

## Summary of Safety and Effectiveness Data

### 1. General Information

Device Generic Name: Carotid Stent with Delivery System

Device Trade Name: Carotid WALLSTENT® Monorail® Endoprosthesis  
(Hereafter referred to as Carotid WALLSTENT Endoprosthesis)

Applicant's Name and Address: Boston Scientific Corporation  
2011 Stierlin Court  
Mountain View, CA 94043-4655  
USA

PMA Number: P050019

Date of Panel Recommendation: None

Date of Notice of Approval to the Applicant: October 23, 2008

### 2. Indications for Use

The Carotid WALLSTENT Endoprosthesis, used in conjunction with the Boston Scientific embolic protection system, is indicated for the treatment of patients at high risk for adverse events from carotid endarterectomy due to either anatomic or comorbid conditions who require carotid revascularization in the treatment of ipsilateral or bilateral carotid artery disease and meet the criteria outlined below:

- Patients with neurological symptoms and  $\geq 50\%$  stenosis of the common, internal carotid artery and/or the bifurcation by ultrasound or angiogram **OR** patients without neurological symptoms and  $\geq 80\%$  stenosis of the common, internal carotid artery and/or the bifurcation by ultrasound or angiogram, **AND**
- Patients must have a reference vessel diameter within the range of 4.0 mm and 9.0 mm at the target lesion.

### 3. Contraindications

The Carotid WALLSTENT Endoprosthesis 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 system or stent system

- Patients with uncorrected bleeding disorders
- Lesions in the ostium of the common carotid artery

#### **4. Warnings and Precautions**

Warnings and Precautions can be found in the Carotid WALLSTENT Endoprosthesis Directions for Use.

#### **5. Device Description**

The Carotid WALLSTENT Endoprosthesis is a self-expanding stent composed of biomedical DFT (Drawn Filled Tubing) alloy monofilament wires braided in a tubular mesh configuration. The wires are manufactured from a biomedical grade cobalt-chromium-iron-nickel-molybdenum alloy (commonly known as Elgiloy<sup>®</sup> or Conichrome) containing an enhanced radiopaque tantalum core. The device has two components: the stent and the stent delivery system. The stent is pre-loaded on the delivery system. During the procedure, the delivery system is delivered over an endovascular guidewire to the target vessel, where the stent is then deployed.

The Monorail delivery system consists of two coaxially arranged shafts: an inner shaft made of stainless steel proximally and thermoplast distally, and an outer sheath made of thermoplast. The central lumen within the inner shaft continues to the distal tip and accepts a 0.014 in. guide wire, which exits the inner lumen through two guide wire holes. Two radiopaque markers on the inner shaft and one radiopaque marker on the retractable outer sheath are used to facilitate stent placement.

The Carotid WALLSTENT Endoprosthesis is pre-loaded on the stent carrier located on the distal segment of the inner shaft. The distal end of the outer sheath covers the Carotid WALLSTENT Endoprosthesis and is used to deploy the stent during the interventional procedure. The proximal end of the Carotid WALLSTENT Endoprosthesis is firmly held on the inner shaft with a holding mechanism, which enables a partially deployed Carotid WALLSTENT Endoprosthesis (up to 50%) to be reconstrained and repositioned in emergency situations.

The available device sizes are provided in Table 1. Two sets of implanted diameters and lengths are provided for the 8 mm and 10 mm stent sizes because these stent models can be used to treat multiple vessel sizes. Due to the design of the stent, the stent length decreases as the diameter expands.

