marketing for any reason relating to the safety and effectiveness of the device.

8.0 POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

8.1 Observed Adverse Events

The SECuRITY Registry Study was a prospective, multi-center, non-randomized study performed to demonstrate the safety and effectiveness of the Xact® Carotid Stent System and Emboshield® Embolic Protection System in treating carotid stenosis in patients at high risk (≥ 50% for symptomatic patients by ultrasound or angiography or ≥ 80% for asymptomatic patients by ultrasound or angiography) for carotid endarterectomy. High-risk patients were defined as having an anatomical risk factor(s) and/or a co-morbidity risk factor(s). A total of three hundred ninety nine (399) patients were enrolled at 30 sites in the United States and Australia. Of the total 399 patients, 93 patients were enrolled in the lead-in phase of the study and one patient was enrolled under the emergent use guidelines, three months following termination of enrollment. Therefore, a total of three hundred five (305) pivotal patients are included in the Intent to Treat (ITT) analysis group.

Serious Adverse Events for the first 30 days of the study and up to one year are presented in tables 2 and 3. Table 4 provides a summary of all causes of death that occurred during the SECuRITY Trial.

Non-stroke neurological includes events such as visual/speech disturbances, confusion, seizure, weakness, and transient ischemic attack (TIA).

Target Lesion Revascularization (TLR) is defined as any repeat invasive procedure, including angioplasty, stenting endarterectomy, or thrombolysis, performed to open or increase the luminal diameter inside or within 10 mm of the previously treated lesion. To be considered clinically indicated, the patient must be symptomatic with > 50% stenosis or asymptomatic with > 80% stenosis.

Adverse events are categorized by body system and are defined as follows:

- Access site complications include events such as bruising, hematoma, and bleeding.
- Vascular includes events such as peripheral vascular disease and deep vein thrombosis.
- Hemodynamic includes events such as hypo- and hypertension, syncope, and dizziness.
- Bleeding includes events such as non-access site bleeding, anemia up to 30 days, and Gastrointestinal (GI) bleeds up to 30 days.
- Blood dyscrasia includes events such as anemia later than 30 days, and thrombocytopenia.
- Respiratory includes events such as pneumonia, embolism, chronic obstructive pulmonary disease (COPD), and respiratory arrest.
- GI includes events such as nausea, ulcers and GI bleeds later than 30 days.
- Genitourinary includes events such as urinary tract infection and prostatic hyperplasia.
- Infection includes events such as abscess, sepsis, and groin infection.
- Metabolic includes events such as electrolyte imbalance, diabetes Mellitus, and renal failure.
- Musculoskeletal includes events such as pain, fractures, and joint replacements.

The numbers and types of adverse events observed were anticipated given the high co-morbid state of these patients.

Table 2: Serious Adverse Events Summary, ≤ 30 days (Non-Hierarchical)

Events	≤ 30 days SECuRITY (N=305)	
	n	%
All Death, Stroke and MI	26	8.52 %
Death	3	0.98 %
Stroke-Related	3	0.98 %
Not Stroke-Related	0	0 %
All Strokes	21	6.89 %
Major	8	2.62 %
Ipsilateral Stroke	7	2.30 %
Non-ipsilateral Stroke	1[1]	0.33 %
Minor	13	4.26 %
Ipsilateral Stroke	12	3.93 %
Non-ipsilateral Stroke	1[2]	0.33 %
Non-Stroke Neurological	25	8.20 %
Restenosis (≥ 50% stenosis as measured by ultrasound)	7	2.29 %
Target Lesion Revascularization (TLR), Clinically Indicated	0	0%
Cardiac	15	4.92 %
MI	2	0.66 %
Arrhythmia	4	1.31 %
Angina	4	1.31 %
Congestive Heart Failure (CHF)	3	0.98 %
Coronary Artery Disease (CAD)	2	0.66 %
Procedural Complication	109	35.74 %
Hypotension	86	28.20 %
Arrhythmia	7	2.30 %
Vasospasm	3	0.98 %
Dissection	10	3.28 %
In-stent Thrombosis	1	0.33 %
Emergent CEA	1	0.33 %
Emergent Intervention -other	1	0.33 %
Access Site Complication Requiring Repair / Transfusion	8	2.62 %
Vascular	3	0.98 %
Hemodynamic	11[3]	3.61 %
Bleeding	6	1.97 %
Requiring transfusion	1	0.33 %
GI Bleeding	5	1.64 %
Blood Dyscrasia	2	0.66 %
Respiratory	5	1.64 %
Gastrointestinal	18	5.90 %
Genitourinary	3	0.98 %
Infection	2	0.66 %
Metabolic	11	3.61 %
Musculoskeletal	32	10.49 %
Miscellaneous[4]	1	0.33 %

[1] Stroke adjudicated as contralateral
[2] Stroke adjudicated as bilateral
[3] Includes hypotension and hypertension not associated with the procedure.

