

SUMMARY OF SAFETY AND EFFECTIVENESS DATA

1.0 GENERAL INFORMATION

Device Generic Name: Carotid Stent

Device Trade Name: Exponent[®] Self-Expanding Carotid Stent with
OTW Delivery System
Exponent[®] Self-Expanding Carotid Stent with
RX Delivery System

**Applicant Name
and Address:** Medtronic Vascular Inc.
3576 Unocal Place
Santa Rosa, CA 95403
USA

PMA Number: P070012

**Date of Panel
Recommendation:** None

**Date of Notice of
Approval to Applicant:** October 23, 2007

2.0 INDICATIONS FOR USE

The Medtronic Vascular Exponent[®] Self-Expanding Carotid Stent System, used in conjunction with a Medtronic Vascular embolic protection system, is indicated for improving carotid luminal diameter in patients at high risk for adverse events from carotid endarterectomy who require carotid revascularization and meet the criteria outlined below.

1. Patients with neurological symptoms and $\geq 50\%$ stenosis of the common or internal carotid artery by either ultrasound or angiogram OR patients without neurological symptoms and $\geq 80\%$ stenosis of the common or internal carotid artery by either ultrasound or angiogram, AND
2. Patients having a vessel with reference diameters between 4.5 mm and 9.5 mm at the target lesion.

3.0 CONTRAINDICATIONS

The Exponent[®] Self-Expanding Carotid Stent with OTW/RX Delivery System is contraindicated for use in:

- Patients in whom anticoagulant and/or antiplatelet therapy is contraindicated.
- Patients with severe vascular tortuosity or anatomy that would preclude the safe introduction of a guide catheter, sheath, embolic protection device, or stent delivery system.
- Patients with known hypersensitivity to Nitinol (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 Exponent[®] Carotid Stent System.

5.0 DEVICE DESCRIPTION

The Exponent[®] Self-Expanding Carotid Stent System is comprised of two main components:

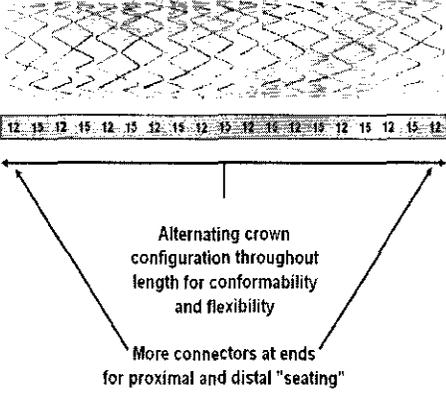
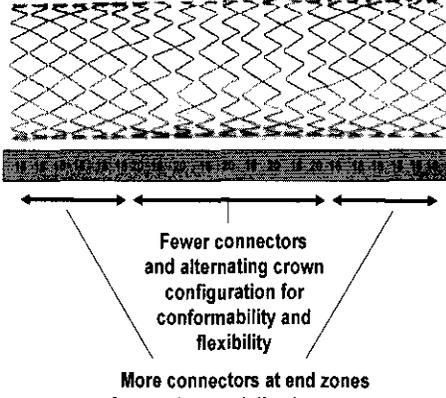
- Exponent[®] Self-Expanding Carotid Stent
- Over-the-Wire (OTW) or Rapid Exchange (RX) Delivery System

5.1 EXPONENT[®] SELF-EXPANDING CAROTID STENT

The Exponent[®] Self-Expanding Carotid Stent is identical for both the OTW and RX delivery system platforms. The stent is laser cut in an open-cell design from a medical grade nickel titanium alloy (nitinol). After manufacture, the stent is compressed and constrained onto the delivery catheter. Upon deployment, the stent expands to its pre-determined diameter and exerts an outward radial force on the arterial wall to establish vessel patency.

The Exponent[®] Self-Expanding Carotid Stent was developed with two configurations, one for the 6.0 and 7.0mm stent diameters and another for the 8.0, 9.0, and 10.0 mm stent diameters. The two configurations are described in Table 1.

Table 1: Exponent® Self-Expanding Carotid Stent Dimensional Specifications

Stent Diameters	6.0 & 7.0 mm	8.0, 9.0, & 10.0 mm
Stent Lengths	20, 30, & 40 mm	
# of Crowns	12 & 15 crowns alternate along the length of the stent	16 & 20 crowns alternate through the middle length of the stent, with 18-crown segments at the ends of the stent
Nominal Segment Length	12-crown segments: 2.2 mm (0.086") 15-crown segments: 2.0 mm (0.078")	16-crown segments: 2.0mm (0.078") 18-crown segments: 1.8 mm (0.071") 20-crown segments: 1.8 mm (0.071")
Strut Cross-Section	Ellipto-Rectangular Thickness: 0.005" nominal Width: 0.005" nominal	Ellipto-Rectangular Thickness: 0.007" nominal Width: 0.004" nominal
# of Connectors	6 at stent ends, 3 in stent middle	6 at stent ends, 5 & 6 alternating in stent middle
Foreshortening	0 – 4%	0 – 6%
Designs	 <p>Alternating crown configuration throughout length for conformability and flexibility</p> <p>More connectors at ends for proximal and distal "seating"</p>	 <p>Fewer connectors and alternating crown configuration for conformability and flexibility</p> <p>More connectors at end zones for proximal and distal "seating"</p>

5.2 EXPONENT® SELF-EXPANDING CAROTID STENT DELIVERY SYSTEMS

The Medtronic Vascular Exponent® Self-Expanding Carotid Stent Delivery Systems are single use devices that consist of the Exponent® Self-Expanding Carotid Stent mounted on either the OTW stent delivery system or the RX stent delivery system. The Exponent® Self-Expanding Carotid Stent Systems are designed to deliver the stent to the carotid arteries via a sheathed catheter. With the stent pre-mounted and constrained on the catheter with a retractable sheath, the delivery system is inserted through a guide catheter or sheath and tracked over a 0.014" embolic protection device guidewire.

For the RX delivery system, two radiopaque marker bands are located on the inner shaft of the delivery system, one proximal to the stent and one distal to the stent, to aid in positioning of the sheathed stent under fluoroscopy.

The OTW delivery system contains a third radiopaque marker band located at the distal end of the outer sheath, which enables visualization of the distal outer sheath position during stent deployment.

Both the OTW and RX delivery system platforms are provided in two sizes, 5F (for the 6.0 & 7.0 mm stent diameters) and 6F (for the 8.0 – 10.0 mm stent diameters); have a 135cm catheter working length; and are compatible with 0.014” guidewires and embolic protection devices. Each of the delivery system platforms has a retractable outer sheath attached to a slider button inside the handle of the device to deploy the stent. The stent is delivered to the intended lesion site and then expanded by retraction of the protective sheath. The stent then remains as a permanent vessel-scaffolding implant.

The Exponent® Self-Expanding Carotid Stent Systems are available in stent diameter of 6.0, 7.0, 8.0, 9.0 and 10.0mm and lengths of 20mm, 30mm, and 40mm. Table 2 lists the available sizes and part number for the Exponent® Self-Expanding Carotid Stent Systems.

Table 2: Exponent® Self-Expanding Carotid Stent with OTW and RX Model Numbers

Stent Diameter (mm)	Stent Length (mm)	Exponent® Self-Expanding Carotid Stent with OTW Delivery System Model Numbers	Exponent® Self-Expanding Carotid Stent with RX Delivery System Model Numbers
6.0	20	620SOCC	620SXCG
7.0	20	720SOCC	720SXCG
8.0	20	820SOCC	820SXCG
9.0	20	920SOCC	920SXCG
10.0	20	1020SOCC	1020SXCG
6.0	30	630SOCC	630SXCG
7.0	30	730SOCC	730SXCG
8.0	30	830SOCC	830SXCG
9.0	30	930SOCC	930SXCG
10.0	30	1030SOCC	1030SXCG
6.0	40	640SOCC	640SXCG
7.0	40	740SOCC	740SXCG
8.0	40	840SOCC	840SXCG
9.0	40	940SOCC	940SXCG
10.0	40	1040SOCC	1040SXCG

6.0 ALTERNATIVE PRACTICES AND PROCEDURES

Alternative practices and procedures for treatment of atherosclerotic disease of the carotid arteries currently include lifestyle modifications, endovascular intervention using other FDA-approved carotid stents and embolic protection systems, carotid endarterectomy, medical therapy, or a combination of these treatments. Lifestyle modifications include measures such as cessation of smoking and changes to diet and alcohol usage. Medical therapy includes use of antiplatelet and/or anticoagulant medicine (aspirin, clopidogrel or ticlopidine) as well as pharmacological treatment of hypertension and hyperlipidemia. The primary treatment used to prevent stroke in

patients with carotid artery disease is surgical removal of the plaque from the stenotic artery by means of an endarterectomy.

7.0 MARKETING HISTORY

The Exponent[®] Self-Expanding Carotid Stent with OTW and RX Delivery System were approved for commercial sale in the European Economic Area (EEA) in August 2003 and subsequently in additional countries. Only the Exponent[®] Self-Expanding Carotid Stent with RX Delivery System has been sold outside the United States. Medtronic Vascular elected to perform a voluntary market withdrawal of the Exponent[®] Self-Expanding Carotid Stent with RX Delivery System from Europe in February 2005, due to field complaints related to stent deployment. The root cause of these failures was identified, and a corrective action was implemented through minor design changes to the device. The Exponent[®] Self-Expanding Carotid Stent with RX Delivery System with design modifications was returned to the market outside the United States in April 2006. The Exponent[®] Self-Expanding Carotid Stent with RX Delivery System that is the subject of this PMA is identical to the version currently marketed outside the United States.

8.0 POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

8.1 OBSERVED ADVERSE EVENTS

The Exponent[®] Self-Expanding Carotid Stent with Over-the-Wire (OTW) Delivery System was evaluated for the treatment of high surgical risk patients with lesions in the common and/or internal carotid artery that are amenable to percutaneous treatment with stenting. A total of 498 patients were enrolled into two separate single-arm trials as follows:

- MAVERIC I, a feasibility study, evaluated the Over-the-Wire (OTW) Exponent[®] Self-Expanding Carotid Stent System with the GuardWire[®] Temporary Occlusion & Aspiration System and included 99 patients. The primary objective of this study was to evaluate the safety and efficacy in treating carotid stenosis in patients at high risk for carotid endarterectomy (CEA) in the population under evaluation.
- MAVERIC II, a pivotal study, evaluated the Over-the-Wire (OTW) Exponent[®] Self-Expanding Carotid Stent System and the GuardWire[®] Temporary Occlusion & Aspiration System and included 399 patients. The primary objective of the study was the same as MAVERIC I in treating carotid stenosis in patients at high risk for CEA. High-risk patients were defined as having anatomical and/or co-morbidity risk factors as defined in the clinical protocols.