**Table 1. Carotid WALLSTENT Endoprosthesis Stent Sizes and Sizing**

Catalog Number	Stent						Delivery Catheter		Compatibility	
	* Fully Open Diameter	* Fully Open Length	Implanted Diameter	Implanted Length	Implanted Diameter	Implanted Length	Outer Diameter	Working Length	Guiding Sheath Minimum ID	Guiding Catheter Minimum ID
	(mm)	(mm)	(mm)	(mm)	(mm)	(mm)	(F / mm)	(cm)	(F / inches)	(F / inches)
71-900	6	22	5	30	4	36	5.0 / 1.67	135	5 / 0.073	7 / 0.073
71-901	8	21	7	30	6	36	5.0 / 1.67	135	5 / 0.073	7 / 0.073
71-902	8	29	7	40	6	48	5.0 / 1.67	135	5 / 0.073	7 / 0.073
71-903	8	36	7	50	6	62	5.0 / 1.67	135	5 / 0.073	7 / 0.073
71-904	10	24	9	30	8	36	5.9 / 1.97	135	6 / 0.086	8 / 0.086
71-905	10	31	9	40	8	49	5.9 / 1.97	135	6 / 0.086	8 / 0.086
71-906	10	37	9	50	8	59	5.9 / 1.97	135	6 / 0.086	8 / 0.086

\* Fully opened stent diameter selected should be 1-2mm larger than nominal vessel diameter.

## 6. Alternative Practices and Procedures

Treatment options for carotid artery disease (CAD) include lifestyle modifications, medical therapy, surgery, and carotid stenting procedures with FDA approved stents and embolic protection systems. Lifestyle modifications are aimed at reducing stroke risk factors such as cigarette smoking and alcohol use. Medical therapy includes use of antiplatelet and/or anticoagulant medicine, such as aspirin, Plavix<sup>®</sup> (clopidogrel), Ticlid<sup>®</sup> (ticlopidine), and Coumadin<sup>®</sup> (warfarin), as well as antihypertensive and antilipidemic drugs. The primary treatment for CAD is carotid endarterectomy, surgical removal of plaque from the affected artery.

## 7. Marketing History

The Carotid WALLSTENT Endoprosthesis has been commercially available in Europe since February 2000, and it is also available in Canada, Australia, South Africa, Mexico, China, India, Egypt, Philippines, Yugoslavia and Greece. The device has not been withdrawn from marketing for any reason relating to the safety and effectiveness of the device.

## 8. Potential Adverse Effects of the Device on Health

### 8.1 Observed Adverse Effects

BEACH (Boston Scientific EPI: A Carotid Stenting Trial for High-Risk Surgical Patients) was a prospective, single-arm, multi-center trial to evaluate the safety and efficacy of the Carotid WALLSTENT Endoprosthesis in conjunction with the FilterWire EX<sup>®</sup>/FilterWire EZ<sup>™</sup> Embolic Protection System to treat surgical high-risk, symptomatic and asymptomatic patients with disease in the carotid artery. The primary objective of the trial was to show equivalence (non-inferiority) between carotid stenting and a historical control, based upon the one-year morbidity and mortality rate including non Q-wave myocardial infarction (MI) to 24 hours; death, stroke, and Q-wave MI through 30 days; and ipsilateral stroke and neurological death from 31 to 360 days. A total of 747 patients were enrolled in the trial: 189 roll-in patients, 480 pivotal patients and 78 bilateral registry patients.

Tables 2 and 3 present the serious adverse events reported in the BEACH trial. A serious adverse event (SAE) may or may not be considered related to the device and may be described as follows:

- Death due to any cause
- Life-threatening condition, (e.g., stroke)
- Persistent or significant disability/incapacity
- Any event resulting in an unscheduled in-patient hospitalization or prolongation of existing hospitalization >72 hours post index procedure

- Any event requiring intervention, except for comorbid scheduled events, which are scheduled and planned during the follow-up period
- Congenital abnormality or birth defect

The events have been coded using the Medical Dictionary for Regulatory Activities (MedDRA™) version 5.0 and are presented by System Organ Class and Preferred Term as follows:

- BLOOD AND LYMPHATIC SYSTEM DISORDERS include events such as anemia and thrombocythemia.
- CARDIAC DISORDERS include events such as angina, arrhythmias, congestive cardiac failure and myocardial infarction.
- GASTROINTESTINAL DISORDERS include events such as gastric ulcer, gastrointestinal hemorrhage, intestinal obstruction, nausea and retroperitoneal hemorrhage.
- GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS include events such as chest pain, death, fall, pyrexia, and weakness.
- HEPATOBILIARY DISORDERS include events such as cholithiasis and gallbladder disorders.
- INFECTIONS AND INFESTATIONS include events such as pneumonia, sepsis and urinary tract infection.
- INJURY, POISONING AND PROCEDURAL COMPLICATIONS include events such as fracture and stent occlusion.
- INVESTIGATIONS include events such as blood creatinine increased, cardiac troponin increased and neurological examination abnormal.
- METABOLISM AND NUTRITION DISORDERS include events such as dehydration and hyperglycemia.
- MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS include events such as arthritis and pain.
- NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCLUDING CYSTS AND POLYPS) include events such as carcinoma and biliary/colon neoplasms.
- NERVOUS SYSTEM DISORDERS include events such as cerebral hemorrhage, cerebrovascular accident, convulsions, dizziness, syncope and transient ischemic attack.
- PSYCHIATRIC DISORDERS include events such as confusion, depression and mental status changes.
- RENAL AND URINARY DISORDERS include events such as renal failure and impairment.

- REPRODUCTIVE SYSTEM AND BREAST DISORDERS include events such as vaginal hemorrhage.
- RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS include events such as chronic obstructive airway disease, dyspnea, pulmonary embolism and respiratory failure.
- SKIN AND SUBCUTANEOUS TISSUE DISORDERS include events such as skin ulcer.
- SURGICAL AND MEDICAL PROCEDURES include events such as aortic valve replacement, carotid endarterectomy, coronary artery surgery and revascularization, and hip arthroplasty.
- VASCULAR DISORDERS include events such as deep venous thrombosis, hematoma, hemorrhage, hypertension, hypotension, peripheral revascularization and vascular pseudoaneurysm.

Tables 2 and 3 include all serious adverse events, regardless of device or procedure relatedness. The tables may also include events that were secondary to a primary event. In addition, Table 4 presents all deaths, regardless of device or procedure relatedness.

**Table 2. BEACH Trial SAEs, ≤ 30 Days**

System Organ Class/Preferred Term	≤ 30 Days	
	Events	Pivotal (N=480)
<b>ANY SAE</b>	<b>220</b>	<b>113 (23.5%)</b>
<b>BLOOD AND LYMPHATIC SYSTEM DISORDERS</b>	<b>12</b>	<b>12 (2.5%)</b>
Anemia Not Otherwise Specified	12	12 (2.5%)
<b>CARDIAC DISORDERS</b>	<b>31</b>	<b>23 (4.8%)</b>
Angina Pectoris	6	6 (1.3%)
Angina Unstable	0	0 (0.0%)
Arrhythmia Not Otherwise Specified	0	0 (0.0%)
Bradycardia Not Otherwise Specified	4	4 (0.8%)
Cardiac Arrest	2	2 (0.4%)
Cardiac Failure Congestive	2	2 (0.4%)
Coronary Artery Disease Not Otherwise Specified	1	1 (0.2%)
Myocardial Infarction	6	6 (1.3%)
Other Cardiac Disorders	10	9 (1.9%)
<b>GASTROINTESTINAL DISORDERS</b>	<b>17</b>	<b>13 (2.7%)</b>
Gastrointestinal Hemorrhage Not Otherwise Specified	6	5 (1.0%)
Retroperitoneal Hemorrhage	4	4 (0.8%)
Other Gastrointestinal Disorders	7	4 (0.8%)
<b>GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS</b>	<b>10</b>	<b>10 (2.1%)</b>
Death Not Otherwise Specified	7	7 (1.5%)
Other General Disorders and Administration Site Conditions	3	3 (0.6%)
<b>HEPATOBIILIARY DISORDERS</b>	<b>0</b>	<b>0 (0.0%)</b>
<b>INFECTIONS AND INFESTATIONS</b>	<b>11</b>	<b>9 (1.9%)</b>
Post Procedural Site Wound Infection	0	0 (0.0%)