Table 3: Serious Adverse Events Summary, Up to 365 Days (Non-hierarchical)

Events	31-365 days SECuRITY (N=302)		0-365 days SECuRITY (N=305)	
	n	%	n	%
Death	26	8.6	29	9.5
Stroke-Related	3	1.0	6	2.0
Not Stroke-Related	23	7.6	23	7.5
Unknown	0	0	0	0
Ipsilateral Stroke	5	1.7	24	7.9
Major	4	1.3	11	3.6
Minor	1	0.3	13	4.3
Non-ipsilateral Stroke	1	0.3	2	0.7
Non-Stroke Neurological	18	6.0	43	14.1
Target Lesion Revascularization (TLR), Clinically Indicated	2	0.7	2	0.7
Restenosis (≥ 50% stenosis as measured by ultrasound)	14	4.6	20	6.6
Cardiac	57	18.9	74	24.3
MI	5	1.7	7	2.3
Arrhythmia	6	2.0	10	3.3
Angina	6	2.0	10	3.3
Congestive Heart Failure (CHF)	10	3.3	15	4.9
Coronary Artery Disease (CAD)	30	9.9	32	10.5
Procedural Complication	0	0	109	35.74
Hypotension	0	0	86	28.20
Arrhythmia	0	0	7	2.30
Vasospasm	0	0	3	0.98
Dissection	0	0	10	3.28
In-stent Thrombosis	0	0	1	0.33
Emergent CEA	0	0	1	0.33
Emergent Intervention -other	0	0	1	0.33
Access Site Complication Requiring Repair / Transfusion	0	0	8	2.62
Vascular	42	13.9	45	14.7
Hemodynamic	25	8.3	36	11.8
Bleeding	4	1.3	10	3.3
Requiring transfusion	1	0.3	2	0.7
GI Bleeding	3	1.0	8	2.6
Blood Dyscrasia	9	3.0	11	3.6
Respiratory	15	5.0	20	6.6
Gastrointestinal	8	2.6	26	8.5
Genitourinary	8	2.6	11	3.6
Infection	6	2.0	8	2.6
Metabolic	14	4.6	25	8.2
Musculoskeletal	19	6.3	51	16.7
Miscellaneous[5]	4	1.3	5	1.6

[4]Aortic aneurysm repair

[5] Adenocarcinoma, Aortic aneurysm repair, aortic valve replacement and malignant hepatic neoplasm.

Table 4: Cause of Death (0-30 days and 31-365 days)

Cause of Death	0-30 Days N=305		31 - 365 days N=302	
	n	%	n	%
Stroke (neurological)	3	0.98	3	0.99
Cardiac	0	0.00	10	3.31
Cancer	0	0.00	4	1.32
Renal Failure	0	0.00	3	0.99
Respiratory	0	0.00	1	0.33
Diabetes	0	0.00	1	0.33
Accidental	0	0.00	1	0.33
Device Related Deaths	0	0.00	0	0.00

8.2 Potential Adverse Events

As reported in the literature, the following adverse events are potentially associated with carotid stents and embolic protection systems:

- Abrupt closure
- Allergic reactions
- Aneurysm
- Angina/Coronary ischemia
- Ateriovenous Fistula
- Bacteremia or septicemia
- Bleeding from anticoagulant or antiplatelet medications
- Bradycardia/arrhythmia
- Cerebral edema
- Cerebral hemorrhage
- Congestive Heart Failure
- Death
- Drug reactions
- Embolism (including air and device)
- Emergent or urgent Endarterectomy
- Fever
- Filter thrombosis/occlusion
- Fluid overload
- Groin hematoma, with or without surgical repair
- Hemorrhage or hematoma
- Hemorrhagic stroke
- Headache
- Hypotension
- Hyperperfusion syndrome
- Hypertension
- Infection/sepsis
- Ischemia/infarction of tissue/organ
- Myocardial Infarction
- Other conduction disturbances
- Pain and tenderness

- Pain, infection, or discomfort at the access site
- Pseudoaneurysm
- Renal failure/insufficiency
- Restenosis of the stented artery
- Seizure
- Stent deformation, collapse, fracture, movement of stent, possibly requiring emergency surgery
- Stent/filter entanglement/damage
- Stroke or other neurological complications
- Thromboembolic episodes
- Thrombophlebitis
- Total occlusion of the artery
- Transient ischemic attacks (TIAs)
- Vascular access complications (e.g. loss of pulse, femoral artery pseudoaneurysm and infection)
- Ventricular fibrillation
- Vessel dissection, rupture, or perforation
- Vessel thrombosis (partial blockage)
- Unstable angina pectoris

9.0 SUMMARY OF PRE-CLINICAL STUDIES

9.1 In Vitro Product Testing

Bench test studies of pre-defined characteristics were conducted with products that were subjected to three different conditions: post sterilization, post product storage and transportation simulation, and post accelerated aging (to simulate a one-year shelf life).

The following characteristics were considered and incorporated into the bench test studies of the Xact®and its components:

Table 5: Summary of Xact®. Delivery System In Vitro Bench Testing

Characteristic	Specification	Pass/Fail
Stent Delivery System Pushability	The delivery system must be capable of being pushed through a simulated tortuous path to a distal location without bending or buckling	Pass
Delivery System Radiopacity	The marker bands on the Delivery Catheter must be visible	Pass
Sheath Retraction Force	The upper 95% / 99% CI of the sheath retraction force recorded must not be greater than 12N	Pass
Stent System Ease of Use	The system shall pass the acceptance criteria specified in the test method 'ease of device preparation and simulated use' when being prepared. The system must also be compatible with the Emboshield Cerebral Protection System	Pass
Stent Placement Accuracy	Delivery system must be capable of deploying and placing a 20mm stent such that it covers a target site 10mm in length within a simulated tortuous path	Pass