The major adverse events that were reported in both studies within the first 30 and 365 days after stenting are provided in Table 3 below. Table 4 includes all other adverse

events. All patient deaths are described in Table 5. No deaths were attributed to device malfunction or failure. All events are patient-based.

Table 3: Major Adverse Events Summary¹

	Events to 30 Days		Events to 365 Days	
	MAVERIC I N = 99 n (%)	MAVERIC II N = 399 n (%)	MAVERIC I N = 99 n (%)	MAVERIC II N = 399 n (%)
Primary endpoint event: (Death, Myocardial Infarction [MI], Stroke to 30 days and Ipsilateral Stroke from 31 – 365 Days)	6 (6.1%)	21 (5.3%)	6 (6.1%)	22 (5.5%)
Any Major Adverse Event (Death, MI, Stroke from 0 – 30 Days)	6 (6.1%)	21 (5.3%)	N/A	N/A
All-cause death ²	1 (1.0%)	4 (1.0%)	1 (1.0%)	37 (9.3%)
Neurological	1 (1.0%)	2 (0.5%)	1 (1.0%)	4 (1.0%)
Cardiac	0 (0.0%)	2 (0.5%)	0 (0.0%)	20 (5.0%)
Other	0 (0.0%)	0 (0.0%)	0 (0.0%)	13 (3.3%)
Myocardial Infarction (Q Wave and Non-Q Wave)	1 (1.0%)	6 (1.5%)	1 (1.0%)	9 (2.3%)
Q Wave MI	0 (0.0%)	2 (0.5%)	0 (0.0%)	2 (0.5%)
Non-Q Wave MI	1 (1.0%)	4 (1.0%)	1 (1.0%)	8 (2.0%)
Stroke	5 (5.1%)	16 (4.0%)	5 (5.1%)	18 (4.5%)
Ipsilateral	4 (4.0%)	13 (3.3%)	4 (4.0%)	14 (3.5%)
Major Ischemic	3 (3.0%)	6 (1.5%)	3 (3.0%)	7 (1.8%)
Minor Ischemic	1 (1.0%)	5 (1.3%)	1 (1.0%)	6 (1.5%)
Major Hemorrhagic	1 (1.0%)	3 (0.8%)	1 (1.0%)	3 (0.8%)
Minor Hemorrhagic	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Non-ipsilateral (to 30 days)	1 (1.0%)	4 (1.0%)	1 (1.0%)	4 (1.0%)
Non-ipsilateral (31 - 365 days)	N/A	N/A	0 (0.0%)	1 (0.3%)
Non-ipsilateral (All)	1 (1.0%)	4 (1.0%)	1 (1.0%)	5 (1.3%)
Major Ischemic	0 (0.0%)	3 (0.8%)	0 (0.0%)	4 (1.0%)
Minor Ischemic	1 (1.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)
Major Hemorrhagic	0 (0.0%)	1 (0.3%)	0 (0.0%)	1 (0.3%)
Minor Hemorrhagic	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

¹ All data based on ITT (intent-to-treat) population, which includes all subjects enrolled in the study regardless of whether they received a stent.

² Death: The Clinical Events Committee (CEC) adjudicated all deaths to determine if the death was defined as neurological (death due to a stroke, a complication of the procedure including bleeding, vascular repair or surgery or any death in which a neurological cause could not be excluded), or non-neurological (defined as death due to either a cardiac-related cause or due to another [other] cause).

Table 4: Other Adverse Events Summary¹

	Events to 30 Days		Events to 365 Days	
	MAVERiC I N = 99 n (%)	MAVERiC II N = 399 n (%)	MAVERiC I N = 99 n (%)	MAVERiC II N = 399 n (%)
Target Lesion Revascularization (TLR) ²	0 (0.0)	0 (0.0)	2 (2.0)	5 (1.3)
Surgery	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Percutaneous	0 (0.0)	0 (0.0)	2 (2.0)	4 (1.0)
Target Vessel Revascularization (not TLR) ³	0 (0.0)	0 (0.0)	2 (2.0)	2 (0.5)
Surgery	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)
Percutaneous	0 (0.0)	0 (0.0)	1 (1.0)	2 (0.5)
Blood and Lymphatic System Disorders ⁴	0 (0.0)	14 (3.5)	0 (0.0)	31 (7.8)
Cardiac Disorders ⁵	2 (2.0)	27 (6.8)	7 (7.1)	72 (18.0)
Congenital, Familial and Genetic Disorders ⁶	0 (0.0)	1 (0.3)	0 (0.0)	2 (0.5)
Ear and Labyrinth Disorders ⁷	0 (0.0)	1 (0.3)	0 (0.0)	1 (0.3)
Eye Disorders ⁸	3 (3.0)	0 (0.0)	3 (3.0)	2 (0.5)
Gastrointestinal Disorders ⁹	0 (0.0)	13 (3.3)	2 (2.0)	38 (9.5)
General Disorders and Administration Site Conditions ¹⁰	0 (0.0)	15 (3.8)	2 (2.0)	55 (13.8)
Hepatobiliary Disorders ¹¹	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
Infections and Infestations ¹²	0 (0.0)	18 (4.5)	3 (3.0)	33 (8.3)
Injury, Poisoning and Procedural Complications ¹³	0 (0.0)	6 (1.5)	3 (3.0)	22 (5.5)
Investigations ¹⁴	1 (1.0)	23 (5.8)	5 (5.1)	34 (8.5)
Metabolism and Nutrition Disorders ¹⁵	0 (0.0)	1 (0.3)	1 (1.0)	11 (2.8)
Musculoskeletal and Connective Tissue Disorders ¹⁶	0 (0.0)	2 (0.5)	1 (1.0)	5 (1.3)
Neoplasms Benign, Malignant and Unspecified (incl Cysts and Polyps) ¹⁷	1 (1.0)	5 (1.3)	3 (3.0)	11 (2.8)
Nervous System Disorders ¹⁸	5 (5.1)	30 (7.5)	9 (9.1)	50 (12.5)
Psychiatric Disorders ¹⁹	0 (0.0)	6 (1.5)	0 (0.0)	9 (2.3)
Renal and Urinary Disorders ²⁰	0 (0.0)	8 (2.0)	3 (3.0)	24 (6.0)
Reproductive System and Breast Disorders ²¹	0 (0.0)		0 (0.0)	1 (0.3)
Respiratory, Thoracic and Mediastinal Disorders ²²	1 (1.0)	8 (2.0)	3 (3.0)	28 (7.0)
Skin and Subcutaneous Tissue Disorders ²³	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Surgical and Medical Procedures ²⁴	2 (2.0)	9 (2.3)	16 (16.2)	47 (11.8)
Vascular Disorders ²⁵	5 (5.1)	28 (7.0)	10 (10.1)	70 (17.5)

¹ All data based on ITT population

² Target Lesion Revascularization: Any 'clinically driven' repeat percutaneous intervention (including angioplasty, stenting, endarterectomy, or thrombolysis) or carotid endarterectomy performed to open or increase the luminal diameter of the previously treated lesion.

³ Target Vessel Revascularization: Any 'clinically driven' repeat percutaneous intervention (including angioplasty, stenting, endarterectomy or thrombolysis) or carotid endarterectomy of the previously treated vessel.

⁴ Blood and Lymphatic System Disorders include: anemia, blood dyscrasia, coagulopathy, iron deficiency anemia, aggravated neutropenia, secondary anemia, thrombocytopenia

⁵ Cardiac Disorders include: Angina pectoris (includes unstable), bradycardia (includes sinus), aortic valve stenosis, atrial fibrillation, atrioventricular block (includes complete), cardiac arrest, coronary artery disease, congestive heart failure, cardiac failure (includes congestive), cardiac tamponade, cardio-respiratory arrest, cardiomyopathy, cardiopulmonary failure, mitral valve incompetence, MI, myocardial ischemia, pulmonary edema (includes acute), coronary artery insufficiency, sick sinus syndrome, tachycardia (includes supraventricular and ventricular), asystole (includes ventricular), ventricular fibrillation

⁶ Congenital, Familial and Genetic Disorders include: Arterio-venous malformation, congenital atrial septal defect