System Organ Class/Preferred Term	≤ 30 Days	
	Events	Pivotal (N=480)
Wound Infection	0	0 (0.0%)
Other Infections and Infestations	11	9 (1.9%)
<b>INJURY, POISONING AND PROCEDURAL COMPLICATIONS</b>	<b>1</b>	<b>1 (0.2%)</b>
Stent Occlusion	0	0 (0.0%)
Other Injury, Poisoning and Procedural Complications	1	1 (0.2%)
<b>INVESTIGATIONS</b>	<b>1</b>	<b>1 (0.2%)</b>
<b>METABOLISM AND NUTRITION DISORDERS</b>	<b>3</b>	<b>2 (0.4%)</b>
<b>MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS</b>	<b>1</b>	<b>1 (0.2%)</b>
<b>NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCLUDING CYSTS AND POLYPS)</b>	<b>0</b>	<b>0 (0.0%)</b>
<b>NERVOUS SYSTEM DISORDERS</b>	<b>55</b>	<b>45 (9.4%)</b>
Carotid Artery Dissection	2	2 (0.4%)
Carotid Artery Occlusion	3	3 (0.6%)
Carotid Artery Stenosis	0	0 (0.0%)
Cerebral Hemorrhage	1	1 (0.2%)
Cerebrovascular Accident	19	19 (4.0%)
Transient Ischemic Attack	16	16 (3.3%)
Vasovagal Attack	1	1 (0.2%)
Other Nervous System Disorders	13	12 (2.5%)
<b>PSYCHIATRIC DISORDERS</b>	<b>4</b>	<b>3 (0.6%)</b>
<b>RENAL AND URINARY DISORDERS</b>	<b>10</b>	<b>10 (2.1%)</b>
<b>REPRODUCTIVE SYSTEM AND BREAST DISORDERS</b>	<b>1</b>	<b>1 (0.2%)</b>
<b>RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS</b>	<b>9</b>	<b>7 (1.5%)</b>
<b>SKIN AND SUBCUTANEOUS TISSUE DISORDERS</b>	<b>0</b>	<b>0 (0.0%)</b>
<b>SURGICAL AND MEDICAL PROCEDURES</b>	<b>19</b>	<b>18 (3.8%)</b>
Carotid Endarterectomy	0	0 (0.0%)
Other Surgical and Medical Procedures	19	18 (3.8%)
<b>VASCULAR DISORDERS</b>	<b>35</b>	<b>28 (5.8%)</b>
Hematoma Not Otherwise Specified	10	10 (2.1%)
Hemorrhage Not Otherwise Specified	3	3 (0.6%)
Hypotension Aggravated	1	1 (0.2%)
Hypotension Not Otherwise Specified	11	11 (2.3%)
Vascular Pseudoaneurysm	2	2 (0.4%)
Other Vascular Disorders	8	8 (1.7%)

**Table 3. BEACH Trial SAEs, Up to 360 Days**

System Organ Class/Preferred Term	31 – 360 Days		0 – 360 Days	
	Events	Pivotal (N=471)	Events	Pivotal (N=480)
<b>ANY SAE</b>	<b>448</b>	<b>183 (38.9%)</b>	<b>668</b>	<b>252 (52.5%)</b>
<b>BLOOD AND LYMPHATIC SYSTEM DISORDERS</b>	<b>14</b>	<b>13 (2.8%)</b>	<b>26</b>	<b>23 (4.8%)</b>
<b>CARDIAC DISORDERS</b>	<b>77</b>	<b>50 (10.6%)</b>	<b>108</b>	<b>69 (14.4%)</b>
Angina Pectoris	17	11 (2.3%)	23	16 (3.3%)
Angina Unstable	3	3 (0.6%)	3	3 (0.6%)