Characteristic	Specification	Pass/Fail
Stent Delivery System Trackability	The delivery system must be capable of being advanced over a guidewire through a simulated tortuous path to a distal location	Pass
Visual and Dimensional Characteristics		
Usable length of system	1366 mm ± 10 mm	Pass
Distance from tip to guide wire exit port	250 mm ± 5 mm	Pass
Largest outer diameter of catheter tip	0.075"±0.002"	Pass
Catheter tip gap	No gap after delivery system preparation	Pass
Outer diameter of distal outer sheath	0.075"±0.001"	Pass
Outer diameter of proximal shaft	Maximum of 0.061"	Pass
Guidewire lumen patency	0.014" guidewire must pass through lumen and exit port	Pass
Tip, distal sheath, exit port and proximal shaft surface characteristics	The external surfaces of the tip, distal sheath, moulding and proximal shaft must be free from extraneous matter, process and surface defects under 2.5 magnification, meeting requirements as outlined in ISO 10555-1.	Pass
Stent device location	The stent shall not be visible at sheath tip	Pass

Table 6: Summary of XACT® Stent In Vitro Bench Testing

In Vitro Bench Test	Summary of Test
Crush Resistance	A specification was defined for recovery of the stent's geometry after crush to a predetermined value. This test is comprised of a uniformly distributed radial constriction of the stent. The stent was removed from the test fixture and its proximal and distal diameters were measured to assess recoverability. The stent met the specification for recovery of geometry.
Outward Radial Force	A specification was defined for the minimum outward radial force the stent should exert and the stent's recovery geometry after crush. The force exerted by the stent when crushed between compression plates to half its diameter was recorded using tensile test equipment. The stent was removed from the test fixture and its proximal and distal diameters were measured to assess recoverability. The stent met the specification for both radial force exerted and recovery of geometry.
MRI Compatibility	Based on the MR testing information the Xact Stent will not present an additional hazard or risk to a patient undergoing an MRI procedure using a scanner operating with a static magnetic field of 3-Tesla or less and under the MRI-related heating conditions used for this evaluation. Therefore, the Xact Stent should be considered "MR-safe" according to the conditions used for this assessment.
Corrosion	An evaluation of the stent's corrosion resistance under conditions simulating the intended *in vivo* conditions was conducted using electrochemical methods. The evaluation comprised a review of the corrosion potential, corrosion rate, anodic and cathodic polarization characteristics, cyclic polarization and crevice corrosion of the Xact® stent. The Xact® showed a good level of resistance to pitting and crevice corrosion. The stent met its specification.

In Vitro Bench Test	Summary of Test
Visual, Dimensional and Surface Characteristics	The visual, dimensional and surface characteristics of the Xact® device and its components were assessed against the product specification. The deployed stent geometry was evaluated as part of this testing. Stent foreshortening was measured by comparing the deployed stent geometry to the specification. The results of these assessments confirmed that the device and its components were appropriate for its intended use. The Xact® met its specifications.
Stent Free Area	The stent free surface area percentage was calculated by subtracting the area covered by the Xact® from the total vessel area stented and dividing by the total vessel area stented. The maximum surface free area must be ≤ 90%. The Xact® met its specifications.

The Xact® and its components were evaluated for these attributes against a performance specification. The results of bench testing indicated that the product performs as intended and is safe and effective for its intended purpose.

In vitro bench test studies demonstrated that the Xact® stent meets its specifications for use under the conditions of the testing performed. In summary, the results of the studies support the safety and performance of the Xact® stent and its components for the intended indication when used in accordance with the Instructions for Use.

9.2 Animal Studies

Three separate animal studies evaluated the performance and safety of the Xact®. The three studies evaluated the performance of the Stent Delivery System, the performance and safety of the stent *in vivo*, and the compatibility of the Xact Carotid Stent System with the Emboshield Embolic Protection System.

The Xact® Stent Delivery Catheter was evaluated in vivo for:

- Delivery, deployment and removal; and
- Damage to the Xact® delivery system and thrombus formation;

The stent was assessed over three time points for:

- Radiopacity;
- Patency rates of the stent over a six month period;
- Biologic response to the stent at 24 hours, one month and six months (histopathology, morphometric analysis, vessel injury); and
- Stent integrity after six months implantation.

The Xact Stent Delivery System was evaluated for compatibility with the Emboshield® Embolic Protection System for the following characteristics:

- The handling characteristics of the Xact stent during delivery and deployment of the stent over the Emboshield Delivery Wire.
- Potential for a Filtration Element containing an embolic load to be retrieved safely through deployed Xact stents (including any snagging).
- The performance of the Filtration Element when retrieved through overlapping stents

Table 7 provides a summary of the In Vivo Animal Testing performed with the Xact Carotid Stent System.