⁷ Ear and Labyrinth Disorders include: Labyrinthitis

- ⁸Eye Disorders include: Transient blindness, blindness (unilateral), blurred vision, reduced visual acuity, visual disturbances
- ⁹Gastrointestinal Disorders include: Abdominal hernia, abdominal pain, small intestinal perforation, colonic perforation, diverticulitis, diverticulum intestinal, duodenal ulcer (hemorrhage), esophageal obstruction, gastric ulcer (hemorrhage), gastritis, gastroduodenal ulcer, gastrointestinal hemorrhage, hematemesis, lower gastrointestinal hemorrhage, melena, mesenteric artery stenosis, discolored feces, nausea, pancreatitis, rectal hemorrhage, retroperitoneal hemorrhage, stomatitis, vomiting
- ¹⁰General Disorders and Administration Site Conditions include: Injection site hemorrhage, peripheral edema, adverse drug reaction, cardiac death, chest pain, death, fall, fatigue, migration of implant, multi-organ failure, peripheral edema, pyrexia, weakness
- ¹¹Hepatobiliary Disorders include: cholecystitis, hepatic failure
- ¹²Infections and Infestations include: Bacteremia, cellulitis, colitis pseudomembranous, Infection, pneumonia, urinary tract infection, bacterial endocarditis, genitourinary tract infections, groin infection, herpes zoster, klebsiella infection, pseudomonas infection, sepsis, upper respiratory tract infection, urosepsis, West Nile viral infection
- ¹³Injury, Poisoning and Procedural Complications include: Accidental overdose, coronary artery restenosis, fracture (includes femur, hip, humerus, lower limb, radius, upper limb), wound evisceration, hemothorax, intraoperative hypotension, postoperative anemia, postoperative hypotension, post-procedure diarrhea, post-procedure hemorrhage, road traffic accident, stent occlusion,
- ¹⁴Investigations include: Decreased hematocrit, decreased hemoglobin, coronary ateriogram, increased cardiac enzymes, abnormal cardiac stress test, increased blood creatinine, decreased blood pressure, increased blood pressure, positive fecal occult blood, prolonged coagulation time, increased intraocular pressure, medical observation, abnormal thoracic cavity drainage test
- ¹⁵Metabolism and Nutrition Disorders include: anorexia, dehydration, diabetes mellitus (includes inadequately controlled), diabetic ketoacidosis, electrolyte imbalance. Hyperglycemia, hyperkalemia, hyponatremia
- ¹⁶Musculoskeletal and Connective Tissue Disorders include: Pain in limb, back pain (includes aggravated), groin pain, peripheral swelling
- ¹⁷Neoplasms Benign, Malignant and Unspecified (incl Cysts and Polyps) include: cancer (includes bladder, breast, colon, gastric, liver, renal cell, pharyngeal, thyroid, ureteric, metastasis), lymphoma, carcinoid tumor, pharyngeal neoplasm
- ¹⁸Nervous System Disorders include: cerebrovascular accident, carotid artery aneurysm, carotid artery stenosis, hemianopia, loss of consciousness, parathesis, convulsions, dizziness, memory impairment, neurological symptoms, aphasia, cerebral hemorrhage, cerebral infarction, clonic convulsion, coma, dementia of the Alzheimers type, dysarthria, embolic stroke, hemorrhagic transformation stroke, hemiparesis, hemiplegia, intraventricular hemorrhage, hypoesthesia, intracranial hemorrhage, ischemic stroke, spinal stenosis (includes lumbar), monoplegia, somnolence, subarachnoid hemorrhage, subdural hematoma, syncope, TIA, vasovagal attack, visual field defect
- ¹⁹Psychiatric Disorders include: Agitation, anxiety (includes aggravated), confusion, disorientation, mental status change
- ²⁰Renal and Urinary Disorders include: Renal calculus, renal colic, renal failure (acute, aggravated and chronic), renal impairment, renal nephropathy, renal artery stenosis, urinary retention
- ²¹Reproductive System and Breast Disorders include: Uterovaginal prolapse
- ²²Respiratory, Thoracic and Mediastinal Disorders include: Dyspnea, pulmonary hemorrhage, respiratory failure (includes acute), asthma (includes aggravated), chronic obstructive airway disease (includes aggravated), dyspnea (includes exertional) pleural effusion, aspiration pneumonia, pneumothorax, pulmonary embolism, pulmonary hypertension, respiratory arrest
- ²³Skin and Subcutaneous Tissue Disorders include: Chronic skin ulcer
- ²⁴Surgical and Medical Procedures include: Aortic aneurysm repair, aortic valve repair, aortic valve replacement, arterial bypass operation, cardiac pacemaker replacement, carotid endarterectomy, cerebrovascular surgery, cervical operation, colon surgery, coronary artery bypass grafting (CABG), coronary artery surgery, coronary revascularization, detached retina repair, endarterectomy, hernia repair, arthroplasty (includes hip, knee), hip surgery, malignant neoplasm excision, malignant breast lump removal, mitral valve replacement, mastectomy (partial), percutaneous transluminal coronary angioplasty (PTCA), percutaneous transluminal angioplasty (PTA), polypectomy, renal vascularization surgery, shoulder surgery, spinal laminectomy, hospitalization, tracheostomy, cardiac valvuloplasty, vascular bypass grafts, whole blood transfusion
- ²⁵Vascular Disorders include: Aortic aneurysm, arterial restenosis, arterial rupture, arterial stenosis, diabetic peripheral angiopathy, femoral arterial stenosis, femoral artery occlusion, gangrene, hematoma, hemorrhage, hypertension (includes aggravated), hypotension (includes aggravated, orthostatic), iliac artery stenosis, intermittent claudication, peripheral artery dissection, peripheral ischemia, peripheral vascular disorder, peripheral revascularization, poor peripheral circulation, vascular pseudoaneurysm, venous thrombosis (deep limb).

Table 5: Cause of Death^{1,2}

	MAVERIC I n (%)	MAVERIC II n (%)
0 - 30 days	n = 99	n = 399
Neurological	1 (1.0%)	2 (0.5%)
Cardiac	0	2 (0.5%)
Other	0	0
Total (0- 30 days)	1 (1.0%)	4 (1.0%)
31 - 365 days	n = 99	n = 399
Neurological	0	2 (0.5)
Cardiac	0	18 (4.5%)
Other:	0	13 (3.3%)
Infection		2
Respiratory		4
Cancer		4
Renal Failure		2
Stroke ³		1
Total (31 - 365 days)	0	33 (8.3)
Total (0 - 365 days)	1 (1.0%)	37 (9.3%)

¹ All data based on ITT population.

² No reported deaths due to device malfunction or failure.

³ Death due to progression of arteriosclerosis; does not meet study definition for neurological death.

8.2 POSSIBLE ADVERSE EVENTS

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

- Abrupt closure
- Acute myocardial infarction
- Allergic reaction (contrast medium; drug; stent or filter material)
- Amaurosis fugax
- Aneurysm or pseudoaneurysm in vessel or at vascular access site
- Angina/ Coronary ischemia
- Arrhythmia (including premature beats, bradycardia, atrial and/or ventricular tachycardia, atrial and/or ventricular fibrillation [VF])
- Asystole or bradycardia requiring placement of a temporary pacemaker
- Arteriovenous fistula
- Bleeding complications from anticoagulant or antiplatelet medication requiring transfusion or surgical intervention
- Cerebral edema
- Cerebral hemorrhage
- Cerebral ischemia
- Congestive heart failure (CHF)
- Death
- Detachment and/or implantation of a component of the system
- Dissection of blood vessel
- Distal embolic protection device thrombosis/ occlusion
- Emboli, distal (air, tissue, plaque, thrombotic material, stent)

- Emergent or urgent surgery (Carotid Endarterectomy [CEA])
- Emergent surgery to remove stent or distal embolic protection device
- Fever
- Hematoma at vascular access site, with or without surgical repair
- Hemorrhagic event, with or without transfusion
- Hyperperfusion syndrome
- Hypotension/Hypertension
- Infection, local or systemic including bacteremia or septicemia
- Ischemia/ infarction of tissue/ organ
- Pain (head/ neck)/ severe unilateral headache
- Pain at catheter insertion site
- Renal failure/ insufficiency secondary to contrast medium
- Restenosis of vessel in stented segment
- Seizure
- Stent/ distal embolic protection device entanglement/ damage
- Stent/ distal embolic protection device collapse or fracture
- Stent malapposition/ migration
- Stent thrombosis/ occlusion
- Stroke / cerebrovascular accident (CVA) / transient ischemic attack (TIA)
- Total occlusion of the carotid artery
- Vascular thrombosis/ occlusion at puncture site, treatment site, or remote site
- Vessel dissection, perforation or rupture
- Vessel spasm or recoil

9.0 SUMMARY OF NON-CLINICAL STUDIES

Non-clinical studies involving the Exponent[®] Self-Expanding Carotid Stent with OTW and RX Delivery Systems are provided below. These sections cover bench testing, *in vivo* studies, biocompatibility, sterilization, packaging, and shelf-life.

9.1 *IN VITRO* STUDIES

In vitro bench testing to support the Exponent[®] Self-Expanding Carotid Stent with OTW and RX Delivery Systems was developed based on internal device guidelines and is consistent with the FDA guidances, *Non-Clinical Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems* (January 2005), and *Guidance for the Submission of Research and Marketing Applications for Interventional Cardiology Devices: PTCA Catheters, Atherectomy Catheters, Lasers, Intravascular Stents* (May 1995), and applicable American Society for Testing and Materials International (ASTM) Standards. Because the Exponent[®] stent is self-expanding, tests specifically recommended for balloon-expandable stents were not conducted.

The specific *in vitro* tests conducted are described below in Tables 6 and 7. All test units were sterilized by E-Beam radiation prior to testing.

Table 6: Summary of *In Vitro* Testing of the Exponent® Stent

Test	Objective	Summary of Methods and Results
Material Analysis	Ensure conformance of stent material composition to required specifications	The composition of the nitinol material used to manufacture the stents was chemically analyzed to determine conformance with material specifications. Certificates of conformance for each incoming material lot are provided by the vendor. The stent material composition is appropriately characterized.
A _f Temperature Testing	Determine the shape memory properties of the stent	The austenitic finish temperature for the stent was measured by chilling the stents and measuring the temperature at which they regained their nominal diameter. The results show that the stent demonstrates acceptable shape memory characteristics.
Mechanical Properties	Ensure acceptable mechanical performance and establish baseline properties for future comparisons	The mechanical properties of the raw nitinol material were measured to ensure conformance with specification. Certificates of conformance are also provided for each incoming material lot. In addition, mechanical properties of processed stent material were calculated. The properties all met established specifications and are similar to historical values for nitinol.
Stent-Free Surface Area	Determine the amount of vessel area in contact with the stent	The amount of vessel area in contact with the stent was calculated using the known stent geometry. The surface areas range from 83 – 89% of the stented area, which does not raise any concerns.
Corrosion Resistance	Evaluate the compatibility of the stent material in the simulated chemical and mechanical service environment	Stents were subjected to potentiodynamic corrosion testing to measure pitting and crevice corrosion. Fretting corrosion was assessed by subjecting overlapping stents to conditions intended to simulate ten years of implant life, followed by visual inspection for signs of wear. The results demonstrate no evidence of corrosion, indicating satisfactory corrosion resistance and acceptably low levels of nickel leaching.
Stent Integrity	Ensure that the stent is free of surface defects	Stent surfaces were examined at 45 – 80X magnification for signs of cracks or defects after expansion. No defects were observed, indicating satisfactory stent integrity.
Kink Resistance	Ensure that the stent is resistant to permanent deformations that may affect patency	Expanded stents were bent around a 1” cylinder to simulate worst-case anticipated bend diameters. None of the stents displayed any protruding struts, suggesting that deployment of the stent in tortuous anatomy is not likely to result in permanent stent deformation.
Dimensional Verification	Ensure stent dimensions meet specifications and are uniform along the stent length and diameter	Stent length and diameter were measured after expansion. Measurements were performed at multiple locations along and around the stent to assess dimensional uniformity. The distance between two successive crowns was also measured. The results demonstrate that stent dimensions after expansion meet the specifications and that they do not significantly vary as a