System Organ Class/Preferred Term	31 – 360 Days		0 – 360 Days	
	Events	Pivotal (N=471)	Events	Pivotal (N=480)
Cardiac Arrest	3	3 (0.6%)	5	5 (1.0%)
Cardiac Failure Congestive	21	16 (3.4%)	23	17 (3.5%)
Coronary Artery Disease Not Otherwise Specified	0	0 (0.0%)	1	1 (0.2%)
Myocardial Infarction	16	14 (3.0%)	22	20 (4.2%)
Other Cardiac Disorders	17	14 (3.0%)	31	24 (5.0%)
<b>GASTROINTESTINAL DISORDERS</b>	<b>24</b>	<b>20 (4.2%)</b>	<b>41</b>	<b>32 (6.7%)</b>
<b>GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS</b>	<b>36</b>	<b>34 (7.2%)</b>	<b>46</b>	<b>43 (9.0%)</b>
Death Not Otherwise Specified	29	29 (6.2%)	36	36 (7.5%)
Other General Disorders and Administration Site Conditions	7	6 (1.3%)	10	8 (1.7%)
<b>HEPATOBIILIARY DISORDERS</b>	<b>3</b>	<b>3 (0.6%)</b>	<b>3</b>	<b>3 (0.6%)</b>
<b>INFECTIONS AND INFESTATIONS</b>	<b>37</b>	<b>26 (5.5%)</b>	<b>48</b>	<b>35 (7.3%)</b>
<b>INJURY, POISONING AND PROCEDURAL COMPLICATIONS</b>	<b>9</b>	<b>8 (1.7%)</b>	<b>10</b>	<b>9 (1.9%)</b>
Stent Occlusion	1	1 (0.2%)	1	1 (0.2%)
Other Injury, Poisoning and Procedural Complications	8	7 (1.5%)	9	8 (1.7%)
<b>INVESTIGATIONS</b>	<b>4</b>	<b>4 (0.8%)</b>	<b>5</b>	<b>5 (1.0%)</b>
<b>METABOLISM AND NUTRITION DISORDERS</b>	<b>5</b>	<b>5 (1.1%)</b>	<b>8</b>	<b>7 (1.5%)</b>
<b>MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS</b>	<b>3</b>	<b>3 (0.6%)</b>	<b>4</b>	<b>3 (0.6%)</b>
<b>NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)</b>	<b>8</b>	<b>8 (1.7%)</b>	<b>8</b>	<b>8 (1.7%)</b>
<b>NERVOUS SYSTEM DISORDERS</b>	<b>43</b>	<b>33 (7.0%)</b>	<b>98</b>	<b>75 (15.6%)</b>
Carotid Artery Occlusion	0	0 (0.0%)	3	3 (0.6%)
Carotid Artery Stenosis	0	0 (0.0%)	0	0 (0.0%)
Cerebral Hemorrhage	3	3 (0.6%)	4	4 (0.8%)
Cerebrovascular Accident	20	20 (4.2%)	39	38 (7.9%)
Transient Ischemic Attack	8	8 (1.7%)	24	24 (5.0%)
Other Nervous System Disorders	12	9 (1.9%)	28	22 (4.6%)
<b>PSYCHIATRIC DISORDERS</b>	<b>7</b>	<b>7 (1.5%)</b>	<b>11</b>	<b>9 (1.9%)</b>
<b>RENAL AND URINARY DISORDERS</b>	<b>12</b>	<b>12 (2.5%)</b>	<b>22</b>	<b>22 (4.6%)</b>
<b>REPRODUCTIVE SYSTEM AND BREAST DISORDERS</b>	<b>0</b>	<b>0 (0.0%)</b>	<b>1</b>	<b>1 (0.2%)</b>
<b>RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS</b>	<b>28</b>	<b>24 (5.1%)</b>	<b>37</b>	<b>29 (6.0%)</b>
<b>SKIN AND SUBCUTANEOUS TISSUE DISORDERS</b>	<b>1</b>	<b>1 (0.2%)</b>	<b>1</b>	<b>1 (0.2%)</b>
<b>SURGICAL AND MEDICAL PROCEDURES</b>	<b>74</b>	<b>59 (12.5%)</b>	<b>93</b>	<b>73 (15.2%)</b>
Carotid Endarterectomy	2	2 (0.4%)	2	2 (0.4%)
Other Surgical and Medical Procedures	72	57 (12.1%)	91	71 (14.8%)
<b>VASCULAR DISORDERS</b>	<b>63</b>	<b>49 (10.4%)</b>	<b>98</b>	<b>77 (16.0%)</b>