Table 7: Summary of Xact® Carotid Stent *In Vivo* Testing

Study	Number of Animals, Timepoints, Devices Tested	Relevant Findings
Performance Evaluation of the Xact Carotid Stent Delivery System	2 animals 10 devices acute study	The RX Xact Carotid Stent delivery system performed satisfactorily in all cases, with successful stent placement. There were no safety issues associated with the system and the performance characteristics received excellent scores in all instances.
Carotid and Iliac Self Expanding Stent Implantations	9 animals 28 devices 24-48 hrs, 1 month 6 months	All animals survived the designated implant intervals and were in excellent health at the conclusion of the study. Stented vessel segments were patent; without evidence of hyperplasia (stenosis). The acute implant arteries were examined histologically and submitted for evaluation of vessel wall injury. The results for the acute implant study were unremarkable with the small amount of acute thrombus formation anticipated. The histological, morphometric and vessel wall injury evaluations of stents explanted at 1 month and 6 months described well healed arterial segments with Nitinol struts contacting the media without significant injury to any segment of the arterial wall.
An Acute In Vivo Safety and Performance Evaluation of the Emboshield® Cerebral Protection System (Generation III) and the Xact® Carotid Stent System	2 animals 6 devices acute study	The Emboshield® Cerebral Protection System and Xact® Carotid Stent System were evaluated acutely in the left and right carotid arteries of two swine. In each vessel, filtration element and single or overlapping Xact® stents were deployed over the filter delivery wire, and a simulated embolic load was injected proximal to the filtration element. The embolic load was then captured with the filtration element, followed by retrieval and removal from the animal. Xact® stents and emboshield® devices were evaluated for performance in relation to specific parameters outlined in the study objectives. Both devices performed as intended and all embolic loads were successfully retrieved through single or overlapping Xact® stents with no resulting snagging or tearing of the emboshield® filtration element.

9.3 Biocompatibility

MedNova reviewed the potential biological effects associated with Xact® Carotid Stent System when used for its intended purpose. The appropriate tests, as recommended by ISO 10993-1, were performed. Where deemed appropriate through the ISO 10993-1 based evaluation of the Xact®Carotid Stent System the following tests were performed:

Table 8: Biocompatibility Testing

Test Performed
Intracutaneous Reactivity
Sensitization (Maximization Method)
Acute Systemic Toxicity
Cytotoxicity (ISO Elution Method)
Hemolysis (Modified ASTM - Extraction Method)
Coagulation (Plasma Recalcification Time Method)
Pyrogenicity (Material Mediated)

The material used in the Xact® stent is Nitinol, which is widely used *in vivo*. MedNova performed a literature evaluation of the available data. Based on this, there was sufficient information available to confirm the safety of Nitinol in terms of genotoxicity, sub-acute toxicity and implantation.

The biocompatibility tests were performed at North American Science Associates, Inc (NAmSA®, Northwood, OH) in accordance with the provisions of the FDA GLP Regulations as outlined in Title 21 Code of Federal Regulations Part 58. All test articles evaluated were manufactured under the control of the MedNova quality system. All tests met appropriate test requirements. The test program performed on the Xact® Carotid Stent System did not identify any biological hazards. The test results demonstrate that the Xact® Carotid Stent System is biocompatible for its intended use.

9.4 Sterilization

MedNova sterilizes the Xact® Carotid Stent System by Ethylene Oxide (EtO). MedNova has validated and is controlling the sterilization cycle in accordance with EN 550 (*Sterilization of Medical Devices - Validation and Routine Control of Ethylene Oxide Sterilization*) and ISO 11135 (*Validation and Routine Control of Ethylene Oxide Sterilization*). The validated sterilization cycle achieves a minimum sterility assurance level (SAL) of 1×10^{-6} for the Xact® Carotid Stent System.

The Xact® Carotid Stent System is non-pyrogenic. On behalf of MedNova, an independent laboratory evaluated the device for its level of pyrogen. The test method used was the Limulus Amebocyte Lysate (LAL) gel clot method. The maximum acceptable level for a device of this nature is 20 EU/device. The test results were less than 20 Endotoxin Units. The device met the acceptance criteria.

Potential toxic residues from ethylene oxide sterilization include ethylene oxide and ethylene chlorohydrin. On behalf of MedNova, the independent laboratory measured the residual levels for the Xact® Carotid Stent System® during sterilization validation and levels were found to be within the limits outlined in ISO 10993-7 (*Biological Evaluation of Medical Devices - Part 7: Ethylene Oxide Sterilization Residuals*).

9.5 Packaging and Shelf Life

The packaging for the Xact® Carotid Stent System was evaluated using the following tests: packaging visual inspection, seal strength evaluation, ship-shake evaluation and dye penetration tests. The pouch evaluation test methods were validated. The results demonstrated that all units met the acceptance criteria. The packaging of the Xact® Carotid Stent System met its specifications.

Samples of the Xact® product was subjected to accelerated aging and evaluated to ensure continued adherence to the product specifications. The data collected to date ensures a shelf life of up to one year for the Xact®Carotid Stent System.

10.0 SUMMARY OF CLINICAL STUDIES

The Registry Study to Evaluate the MedNova Emboshield® Bare Wire Cerebral Protection System and Xact® Stent in Patients at High Risk for CarotId EndarterecTomY (SECuRITY) was a prospective, multi-center, non-randomized study performed to demonstrate the safety and effectiveness of the Emboshield® Cerebral Protection System (Emboshield®) and Xact® Carotid Stent System (Xact®) in treating carotid stenosis in patients at high risk (≥ 50% for symptomatic patients by ultrasound or angiography or ≥ 80% for asymptomatic patients by ultrasound or angiography) for carotid endarterectomy. High-risk patients were defined as having an anatomical risk factor(s) and/or a co-morbidity risk factor(s). A total of three hundred ninety nine (399) patients were enrolled at 30 sites in the United States and Australia. Of the total 399 patients, 93 patients were enrolled in the lead-in phase of the study and one patient was enrolled under the emergent use guidelines, three months following termination of enrollment. Therefore, a total of three hundred five (305) pivotal patients are included in the ITT analysis group.