Test	Objective	Summary of Methods and Results
		function of location.
Crush Resistance	Ensure that the stent is resistant to large externally-applied deformations	Stents were subjected to flat-plate compression. Samples recovered to their nominal diameter after removal of the applied load, indicating sufficient resistance to external crushing.
Foreshortening	Evaluate the extent of length decrease after expansion	The length of the stent was measured before and after deployment. The extent of foreshortening due to stent expansion met specifications, and is recorded in the device labeling to ensure accurate device placement.
Radial Stiffness and Outward Force	Ensure that the stent can withstand uniformly radially-applied loads without compression. Ensure that the outward expansion force provided by the stent is capable of maintaining patency without provoking injury.	The effect of stent diameter on the magnitude of the applied inwardly-directed radial force was measured. In addition, the magnitude of the radial force exerted by the stent during expansion was measured. The results suggest that the stent is resistant to collapse and capable of providing sufficient radial force to the vessel wall.
Stress and Fatigue Analysis	Calculate the anticipated stresses within the stent and ensure sufficient stent durability	Finite element analysis methods were used to simulate stent manufacture, compression onto the delivery catheter, stent expansion after deployment, and compression to the simulated vessel diameter. Maximum radial stresses resulting from this strain history were calculated. The safety factors for the stents under these conditions all exceeded 1.0, suggesting sufficient durability under clinically anticipated conditions.
Accelerated Pulsatile Durability	Determine whether stents fracture when subjected to physiologically relevant radial fatigue loads	Stents were deployed in flexible tubing, and subjected to a total of 420 million physiologically relevant radial deformations to simulate ten years of implant life. No stent fractures, cracks, or other defects were observed during or after the durability test, suggesting satisfactory durability to anticipated radial loads.
Magnetic Resonance Imaging (MRI) Compatibility	Ensure that the stented area can be safely imaged using MRI	Stent deflection, torque, heating and imaging artifacts resulting from a 15-minute exposure to a 3 Tesla MRI system were measured. The results suggest satisfactory performance in MR fields of 3 Tesla or less, spatial gradient field strengths of 720 Gauss/cm or less, and a maximum whole-body-averaged specific absorption rate of 3.0 W/kg for 15 minutes of scanning. The device labeling states that the stent is "MR Compatible" under these conditions. Image quality in the area near the stented location may be compromised.
Radiopacity	Ensure that deployed stents can be observed under fluoroscopy	The visibility of the stent under fluoroscopy was assessed during animal studies. The radiopacity of the radiopaque markers of the delivery system was also assessed. The results demonstrated that deployed stents and the delivery system are sufficiently radiopaque.

Table 7: Summary of *In Vitro* Testing of the OTW and RX Systems

Test	Objective	Summary of Methods and Results
Stent Deployment Force	Ensure that excessive force is not required to deploy the stent	Stents were deployed in a fixture simulating challenging target anatomy. The force required to retract the sheath and deploy the stent was measured and met specifications. The results indicate appropriate ease of deployment.
Stent Deployment Accuracy	Ensure that stents can be deployed in the target region	Stents were deployed in a fixture simulating challenging target anatomy. The distance between the stent and the target location was measured and met specifications. The results demonstrate that the stent can be deployed at the intended location with sufficient accuracy.
Delivery System Dimensions	Ensure delivery system dimensions meet specifications and are compatible with accessory devices	The key delivery system dimensions, including working length, guidewire lumen length, tip internal diameter, and proximal shaft outer diameter, were measured and evaluated against specifications. All dimensions measured met the specification requirements.
Crossing Profile	Ensure that the stent system can cross lesions without interaction	The maximum diameter, or crossing profile, of the stent system was measured and evaluated against specifications. The crossing profile met the specification requirements, indicating sufficient ability to cross lesions. This information is incorporated in the device labeling.
Sheath/Guide Catheter Compatibility	Demonstrate compatibility between the stent system and sheaths and guide catheters used to deliver the stent	The force needed to insert a stent system through representative introducer sheaths and guide catheters was measured and evaluated against specifications. The stent system was able to pass through all tested devices using forces below the specified limits, suggesting adequate device compatibility.
Embolic Protection Device Compatibility	Demonstrate compatibility between the stent system and the Medtronic GuardWire embolic protection device	GuardWire devices were back-loaded through the guidewire lumen of stent systems and passed through the entire length of the catheter without difficulty. The results suggest that the Exponent and GuardWire systems are compatible.
Tensile Strength	Ensure the durability of the stent system	The tensile strength of key bond joints in the stent system was measured using a pull tester. All bond joint tensile strengths met the specification requirements, indicating sufficient resistance to tensile forces.
Air Entrainment and Embolization	Assess the potential for air entrainment and embolization during stent system introduction	Following stent system flushing, stents were deployed under water, and the presence and size of air bubbles was recorded. The volume of air released was comparable between the OTW and RX systems, which were comparable to the air released during the deployment of a currently marketed carotid stent. The results suggest that the amount of air liberated during deployment does not raise any concerns.

The *in vitro* test results support adequate performance of the device.

9.2 ANIMAL STUDIES

Five *in vivo* studies were performed to evaluate the acute and chronic safety of the Exponent® Self-Expanding Carotid Stent with OTW and RX Delivery Systems. All studies were conducted in accordance with Good Laboratory Practices (GLP) per 21 CFR §58. These studies are summarized in Table 8.

Table 8: Summary of Animal Studies

Study	Number of Animals, Time Points, Devices Tested, and Implant Sites	Relevant Findings
FS40: Acute delivery, mechanical performance and vascular response versus a control in normal porcine peripheral arteries	8 animals (porcine) 28 days 8 test articles, 5 controls Carotid and iliac arteries	All stent delivery and deployment procedures were rated well. Vascular injury and neointimal thickness scores were low.
FS41: Acute delivery, mechanical performance and chronic vascular response versus a control in normal porcine peripheral arteries	8 animals (porcine) 6 months 13 test articles, 6 controls Carotid and iliac arteries	All stent delivery and deployment procedures were rated well. Vascular injury and neointimal thickness scores were low.
FS55: Acute performance compatibility of the Self-Expanding Carotid Stent with the GuardWire Temporary Occlusion and Aspiration System in carotid swine arteries	1 animal (porcine) Acute 4 stents, 2 embolic protection devices Carotid arteries	The Exponent and GuardWire devices were used together as a system without observed difficulty. Device compatibility, trackability, stent crossing, and device retrieval were all rated well.
FS70: Vascular response and mechanical performance in the swine iliac and carotid arteries.	10 animals (porcine) 28 days 20 test articles, 10 controls Carotid and iliac arteries	All stent delivery and deployment procedures were rated well. Vascular injury scores were generally low. One animal experienced severe in-stent granulomas, which is a known potential reaction with nickel-titanium stents.
FS139: Mechanical performance of the RX delivery system versus the OTW delivery system, and compatibility with embolic protection systems in target vessels.	2 animals (ovine) Acute 8 RX systems and 4 OTW systems, plus the GuardWire® Temporary Occlusion and Aspiration System	Acute performance of the RX system, including both mechanical performance and compatibility with embolic protection systems, was acceptable and equivalent to the performance of the OTW system. No complications were reported.

The animal study results suggest satisfactory device safety *in vivo*.

9.3 BIOCOMPATIBILITY

The Exponent[®] Self-Expanding Carotid Stent Systems were tested for biocompatibility in accordance with International Organization for Standardization (ISO) 10993-1, "Biological Evaluation of Medical Devices Part 1: Evaluation of Testing," FDA's Blue Book Memorandum dated May 1, 1995, and FDA 21 CFR Part 58. All testing was conducted using finished, sterilized stent systems in accordance with FDA/ISO guidelines for blood contact/implant materials.

The stent is considered an implant with permanent blood contact (> 30 days). Both the OTW and RX delivery systems are categorized as external communicating devices that contact circulating blood for less than 24 hours. The biocompatibility test regimen is outlined in Table 9.

Table 9: Summary of Biocompatibility Testing

Test Performed	Test Result
Cytotoxicity (MEM elution)	Pass
<i>In vitro</i> hemolysis	Pass
Acute intracutaneous reactivity	Pass
Acute systemic toxicity	Pass
Material-mediated pyrogenicity	Pass
Sensitization (Maximization)	Pass
<i>In vivo</i> thromboresistance	Pass
C3a complement activation	Pass
Plasma recalcification/ coagulation time	Pass
Muscle implantation	Pass

Evaluation of chronic toxicity and carcinogenicity was not necessary due to the extensive clinical history of the device materials and their well-characterized long-term safety profile.

The test results demonstrate that both the stent and delivery systems are biocompatible and non-pyrogenic.

9.4 STERILIZATION

The Medtronic Vascular Exponent[®] Self-Expanding Carotid Stent Systems are E-beam sterilized in compliance with AAMI/ISO 11137:1995 (*Sterilization of health care products: requirements for validation and routine control: radiation sterilization*). Quarterly sterilization dose audits and monitoring of bioburden levels are performed to confirm that the sterilization process is effective in eradicating viable microorganisms. The audit results indicate that the carotid system will maintain a Sterility Assurance Level of 10^{-6} when sterilized at a minimum dose of 25 kGy.

Limulus Amoebocyte Lysate (LAL) testing of finished lot demonstrates acceptable levels of pyrogenicity.

9.5 PACKAGING AND SHELF LIFE

A three-year shelf life has been substantiated for the Exponent[®] Self-Expanding Carotid Stent with OTW Delivery System, and a one-year shelf-life has been substantiated for the Exponent[®] Self-Expanding Carotid Stent with RX Delivery System. Shelf-life values were based on demonstration of acceptable packaging integrity and device performance using sterilized samples subjected to real-time and accelerated aging.