Table 9: Overview of the SECuRITY Trial

Characteristic	SECuRITY Trial
Product Evaluated	Xact® Carotid Stent System (Xact®) Emboshield® Cerebral Protection System (Emboshield®)
Study Design	Prospective, multi-center, non-randomized study
Sample Size	305 (plus 93 lead-in patients)
Number of Sites	30 sites in the United States (29) and Australia (1)
Primary Endpoint	Xact® stent: Incidence of major adverse events (MAEs), defined as death, stroke or myocardial infarction (Q-wave and non Q-wave) at 30-days post-procedure and the incidence of ipsilateral stroke at one year. Emboshield®: Incidence of major adverse events (MAE), defined as death, stroke or myocardial infarction (Q-wave and non Q-wave) at 30-days post procedure.
Secondary Endpoints	Safety: Incidence of vascular complications (other than MAE) at 30 days. Lesion Success [1] Device Success [2] Procedure Success [3] Long Term Success [4]

Characteristic	SECuRITY Trial
	Device performance of the distal protection device and stent, and overall procedural success. Long-term success for the Xact® stent was defined as the occurrence of restenosis and the incidence of target lesion revascularization at 6 and 12 months post procedure.
Patient Follow-up	30-days, 6-months and12-months.[5]

1 Defined as <50% residual stenosis of the target lesion using the Xact® stent and Emboshield® filter .

2 Xact® stent: <50% residual stenosis in the target lesion. Emboshield®: deployment and retrieval of the device during the procedure, in the absence of angiographic distal embolization.

3 Defined as <50% residual stenosis in the target lesion using any method, and the absence of major adverse events at 30 days.

4 Restenosis: defined as a narrowing >50% at 6 and 12 months post-procedure, as determined by ultrasound. Revascularization: target lesion revascularization associated with a narrowing of >80% within 12 months post-procedure.

5 Each of these visits included a clinical evaluation, neurological assessment and a carotid duplex exam. An ECG was also obtained at the 30-day visit.

Statistical Methods

The proportion of patients experiencing a primary endpoint adverse event in the SECuRITY Registry was compared to a weighted historical control (WHC) rate based on a review of outcome assessments for endarterectomy published in peer reviewed literature. It was established that the one-year control rate for patients having high-risk co-morbidities was 14% and the one-year control rate for patient with anatomic risk factors was 11%. The WHC rate for this trial was then computed by weighting these rates by the actual proportion of patients in the study with co-morbidities versus anatomic risk factors.

- Patients with at least one high-risk co-morbidity: 266/303 = 87.8%
- Patients with anatomic risk factors only: 37/303 = 12.2%
- WHC = (87.8% x 14%) + (12.2% x 11%) = 13.6%

All patients who met eligibility requirements, and who were available for clinical follow-up, were included in the denominator. Two (2) patients had neither high-risk co-morbidities nor anatomic risk factors and were excluded from the calculation of the weighted historic control.

The analysis and subsequent interpretation of the results from this study are based on inferential statistics. The test statistic used for this analysis was the Clopper-Pearson method for calculating 95% binomial confidence intervals, based on the observed primary composite endpoint failure rate. If the upper bound of the 95% binomial confidence interval was found to be less than the WHC plus the margin of clinical equivalence, the null hypothesis would be rejected and non-inferiority of the Xact® stent to CEA would be demonstrated.

The SECuRITY protocol required regular patient follow-up by the treating physician and follow-up neurological assessments by a neurologist. Core laboratories provided independent assessments for the angiographic, ultrasound, ECG, and pathologic evaluation of captured debris (Emboshield® only). Medical monitors reviewed all safety data to ensure appropriate reporting of adverse events. A Clinical Adjudication Committee adjudicated suspected primary endpoint events. A Data Safety Monitoring Board monitored adverse events to ensure patient safety.

10.1 Eligibility Criteria Summary

The study population consisted of male and female patients, at least 18 years of age and at least one year life expectancy, with a lesion located in the internal carotid artery. Key inclusion criteria included:

- Target Internal Carotid Artery (ICA) vessel diameter was visually estimated to be ≥ 4.0 mm and ≤ 9.0 mm for Xact® stent treatment segment and to be ≥ 3.5 mm and ≤ 6.0 mm for the Emboshield ®
- The patient had a 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

Each patient had to fulfill at least one (1) of the following anatomical or co-morbid risk factors to be included in the study:

Anatomic Risk Factors

- Previous radiation treatment to the neck or radical neck dissection
- Target lesion was at or above the second vertebral body C2 (level of jaw)
- Inability to extend the head due to cervical arthritis or other cervical disorders
- Tracheostomy or tracheal stoma
- Laryngectomy
- Contralateral laryngeal nerve palsy
- Severe tandem lesions

Co-morbid Risk Factors

- Previous carotid endarterectomy with significant restenosis (as defined above for symptomatic or asymptomatic patients)
- Total occlusion of the contralateral carotid artery
- Left ventricular ejection fraction < 35%
- Congestive Heart Failure New York Heart Association (NYHA) Functional Class III or higher
- Dialysis dependent renal failure
- Canadian Cardiovascular Society Angina Classification III or higher or unstable angina
- Requires simultaneous or staged coronary artery bypass surgery, cardiac valve surgery, peripheral vascular surgery, or abdominal aortic aneurysm repair within 60 days
- > 80 years of age
- Myocardial infarction within previous 6 weeks
- Abnormal stress test. Treadmill, thallium or dobutamine echo were acceptable. The stress tests had to be sufficiently abnormal to place the patient at an increased risk for CEA

- Severe pulmonary disease, including at least one of the following: requirement chronic O2 therapy, resting PO2 ≤ 60 mm Hg, Hematocrit ≥ 50%, FEV1 or DLCO ≤ 50% of normal

10.2 Description of Patients Evaluated

Attempts were made to contact patients even if they had missed the previous visit. This action resulted in several patients returning for a subsequent follow-up visit, even if they had missed the prior visit.