10.0 SUMMARY OF CLINICAL STUDIES

The MAVERIC (Evaluation of the Medtronic AVE Self-Expanding Carotid Stent System with Distal Protection in the Treatment of Carotid Stenosis) I and II studies were two prospective, single-arm, multi-center, consecutively enrolling clinical studies performed in the United States to demonstrate the safety and efficacy of the Medtronic Exponent[®] Self-Expanding Carotid Stent with OTW Delivery System in conjunction with the GuardWire[®] Temporary Occlusion and Aspiration System. In both studies, the devices were used to treat subjects with occlusive disease of the common or internal carotid artery who were either symptomatic ($\geq 50\%$ stenosis) or asymptomatic ($\geq 80\%$ stenosis), and possessed anatomic and/or co-morbidity risk factors for surgical revascularization. MAVERIC I enrolled a total of 99 patients at 16 U.S. clinical sites and MAVERIC II enrolled 399 patients at 34 U.S. clinical sites in the U.S. An overview of the MAVERIC I & II studies is presented in Table 10.

Table 10: Overview of MAVERIC I and II Studies

	MAVERIC I	MAVERIC II
Products Evaluated	Exponent [®] Self-Expanding Carotid Stent with Over-the-Wire (OTW) Delivery System and the GuardWire [®] Temporary Occlusion & Aspiration System	
Study Design	Non-randomized, multi-center, single-arm, prospective clinical trials	
Sample Size	99 patients	399 patients
Number of Sites	16 in the U.S.	34 in the U.S.
Primary Endpoint	Any death, MI, stroke to 30 days and ipsilateral stroke from 31 – 365 days	
Secondary Endpoints	<p>Safety:</p> <ul style="list-style-type: none"> Freedom from any stroke, MI or death at 30 days Freedom from target lesion revascularization at one year <p>Efficacy:</p> <ul style="list-style-type: none"> Acute success defined by: <ul style="list-style-type: none"> lesion¹ device (stent delivery system and distal protection device)² procedure³ 	<p>Safety:</p> <ul style="list-style-type: none"> Major Adverse Events at 30 days post procedure, defined as any stroke, MI, and/or death <p>Efficacy:</p> <ul style="list-style-type: none"> Acute success defined by: <ul style="list-style-type: none"> lesion¹ device (stent delivery system and distal protection device)² procedure³ Freedom from stroke at one year
Study Hypothesis	Results meet the performance goal (PG) derived from historical carotid endarterectomy data	
Patient Follow-Up	<ul style="list-style-type: none"> Neurological evaluation by an independent neurologist at 30 days, 6 months, and 365 days Clinical assessment via telephone call at 14 days and physical assessment (office visit) at 30 days, 6 months, and 365 days, and annually for 3 years thereafter Carotid duplex scans performed at 2 weeks and 365 days 	<ul style="list-style-type: none"> Neurological evaluation by an independent neurologist or NIHSS stroke-certified surrogate at 30 days, 6 months, and 365 days Physical assessment (office visit) at 30 days, 6 months, and 365 days, and annually for 3 years thereafter Carotid duplex scans performed at 4 weeks and 365 days

¹ Attainment of < 30% residual in-stent stenosis of the target lesion; if in-stent measurements not available, then in-lesion measurements were used; if in-lesion measurements not available, then visual estimates were used.

² Attainment of <30% residual in-stent stenosis of the target lesion using the study devices; this measure is a union of stent and embolic protection device success.

³ Attainment of residual in-stent stenosis of the target lesion and no in-hospital major adverse events. If in-stent measurements not available, then in-lesion measurements were used; if in-lesion measurements not available, then visual estimates were used.

The protocol required regular patient follow-up by the treating physician and follow-up neurological assessment by either an independent neurologist or an NIH Stroke Scale (NIHSS)-certified evaluator. Core laboratories provided independent assessments for angiographic, ultrasound, and electrocardiogram results. Medical monitors reviewed all safety data to ensure appropriate reporting of adverse events. A Clinical Events Committee adjudicated suspected primary endpoint events. A Data Safety Monitoring Board monitored adverse events to ensure patient safety.

Statistical Methods

The statistical analyses of MAVERIC I and II were designed to demonstrate that the primary endpoint event rates were significantly less than a performance goal derived

from available carotid endarterectomy (CEA) literature, which represented the standard of care for carotid revascularization at the time of study initiation.

The one-year major event rate from CEA was estimated as $\omega_A \times 11\% + \omega_C \times 14\%$, where ω_C = the proportion of subjects with co-morbidity risk factors and ω_A = the proportion of subjects with anatomic risk factors. Based on this estimate, the study hypotheses were established as:

$$\begin{aligned} H_0: \pi_{\text{Medtronic AVE}} &\geq \omega_A \times 11\% + \omega_C \times 14\% + 4\% \\ H_A: \pi_{\text{Medtronic AVE}} &< \omega_A \times 11\% + \omega_C \times 14\% + 4\%, \end{aligned}$$

where $\pi_{\text{Medtronic AVE}}$ = the one-year primary endpoint event rate and where ω_A and ω_C are based on the observed mix of subjects enrolled with each type of surgical risk factor. With a one-sided type I error of 5% and a type II error of 20%, the upper bound of the one-sided 95% confidence interval for the primary endpoint event rate must be less than the calculated performance goal for the null hypothesis to be rejected.

Eligibility Requirements

The study population included male and female subjects of at least 18 years of age, with a lesion located between the origin of the common carotid artery and the intracranial segment of the internal carotid artery.

Key inclusion criteria included:

- Neurological symptoms and $\geq 50\%$ stenosis of the common or internal carotid artery by either ultrasound or angiogram, or absence of neurological symptoms and $\geq 80\%$ stenosis of the common or internal carotid artery by either ultrasound or angiogram, and
- Reference diameters between 5.5 mm and 9.5 mm at the target lesion.

Symptomatic patients were defined as having:

- sudden numbness or weakness of face, arm or leg – especially on one side of the body,
- sudden confusion, trouble speaking or understanding,
- sudden trouble seeing in one or both eyes,
- sudden trouble walking, dizziness, loss of balance or coordination, or
- sudden severe headache with no known cause.

Patients were excluded from eligibility if they had an occurrence of non-disabling stroke, disabling stroke within 4 weeks of the index procedure or symptoms of a TIA or amaurosis fugax within 24 hours of the index procedure.

Each subject must have been considered at high risk for adverse events from carotid endarterectomy, as evidenced by the presence of at least one anatomic or co-morbidity risk factors. These risk factors and their prevalence in the enrolled population are identified in Table 11 below.

Table 11: Surgical High Risk Criteria

RISK FACTORS	MAVERIC I (N=99 Patients)	MAVERIC II (N=399 Patients)
ANATOMIC		
Previous Carotid Endarterectomy	59.6% (59/99)	28.6% (114/399)
Contralateral Carotid Artery Occlusion	5.1% (5/99)	8.5% (34/399)
Previous Radical Neck Dissection Or Radiation Therapy To Neck Region	11.1% (11/99)	9.3% (37/399)
Target Lesion Above C-2 (Level Of Jaw)	7.1% (7/99)	10.3% (41/399)
Low Cervical Carotid Lesions	1.0% (1/99)	1.0% (4/399)
Dissection	1.0% (1/99)	0.0% (0/399)
Inability To Extend Neck (I.E. Cervical Osteoarthritis, Mobility Limitations)	8.1% (8/99)	7.3% (29/399)
Tandem Lesions \geq 70% Stenosis	2.0% (2/99)	1.3% (5/399)
Contralateral Laryngeal Palsy	1.0% (1/99)	1.3% (5/399)
At Risk For Wound Infection	5.1% (5/99)	3.3% (13/399)
Tracheostomy	1.0% (1/99)	1.5% (6/399)
CO-MORBIDITY		
Patients > 80 Years Of Age	10.1% (10/99)	35.3% (141/399)
Two Or More Major Diseased Coronary Arteries With >70% Stenosis At The Time Of Index Procedure In Patients With A History Of Angina ¹	N/A	15.3% (61/399)
Myocardial Infarction Within Previous 6 Weeks	0.0% (0/99)	0.8% (3/399)
NYHA Class III Or IV Heart Failure	15.2% (15/99)	12.8% (51/399)
Unstable Angina (Defined As Resting Pain With ECG Changes)	3.0% (3/99)	3.3% (13/399)
History Of Liver Failure With Elevated Prothrombin Time	0.0% (0/99)	0.3% (1/399)
Requires Concurrent CABG, AAA Repair Or Peripheral Vascular Surgery	0.0% (0/99)	0.0% (0/399)
COPD With FEV1 < 30% Predicted	3.0% (3/99)	1.8% (7/399)

¹ Part of the MAVERIC II clinical protocol but not a co-morbidity risk factor for the MAVERIC I clinical protocol.

Description of Subjects Evaluated

Table 12 summarizes patient follow-up compliance at the endpoint evaluation time points.

Table 12: Subject Follow-up Compliance

	MAVERIC I (N = 99) % (n/N)	MAVERIC II (N = 399) % (n/N)
30 Days		
Patients Enrolled	100.0% (99/99)	100.0% (399/399)
Cumulative Death	1.0% (1/99)	1.0% (4/399)
Cumulative Withdrawn/Lost to Follow-Up (LTF)	0.0% (0/99)	1.5% (6/399)
Patients Evaluable	99.0% (98/99)	97.5% (389/399)
Patients Evaluated ¹	97.0% (96/99)	94.5% (377/399)
Neurological Evaluation ²	88.9% (88/99)	89.0% (355/399)
Ultrasound Evaluation ³	90.9% (90/99)	86.4% (345/399)
Other Clinical Evaluation Only ⁴	8.1% (8/99)	5.5% (22/399)
365 Days		
Cumulative Death	1.0% (1/99)	9.3% (37/399)
Cumulative Withdrawn or LTF	1.0% (1/99)	7.5% (30/399)
Patients Evaluable	98.0% (97/99)	83.2% (332/399)
Patients Evaluated ¹	96% (95/99)	79.7% (318/399)
Neurological Evaluation ²	78.8% (78/99)	72.7% (290/399)
Ultrasound Evaluation ³	79.8% (79/99)	73.2% (292/399)
Other Clinical Evaluation Only ⁴	17.2% (17/99)	7.0% (28/399)

¹ Patients evaluated defined as a complete 30 or 365 day contact form

² Neurological assessment defined as a complete NIH Stroke Scale form

³ Ultrasound evaluation took place at 14 days for MAVERIC I

⁴ Other Clinical Evaluation Only defined as a complete 30 or 365 day contact form with no neurological evaluation

Description of Patient Demographics

Table 13 summarizes demographic information for the MAVERIC I and II subjects.

Table 13: MAVERIC I and II Subject Demographics

Subject Characteristics	MAVERIC I	MAVERIC II
Age (yrs)		
Mean ± SD (N)	69.26 ± 10.20 (99)	74.08 ± 9.39 (399)
Range (Min, Max)	43, 89	41, 95
Gender, % (n/N)¹		
Male	57.6% (57/99)	58.6% (234/399)
Female	42.4% (42/99)	41.4% (165/399)
Race, % (n/N)¹		
White	89.9% (89/99)	91.2% (364/399)
Black	5.1% (5/99)	3.8% (15/399)
Hispanic	3.0% (3/99)	3.0% (12/399)
Asian	1.0% (1/99)	0.8% (3/399)
Other	1.0% (1/99)	1.3% (5/399)
Medical History, % (n/N)¹		
Left Ventricular Function		
Normal (ejection fraction >55%)	45.0% (27/60)	51.6% (126/244)
Mildly Impaired (ejection fraction 46% to 55%)	25.0% (15/60)	12.3% (30/244)
Moderately Impaired (ejection fraction 30% to 45%)	15.0% (9/60)	22.1% (54/244)
Severely Impaired (ejection fraction <30%)	15.0% (9/60)	13.9% (34/244)
Clinical Congestive Heart Failure	26.5% (26/98)	24.8% (96/387)
Peripheral Vascular Disease	52.6% (51/97)	44.0% (171/389)

Subject Characteristics	MAVERiC I	MAVERiC II
Gastrointestinal/Genitourinary Bleeding	8.2% (8/97)	5.3% (21/397)
Diabetes Mellitus	27.3% (27/99)	34.1% (136/399)
History of Liver Failure	0.0% (0/97)	0.3% (1/386)
Dyslipidemia Requiring Medication	68.7% (68/99)	70.8% (281/397)
History of Hypertension	91.8% (90/98)	87.9% (350/398)
Uncontrolled Systemic Hypertension	2.2% (2/91)	1.5% (6/393)
Cigarette Smoking (Ever)	72.7% (72/99)	67.3% (266/395)
Family History of Premature Atherosclerosis	41.9% (26/62)	Not Captured
Significant Aortic Arch Atherosclerosis	1.1% (1/93)	Not Captured
History of Cardiac arrhythmia	17.7% (17/96)	Not Captured
Severe Aortic/Mitral Valvular Disease	7.4% (7/95)	Not Captured
Renal Insufficiency	11.1% (11/99)	Not Captured
Clinical COPD	3.4% (3/88)	Not Captured
Coronary Artery Disease	66.3% (63/95)	Not Captured
Unstable Angina	3.1% (3/98)	Not Captured
Current Smoking	19.4% (19/98)	Not Captured
Previous Q wave or Non-Q wave MI	28.0% (26/93)	27.8% (107/385)
Prior Cardiovascular Procedures, % (n/N)¹		
Previous PTCA (coronary)	23.5% (23/98)	Not Captured
Previous Atrial Valve Repair (AVR)	3.0% (3/99)	Not Captured
Previous Mitral Valve Repair (MVR)	1.0% (1/99)	Not Captured
Previous CABG	33.3% (33/99)	Not Captured
Neurological History, % (n/N)¹		
Previous PTA (Carotid)	0.0% (0/97)	2.3% (9/399)
Previous CEA	60.6% (60/99)	33.6% (134/399)
History of TIA	23.5% (23/98)	29.3% (115/392)
History of Stroke	21.9% (21/96)	22.5% (89/396)
Target Lesion Location, % (n/N)¹		
Right Carotid		
Common	6.2% (6/97)	3.1% (12/389)
Internal	44.3% (43/97)	48.3% (188/389)
Left Carotid		
Common	11.1% (11/97)	4.9% (19/389)
Internal	38.1% (37/97)	43.7% (170/389)
Baseline Target Lesion Characteristics, % (n/N)¹		
Lesion location, %		
Contiguous	43.3% (42/97)	50.1% (194/387)
Remote	48.5% (47/97)	37.7% (146/387)
Sequential	8.2% (8/97)	12.1% (47/387)
Distance from Ostium (mm)		
Mean±SD (N)	6.01±7.87 (97)	3.63±5.73 (387)
Minimum, maximum	0.00, 42.40	0.00, 34.40
Lesion Length (mm)		
Mean±SD (N)	14.71±6.99 (96)	15.17±6.83 (387)
Minimum, maximum	2.29, 33.71	4.56, 39.73

Subject Characteristics	MAVERIC I	MAVERIC II
Discrete (<10 mm), % (n/N)	26.0% (25/96)	25.1% (97/387)
Tubular (10 to 20 mm), % (n/N)	53.1% (51/96)	54.0% (209/387)
Diffuse (≥20 mm), % (n/N)	20.8% (20/96)	20.9% (81/387)
Lesion Eccentricity, % (n/N)	35.1% (34/97)	29.2% (113/387)
Thrombus, % (n/N)		
None	93.8% (91/97)	94.3% (365/387)
Possible	6.2% (6/97)	5.7% (22/387)
Mild	0.0% (0/97)	0.0% (0/387)
Moderate	0.0% (0/97)	0.0% (0/387)
Large	0.0% (0/97)	0.0% (0/387)
Total occlusion	0.0% (0/97)	0.0% (0/387)
Access tortuosity (any), % (n/N)	2.1% (2/97)	3.9% (15/387)
Distal tortuosity (any), % (n/N)	33.0% (32/97)	34.9% (135/387)
Calcification (unilateral or bilateral), % (n/N)	49.5% (48/97)	53.7% (208/387)
Ulceration, % (n/N)	23.7% (23/97)	27.4% (106/387)
Aneurysm, % (n/N)	6.2% (6/97)	3.1% (12/387)
Baseline TIMI flow, % (n/N)		
0, 1	0.0% (0/59)	0.0% (0/221)
2	3.4% (2/59)	5.9% (13/221)
3	96.6% (57/59)	94.1% (208/221)

¹Denominators indicate the total number of patients with available data for the related parameter.

Table 14 summarizes quantitative angiographic findings for the MAVERIC I trial.

Table 14: Quantitative Angiographic Findings, MAVERIC I

Parameter	Pre-procedure	Final Assessment
Reference diameter		
Common carotid (mm)		
Mean ± SD (N ¹)	6.64±1.33 (97)	6.65±1.33 (96)
Minimum, maximum	3.60, 10.00	3.66, 10.00
Internal carotid (mm)		
Mean ± SD (N ¹)	4.56±0.88 (97)	4.70±0.93 (96)
Minimum, maximum	2.78, 6.51	3.02, 7.75
RVD (mm)		
Mean ± SD (N ¹)	4.99±1.32 (97)	5.12±1.31 (96)
Minimum, maximum	2.78, 9.17	3.02, 8.89
MLD (mm)		
Mean ± SD (N ¹)	1.48±0.76 (97)	3.81±0.75 (96)
Minimum, maximum	0.21, 3.30	1.57, 5.59
% Diameter stenosis		
Mean ± SD (N ¹)	70.59±12.30 (97)	23.41±13.51 (96)
Minimum, maximum	38.93, 94.05	2.58, 63.99

¹Denominators indicate the total number of patients with available data for the related parameter.

Table 15 summarizes quantitative angiographic findings for the 399 patients enrolled into the MAVERIC II trial.

Table 15: Quantitative Angiographic Findings, MAVERIC II

Parameter	Pre-procedure	Final Assessment
Reference diameter		
Common carotid (mm)		
Mean±SD (n) ¹	6.51±1.19 (387)	6.48±1.19 (385)
Minimum, maximum	4.11, 10.45	4.03, 10.73
Internal carotid (mm)		
Mean±SD (n) ¹	4.25±0.79 (387)	4.32±0.74 (385)
Minimum, maximum	2.22, 6.83	2.66, 6.82
RVD (mm)		
Mean ±SD (n) ¹	4.40±0.93 (387)	4.46±0.89 (385)
Minimum, maximum	2.38, 9.55	2.66, 9.25
MLD (mm)		
Mean±SD (n) ¹	1.34±0.54 (387)	3.64±0.72 (385)
Minimum, maximum	0.34, 3.62	(1.79,5.84)
% Diameter stenosis		
Mean±SD (n) ¹	69.60±9.88 (387)	17.45±12.42 (385)
Minimum, maximum	36.07, 90.96	-25.54, 60.98

¹Denominators indicate the total number of patients with available data for the related parameter.

Clinical Results Summary

Primary endpoint events (defined as any death, MI, or stroke reported from 0 to 30 days and any ipsilateral stroke reported from 31 – 365 days) occurred in 6 patients in the MAVERIC I clinical trial, for a rate of 6.1% at both 30 days and 365 days. In the MAVERIC II trial, primary endpoint events occurred in 21 patients at 30 days, for a rate of 5.3%, and occurred in 22 patients from 0 - 365 days for a rate of 5.5%. No deaths were attributed to device malfunction or failure. Table 16 summarizes the safety and effectiveness measures for both studies.

Table 16: Safety and Efficacy Measures¹

Safety and Efficacy Measures	MAVERIC I (N = 99) % (n/N)	MAVERIC II (N = 399) % (n/N)
Primary Endpoint		
Death, MI, Stroke to 30 days and Ipsilateral Stroke from 31-365 Days	6.1% (6/99)	5.5% (22/399)
30 Day Death	1.0% (1/99)	1.0% (4/399)
30 Day MI	1.0% (1/99)	1.5% (6/399)
30 Day Stroke	5.1% (5/99)	4.0% (16/399)
31-365 Day Ipsilateral Stroke	0.0% (0/99)	0.3% (1/399)
Secondary Endpoint		
Any MAE to 30 days (Death, MI, Stroke)	6.1% (6/99)	5.3% (21/399)
Target Lesion Revascularization (TLR)	2.0% (2/99)	1.3% (5/399)
Target Vessel Revascularization (TVR)	2.0% (2/99)	0.5% (2/399)
Primary Patency at 1 year	85.9% (85/99)	92.1% (363/394)
Technical Success	80.8% (80/99)	87.0% (347/399)
Acute Procedure Success	81.8% (81/99)	88.6% (350/395)

¹ All data based on ITT population

Table 17 includes the results of primary endpoint event hypothesis testing for the MAVERIC I and II studies. The 95% one-sided upper confidence interval of the MAVERIC primary endpoint event rate is less than the hypothesized value ($\omega_A \times 11\% + \omega_C \times 14\% + 4\%$), demonstrating that the MAVERIC study results met the pre-specified performance goal.