Upon completion of the study, a study termination form was completed for each patient. A number of reasons were given for why patients were terminated, including a patient's refusal of any additional follow-up, death, and patients that were lost to any additional follow-up. Table 10 summarizes the patient follow-up and includes one patient that died 374 days post index procedure. Table 11 provides the baseline demographics of the patients.

Table 10: SECuRITY Patient Follow-up

	30-days	6-months	12-months
Patients Enrolled	305		
Cumulative Death	3	13	26
Cumulative Withdrawal or Loss-to-Follow-up	10	26	36
Patients Evaluable	302	292	279
Patients Evaluated	292	266	243
Follow-up Rate (%)	96.7	91.1	87.1

Table 11: Baseline Patient Demographics

Demographic	SECuRITY Trial
Age	
Mean ± SD	74.5 ± 9.1
Range (min, max)	48.0, 92.2
Age > 80 year	33.8% (103/305)
Gender	
Male	63.6% (194/305)
Females	36.4% (111/305)
Medical History	
Diabetes	30.8% (94/305)
Hypertension requiring treatment	86.6% (264/305)
Hyperlipidemia	73.8% (225/305)
Current Smoker	72.5% (221/305)
Number of Symptomatic Patients (TIA,/stroke within 180 days)	21% (64/305)
Baseline Lesion & Vessel Characteristics	
Eccentric	29.0% (87/300)
Concentric	71.0% (213/300)
Calcified	21.0% (63/300)
Ulcerated	23.0% (69/300)
Lesion Length (mm)	
Mean ± SD	15.0 ± 6.5
Range (min, max)	2.0, 46.8

Demographic	SECuRITY Trial
Minimum Lumen Diameter (MLD, mm)	
Mean ± SD	4.8 ± 0.9 (n=299)
Range (min, max)	0.8, 9.5
Percent Diameter Stenosis (%DS)	
Mean ± SD	73.2 ± 17.3 (n=299)
Range (min, max)	-160, 93.2
High-Risk Inclusion Criteria	
Anatomic Risk Factors	
Previous Radiation Treatment to Neck or Radical Neck Dissection	5.9% (18/305)
Target Lesion At or Above Second Vertebral Body C2	9.2% (28/305)
Inability to Extend the Head Due to Cervical Arthritis or Other Cervical Disorders	3.0% (9/305)
Tracheostomy or Tracheal Stoma	0.0% (0/305)
Laryngectomy	0.3% (1/305)
Contralateral Laryngeal Nerve Palsy	0.0% (0/305)
Severe Tandem Lesions	1.3% (4/305)
Co-Morbid Risk Factors	
Previous Carotid Endarterectomy with Significant Restenosis	21.0% (64/305)
Total occlusion of the Contralateral Carotid Artery	8.9% (27/305)
Left Ventricular Ejection Fraction <35%	79.% (24/305)
Congestive Heart Failure NYHA III or Higher	6.2% (19/305)
Dialysis Dependent Renal Failure	1.6% (5/305)
CCSAC III or Higher or Unstable Angina	7.5% (23/305)
Requires Simultaneous or Staged CABG, Cardiac Valve Surgery, Peripheral Vascular Surgery, or Abdominal Aortic Aneurysm Repair Within 60 Days	7.2% (22/305)
>80 Years of Age	33.8% (103/305)
MI Within Previous 6 Weeks	0.7% (2/305)
Abnormal Stress Test	12.1% (37/0305)
Severe Pulmonary Disease	2.0% (6/305)

10.3 Results

At 30 days following the study procedure, 92.5% of the treated patients were free of major adverse events (MAEs), defined as death, stroke or myocardial infarction. The primary endpoint of the study was a composite rate of the 30-day MAEs *and* ipsilateral strokes at one year. The composite rate of occurrence for the primary endpoint measure at 12 months was 8.5%.

Acute success in effectively treating the target lesion was demonstrated in 96.7% (295/305) of the patients undergoing the study procedure. Device success was also achieved in a majority of the study procedures for both study devices: 94.1% (287/305) for the Xact® stent and 96.7% (295/305) for the Emboshield® distal protection device.

Overall procedural success was demonstrated in 269 patients (88.2%), as measured by a residual stenosis of < 50% at the completion of the procedure *and* the absence of major adverse events (Stroke, Death, or MI) at 30 days. Five (5) patients (1.6%, 5/305), experienced a vascular complication that required treatment with additional therapeutic measures, including aspiration of a stagnate column of blood prior to filter retrieval, placement of a second stent, application of a pressure dressing to the access site and surgical drainage for a groin abscess.

Change to Minimum Lumen Diameter (MLD) was calculated for 299 patients where the MLD measured was the section (segment) of the carotid considered for stenting. The average change was 2.3mm and the average percent change in lumen diameter was –55.5%.

At 12 months, long-term durability of the procedure was also demonstrated by 99.3% (0.7%, 2/305) of the treated patients being free from repeat revascularization. Additionally, at 6 months and 12 months post-procedure, restenosis was demonstrated in a small percentage of the patient population, 4.9% and 4.1%, respectively.