Table 17. MAVERIC I and II Statistical Analysis for Primary Endpoint Events

	Primary Endpoint Events to 365 days ¹	Weighted PG	Weighted PG + 0.04	Upper Bound of 1-Sided 95% CI
MAVERIC I	6.1% (6/98)	11.765%	15.765%	11.73%
MAVERIC II	5.9% (22/375)	12.728%	16.728%	8.27%

¹ Data based on analysis population (AP), defined as ITT population minus patients lost to follow-up.

A primary endpoint event is defined as death, MI, stroke to 30 days and ipsilateral stroke from 31 - 365 days.

In MAVERIC I, the PG (performance goal) for the AP population was based on 25 patients with co-morbid risk factors and 73 patients with anatomic risk factors. In MAVERIC II, the PG was based on 216 patients with co-morbid risk factors and 159 patients with anatomic risk factors (2 patients with missing high-risk data were considered to have anatomic risk factors).

One-year complication rates of 11% for patients with anatomic risk factors and 14% For patients with co-morbid risk factors were used to calculate the weighted PG for both studies.

The Kaplan-Meier estimates for freedom-from-primary endpoint events to 365 days for the MAVERIC I & II trials for all subjects, symptomatic subjects, and asymptomatic subjects are provided in Tables 18 - 23. All analyses are based on the intent-to-treat population.

Table 18. MAVERIC I Kaplan-Meier Estimate for Freedom-from-Primary Endpoint Events to 365 Days For All Subjects

	Time Intervals (Days)										
	0*	1-30	31-60	61-120	121-150	151-180	181-240	241-270	271-300	301-330	331-365
# Entered	99	96	93	93	93	93	93	92	92	92	92
# Censored	0	0	0	0	0	0	1	0	0	0	2
# Incomplete	0	0	0	0	0	0	0	0	0	0	0
# Events	3	3	0	0	0	0	0	0	0	0	0
Cumulative % Event-Free	97.0%	93.9%	93.9%	93.9%	93.9%	93.9%	93.9%	93.9%	93.9%	93.9%	93.9%
SE	1.7%	2.4%	2.4%	2.4%	2.4%	2.4%	2.4%	2.4%	2.4%	2.4%	2.4%

* Peri-procedural events

Entered: The number of patients entering the interval

Censored: The number of patients who prematurely withdrew without an event in the interval

Incomplete: The number of patients who died in the interval without event

Events: The number of patients with event in the interval

Cumulative % Event-Free: Kaplan-Meier estimate of percentage of patients without an event at the end of the specified interval

SE: Kaplan-Meier estimate of standard error

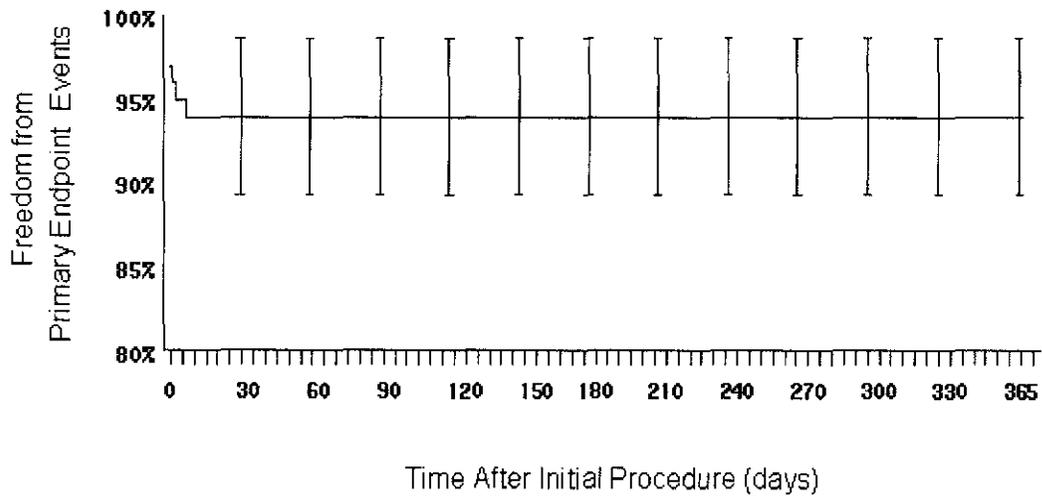


Table 19. MAVERIC I Kaplan-Meier Estimate for Freedom-from-Primary Endpoint Events to 365 Days for Symptomatic Subjects

	Time Intervals (Days)										
	0*	1-30	31-60	61-120	121-150	151-180	181-240	241-270	271-300	301-330	331-365
# Entered	38	35	33	33	33	33	33	33	33	33	33
# Censored	0	0	0	0	0	0	0	0	0	0	1
# Incomplete	0	0	0	0	0	0	0	0	0	0	0
# Events	3	2	0	0	0	0	0	0	0	0	0
Cumulative % Event-free	92.1%	86.8%	86.8%	86.8%	86.8%	86.8%	86.8%	86.8%	86.8%	86.8%	86.8%
SE	4.4%	5.5%	5.5%	5.5%	5.5%	5.5%	5.5%	5.5%	5.5%	5.5%	5.5%

* Peri-procedural events

Entered: The number of patients entering the interval

Censored: The number of patients who prematurely withdrew without an event in the interval

Incomplete: The number of patients who died in the interval without event

Events: The number of patients with event in the interval

Cumulative % Event-Free: Kaplan-Meier estimate of percentage of patients without an event at the end of the specified interval

SE: Kaplan-Meier estimate of standard error

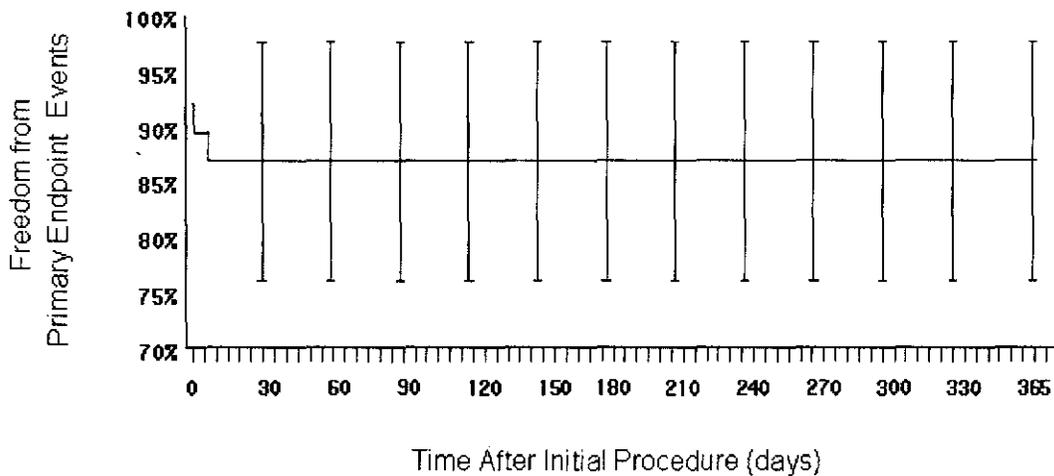


Table 20. MAVERIC I Kaplan-Meier Estimate for Freedom-from-Primary Endpoint Events to 365 Days for Asymptomatic Subjects

	Time Intervals (Days)										
	0*	1-30	31-60	61-120	121-150	151-180	181-240	241-270	271-300	301-330	331-365
# Entered	59	59	58	58	58	58	58	57	57	57	57
# Censored	0	0	0	0	0	0	1	0	0	0	1
# Incomplete	0	0	0	0	0	0	0	0	0	0	0
# Events	0	1	0	0	0	0	0	0	0	0	0
Cumulative % Event-free	100%	98.3%	98.3%	98.3%	98.3%	98.3%	98.3%	98.3%	98.3%	98.3%	98.3%
SE	0.0%	1.7%	1.7%	1.7%	1.7%	1.7%	1.7%	1.7%	1.7%	1.7%	1.7%

* Peri-procedural events

Entered: The number of patients entering the interval

Censored: The number of patients who prematurely withdrew without an event in the interval

Incomplete: The number of patients who died in the interval without event

Events: The number of patients with event in the interval

Cumulative % Event-Free: Kaplan-Meier estimate of percentage of patients without an event at the end of the specified interval

SE: Kaplan-Meier estimate of standard error

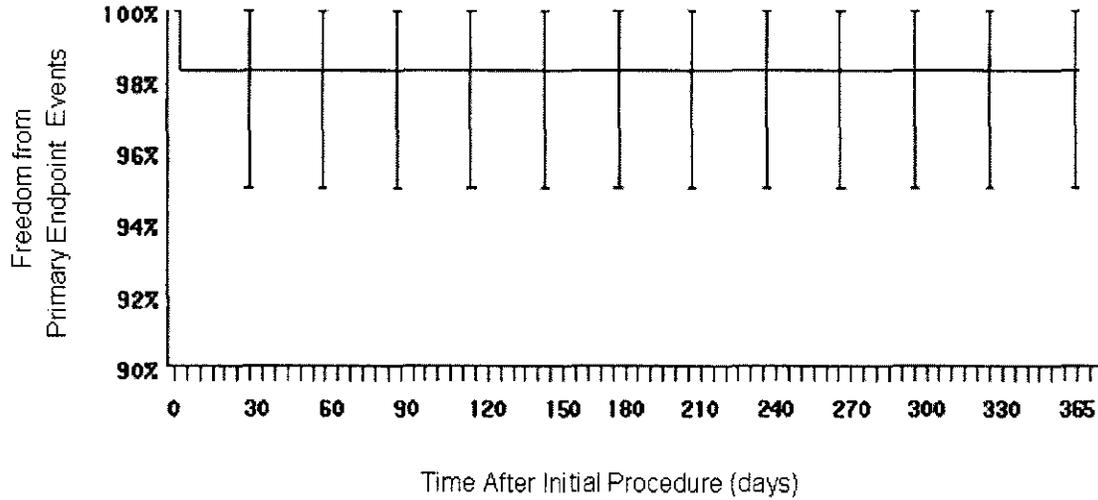


Table 21. MAVERIC II Kaplan-Meier Estimate for Freedom-from-Primary Endpoint Events to 365 Days for All Subjects

	Time Intervals (Days)										
	0*	1-30	31-60	61-120	121-150	151-180	181-240	241-270	271-300	301-330	331-365
# Entered	399	390	369	367	361	359	353	341	336	333	326
# Censored	0	9	2	2	0	3	4	3	0	1	9
# Incomplete	0	0	0	4	2	3	7	2	3	6	2
# Events	9	12	0	0	0	0	1	0	0	0	0
Cumulative % Event-free	97.7%	94.7%	94.7%	94.7%	94.7%	94.7%	94.4%	94.4%	94.4%	94.4%	94.4%
SE	0.7%	1.1%	1.1%	1.1%	1.1%	1.1%	1.2%	1.2%	1.2%	1.2%	1.2%

* Peri-procedural events

Entered: The number of patients entering the interval

Censored: The number of patients who prematurely withdrew without an event in the interval

Incomplete: The number of patients who died in the interval without event

Events: The number of patients with event in the interval

Cumulative % Event-Free: Kaplan-Meier estimate of percentage of patients without an event at the end of the specified interval

SE: Kaplan-Meier estimate of standard error

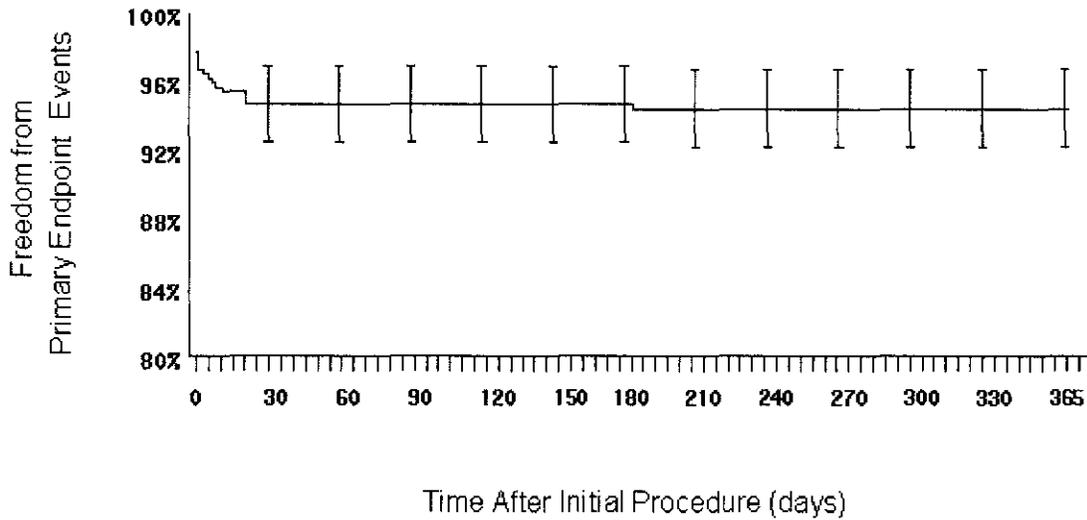


Table 22. MAVERIC II Kaplan-Meier Estimate for Freedom-from-Primary Endpoint Events to 365 Days for Symptomatic Subjects

	Time Intervals (Days)										
	0*	1-30	31-60	61-120	121-150	151-180	181-240	241-270	271-300	301-330	331-365
# Entered	175	171	158	157	153	153	150	145	142	142	139
# Censored	0	5	1	1	0	1	3	2	0	0	5
# Incomplete	0	0	0	3	0	2	2	1	0	3	0
# Events	4	8	0	0	0	0	0	0	0	0	0
Cumulative % Event-free	97.7%	93.1%	93.1%	93.1%	93.1%	93.1%	93.1%	93.1%	93.1%	93.1%	93.1%
SE	1.1%	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%

* Peri-procedural events

Entered: The number of patients entering the interval

Censored: The number of patients who prematurely withdrew without an event in the interval

Incomplete: The number of patients who died in the interval without event

Events: The number of patients with event in the interval

Cumulative % Event-Free: Kaplan-Meier estimate of percentage of patients without an event at the end of the specified interval

SE: Kaplan-Meier estimate of standard error

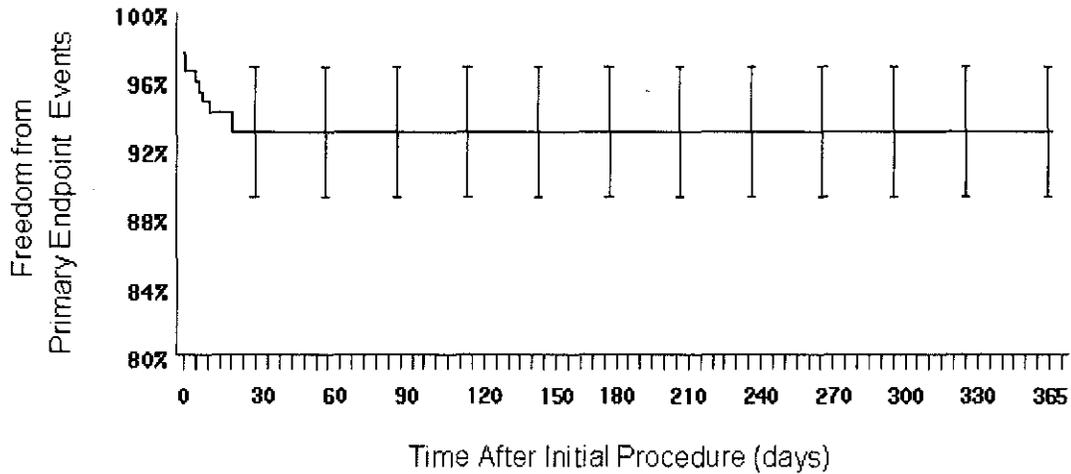


Table 23. MAVERIC II Kaplan-Meier Estimate for Freedom-from-Primary Endpoint Events to 365 Days for Asymptomatic Subjects

	Time Intervals (Days)											
	0*	1-30	31-60	61-120	121-150	151-180	181-240	241-270	271-300	301-330	331-365	
MAVERIC II												
# Entered	219	214	207	206	204	202	199	192	190	187	183	
# Censored	0	3	1	1	0	2	1	1	0	1	4	
# Incomplete	0	0	0	1	2	1	5	1	3	3	2	
# Events	5	4	0	0	0	0	1	0	0	0	0	
Cumulative % Event-free	97.7%	95.9%	95.9%	95.9%	95.9%	95.9%	95.4%	95.4%	95.4%	95.4%	95.4%	
SE	1.0%	1.3%	1.3%	1.3%	1.3%	1.3%	1.4%	1.4%	1.4%	1.4%	1.4%	

* Peri-procedural events

Entered: The number of patients entering the interval

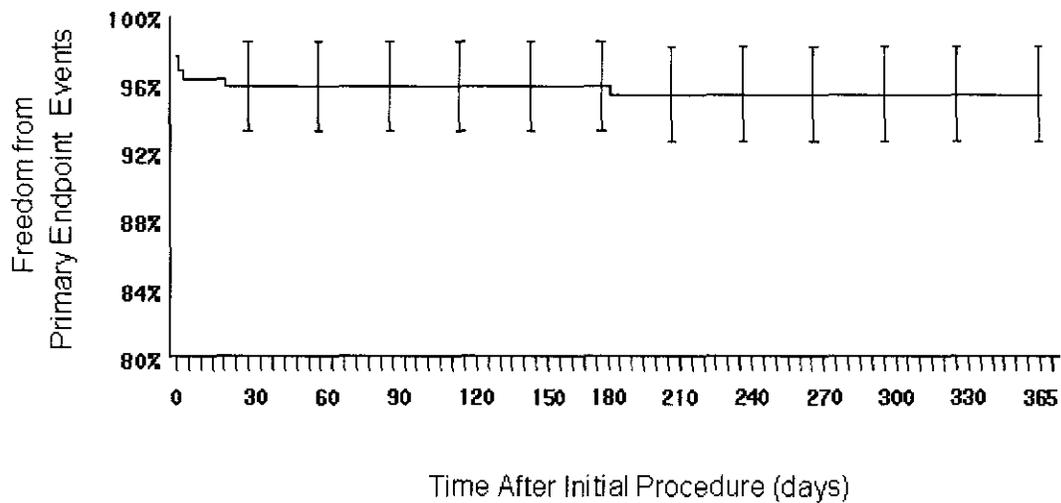
Censored: The number of patients who prematurely withdrew without an event in the interval

Incomplete: The number of patients who died in the interval without event

Events: The number of patients with event in the interval

Cumulative % Event-Free: Kaplan-Meier estimate of percentage of patients without an event at the end of the specified interval

SE: Kaplan-Meier estimate of standard error



11.0 CONCLUSIONS DRAWN FROM CLINICAL STUDIES

Pre-clinical studies indicate that the Exponent® Self-Expanding Carotid Stent with OTW and RX Delivery Systems meet or exceed safety and performance specifications. The Exponent® Self-Expanding Carotid Stent with RX Delivery System is expected to perform similarly to the OTW stent system in clinical use based on similarities in design and non-clinical performance between the two systems. The multi-center clinical studies indicate that the Exponent® Self-Expanding Carotid Stent with OTW Delivery System, used with the GuardWire® Temporary Occlusion and Aspiration System, is safe and effective as a treatment for carotid artery disease in the population indicated.

Results from the pre-clinical and clinical evaluations provide valid scientific evidence and reasonable assurance that the devices are safe and effective when used in accordance with their labeling.

12.0 PANEL RECOMMENDATION

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

13.0 CDRH DECISION

FDA issued an approval order on October 23, 2007. The conditions of approval require a post-approval study of 1,500 new patients to be evaluated at 30 days and 365 days post-procedure, as well as the continued follow-up of the existing cohort of patients from the MAVERIC II study for a total of three years. The results of these studies will be evaluated to determine whether any changes should be made to the device labeling to ensure that the information available to physicians is complete, appropriate, and up-to-date.

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

14.0 APPROVAL SPECIFICATIONS

Instructions for Use: See labeling.

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

Post-Approval Requirements and Restrictions: See approval order.