In the SECuRITY trial the median number of days-to-discharge was 1.7. The longest hospital stay post-stenting in each study was 16 days. Approximately, 70% of patients in the SECuRITY Trial remained in the hospital for 1 day following the carotid stenting procedure. Additionally, 6% of patients stayed 5 or more days, generally for the treatment of a co-morbid condition.

The primary objective of the SECuRITY trial was met. The upper bound of the 95% one-sided binomial confidence interval was found to be less than the WHC plus the margin of clinical equivalence, demonstrating that the carotid stenting with the Xact® stent is non-inferior to carotid endarterectomy.

The clinical results of this study indicate that the Xact® Carotid Stenting System, when used in conjunction with the Emboshield® Embolic Protection System, provides a safe, effective and durable method for the treatment of carotid stenosis in patients at high-risk for carotid endarterectomy.

Tables 12 through 14 present a Summary of Safety and Efficacy Measures, respectively.

Table 12: Summary of Safety in the SECuRITY Trial

Events	≤ 30 Days SECuRITY (N=305)			
	n	%	LCL*	UCL**
30 Day Primary Endpoint (Death, Stroke and MI)	23	7.5 %	0.048	0.111
Death	3	0.98 %	0.002	0.029
Stroke-Related	3	0.98 %	0.002	0.029
Not Stroke-Related	0	0 %	0.000	0.01
All Strokes	21	6.89 %	0.043	0.103
Major	8	2.62 %	0.011	0.051
Ipsilateral Stroke	7	2.30 %	0.009	0.047
Non-ipsilateral Stroke	1[6]	0.33 %	0.000	0.018
Minor	13	4.26 %	0.023	0.0712
Ipsilateral Stroke	12	3.93 %	0.021	0.068
Non-ipsilateral Stroke	1[7]	0.33 %	0.000	0.018
Non-Stroke Neurological	25	8.20 %	0.054	0.119
Cardiac	15	4.92 %	0.028	0.08
MI	2	0.66 %	0.001	0.024
Arrhythmia	4	1.31 %	0.004	0.033

[6] Stroke adjudicated as contralateral
[7] Stroke adjudicated as bilateral

Events	≤ 30 Days SECuRITY (N=305)			
	n	%	LCL*	UCL**
Angina	4	1.31 %	0.004	0.033
Congestive Heart Failure (CHF)	3	0.98 %	0.002	0.029
Coronary Artery Disease (CAD)	2	0.66 %	0.001	0.024
Procedural Complication	109	35.74 %	0.304	0.414
Hypotension	86	28.20 %	0.232	0.336
Arrhythmia	7	2.30 %	0.009	0.047
Vasospasm	3	0.98 %	0.002	0.029
Dissection	10	3.28 %	0.016	0.06
In-stent Thrombosis	1	0.33 %	0.000	0.018
Emergent CEA	1	0.33 %	0.000	0.018
Emergent Intervention -other	1	0.33 %	0.000	0.018
Access Site Complication Requiring Repair / Transfusion	8	2.62 %	0.011	0.051
Vascular	3	0.98 %	0.002	0.029
Hemodynamic	11[8]	3.61 %	0.018	0.064
Bleeding	6	1.97 %	0.007	0.042
Requiring transfusion	1	0.33 %	0.000	0.018
GI Bleeding	5	1.64 %	0.005	0.038
Blood Dyscrasia	2	0.66 %	0.001	0.024
Respiratory	5	1.64 %	0.005	0.038
Gastrointestinal	18	5.90 %	0.035	0.092
Genitourinary	3	0.98 %	0.002	0.029
Infection	2	0.66 %	0.001	0.024
Metabolic	11	3.61 %	0.018	0.064
Musculoskeletal	32	10.49 %	0.073	0.145
Miscellaneous[9]	1	0.33 %	0.000	0.018

*LCL –Lower Confidence Level

** UCL Upper Confidence Level

[1] Includes hypotension and hypertension not associated with the procedure.
[1] Aortic Aneurysm

Table 13: Change in Quantitative Angiographic Analysis

	Pre-Procedure to Post-Procedure Change (n=295**)		
	Change Mean	S.D.	95% CI
In Lesion MLD* (mm)	2.3mm	0.7mm	(2.3, 2.4) -
In Lesion Diameter Stenosis (%)	-55.5%	15.6%	(-57.3, -53.7)

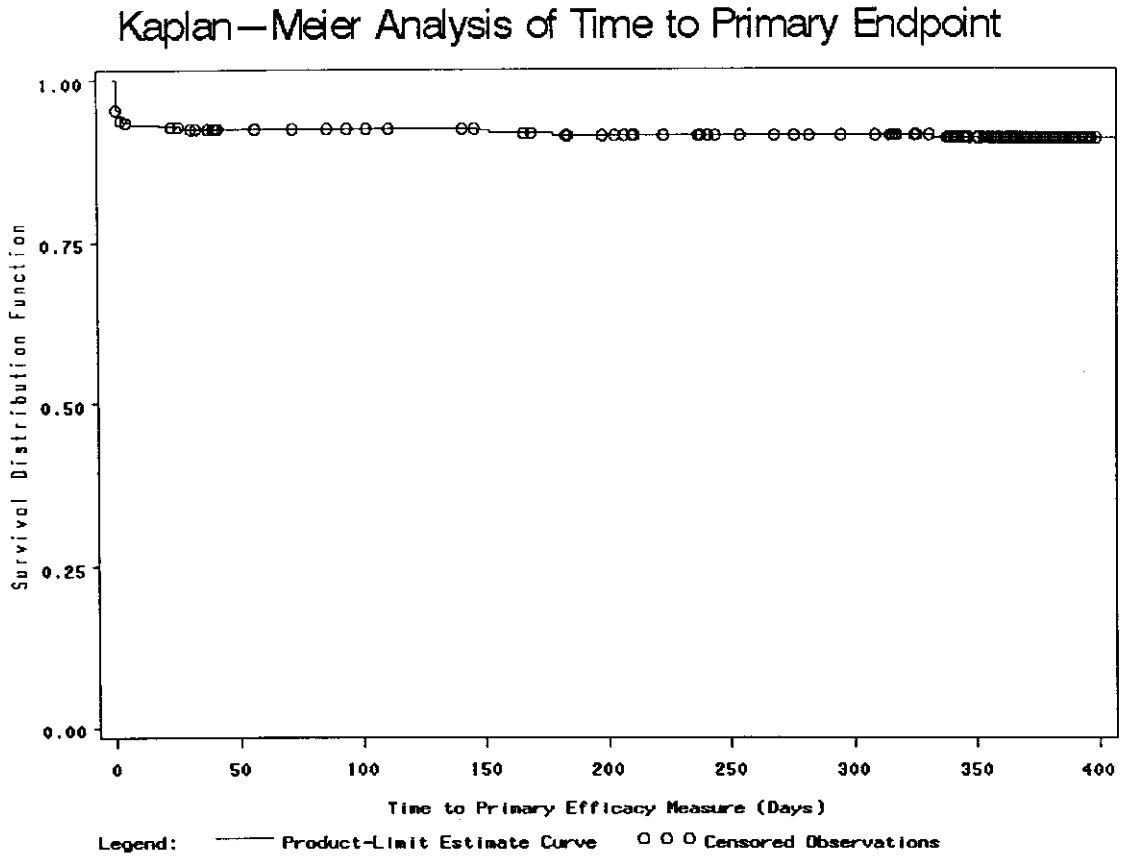
*Minimum Lumen Diameter of the section (segment) of the carotid considered for stenting
**Number of patients for which pre- and post- angiographic data was available.

Table 14: Efficacy Measures

Efficacy Measures	%	95% CI	X/n
Lesion Success (< 50% stenosis using the Xact stent and Emboshield filter)	96.7%	(0.941, 0.984)	(295/305)
Device Success - Xact Stent (< 50% residual stenosis, successful delivery of the stent)	94.1%	(0.908, 0.965)	(287/305)
Device Success - Embolic Protection Device (Successful deployment/retrieval of the filter, absence of angiographic distal embolization)	96.7%	(0.941, 0.984)	(295/305)
Procedural Success (< 50% stenosis using any method and freedom from MAE at 30 days)	88.2%	(0.840, 0.916)	(269/305)
Long Term Success (absence of Ipsilateral stroke at 365 days post-procedure [0-365 days])	92.2%	(0.889, 0.952)	(24/305)
Restenosis[10] (≥ 50% stenosis as measured by ultrasound)			
At 6 Months post-procedure	4.9%	(0.020, 0.067)	(12/246)
At 12 Months post-procedure	4.1%	(0.014,0.055)	(9/221)
Target Lesion Revascularization (Surgical/percutaneous revascularization involving the target lesion within 365 days)	0.65%	(0.000, 0.018)	(2/305)
Total Vascular Complications	1.6%	(0.005, 0.038)	(5/305)

[10] At the end of the one year follow-up period only two subjects had a clinically indicated need for revascularization.

Figure 1: Freedom from Composite Endpoint of Stroke, Death and MI (0-365 days)



Months after Index Procedure	0	1	3	6	12
Days after Index Procedure	0	30	90	180	365
Number at Risk	305	276	264	253	157
Number Censored	0	6	18	26	121
Number of Events	0	23	23	26	27
Percent Event Free	100%	92.4%	92.4%	91.4%	91.0%
One-Sided Lower 95% CI	100%	89.9%	89.9%	88.6%	87.4%

11.0 CONCLUSIONS FROM STUDIES

The preclinical studies indicate that the Xact® Carotid Stent System meets or exceeds safety and performance specifications. Multicenter clinical data have demonstrated that the Xact® Carotid Stent System is safe and effective for its intended use. Results from preclinical and clinical evaluations provide valid scientific evidence and reasonable assurance that the device is safe and effective; therefore, it is reasonable to conclude that the benefits of use of the device for the target population outweigh the risk of illness or injury when used as indicated in accordance with the directions for use.

12.0 PANEL RECOMMENDATION

In accordance with the provisions of section 515 (c)(2) of the Act as amended by the Safe Medical Devices Act of 1990, the PMA was not referred to the Circulatory Systems Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by the panel.

13.0 CDRH DECISION

FDA issued an approval order on September 6, 2005. The conditions of approval require a post-approval study consisting of at least 1,500 new patients. The endpoints for this study are death, Q-wave and non-Q-wave MI, and stroke at 30 days and ipsilateral stroke at 365 days for a 500-patient subset Ipsilateral stroke at 12, 24, and 36 months will also be assessed in a separate 305-patient cohort.

The applicant's manufacturing facilities were inspected and found to be in compliance with the Quality System Regulation (21 CFR 820).

14.0 APPROVAL SPECIFICATIONS

Directions for Use: See product labeling

Hazards to Health from Use of these Devices: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in labeling.

Post-approval Requirements and Restrictions: See approval order.