Table 4. Causes of Death

Death (by type)	0-30 Days	31-360 Days
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	(N=480)		(N=471)	
	n	%	n	%
Neurologic	2	0.4	7	1.5
Cardiac	3	0.6	8	1.7
General	2	0.4	7	1.5
Respiratory/Pulmonary	0	0.0	5	1.1
Infectious/Inflammatory	0	0.0	2	0.4

## 8.2 Potential Adverse Events

Based on the literature, and on clinical and commercial experience with carotid stents and embolic protection systems, potential adverse events include, but are not limited to:

- Acute occlusion of the stented artery
- Allergic reactions to antiplatelet agents / contrast medium
- Aneurysm
- Angina / coronary ischemia
- Arrhythmia
- Arterial occlusion / thrombosis at puncture site or remote site
- Arteriovenous fistula
- Bacteremia or septicemia
- Bleeding or hematoma from anticoagulant or antiplatelet medications
- Bradycardia
- Cerebral vascular event such as edema or hemorrhage
- Cerebral ischemia / transient ischemic attack (TIA)
- Congestive heart failure (CHF)
- Death
- Detachment and/or implantation of a component of the system
- Dissection, intimal flap, perforation or rupture
- Emboli, distal (air, tissue or thrombotic emboli)
- Carotid endarterectomy (CEA) surgery
- Fever
- Filter thrombosis / occlusion
- Groin hematoma, with or without surgical repair
- Hemorrhage, with or without transfusion
- Hyperperfusion syndrome
- Hypotension / hypertension
- Hypotonia
- Infection and pain at insertion site
- Ischemia / infarction of tissue or organ
- Insufficient anchoring or possible intimal trauma due to inadequate Carotid WALLSTENT Endoprosthesis selection
- Myocardial Infarction (MI)
- Pain (head, neck)

- Perforation or rupture of the stented artery
- Pseudoaneurysm at catheterization site
- Occlusion of carotid artery
- Renal failure / insufficiency
- Restenosis of stented segment
- Seizure
- Severe unilateral headache
- Stent embolization
- Stent / filter entanglement or damage
- Stent migration
- Stent misplacement
- Stent thrombosis / occlusion
- Stroke / cerebrovascular accident (CVA)
- Vessel spasm or recoil

**9. Summary of Pre-Clinical Studies**

**9.1 In Vitro Testing**

Boston Scientific has conducted in vitro testing to verify that the Carotid WALLSTENT Endoprosthesis meets performance specifications as specified by and in compliance with the following documents and standards:

- Carotid WALLSTENT Monorail Endoprosthesis Product Specification
- CDRH guidance, Guidance for Industry and FDA Staff, Non-Clinical Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems, issued January 13, 2005 (<http://www.fda.gov/cdrh/ode/guidance/1545.pdf>)

The Carotid WALLSTENT Endoprosthesis materials and design have been subjected to chemical, mechanical, dimensional, analytical, stress, and fatigue analysis. The stent and its delivery system have undergone performance testing. Data resulted from a combination of vendor testing (chemical analysis), analytical modeling, and in vitro bench testing. Table 5 summarizes the tests / characterizations that were performed in accordance with the referenced CDRH Guidance document. Requirements and tests for balloon-expandable or covered stents were not included in the summary table since they are not applicable to the Carotid WALLSTENT Endoprosthesis. The test results demonstrate that the Carotid WALLSTENT Endoprosthesis meets performance specifications under clinically relevant conditions.

**Table 5. Summary of the Carotid WALLSTENT Endoprosthesis In Vitro Testing**

In Vitro Test	Significance/ Relevant Functional Requirement	Summary of Tests/Results
<b>Stent Material Characterization</b>		

In Vitro Test	Significance/ Relevant Functional Requirement	Summary of Tests/Results
Stent Material Composition	<p>Integrity and suitability of metal wire for implant.</p> <p>Baseline for evaluation of the effects of future changes in materials.</p>	<p>Certificates of Conformance accompanying each lot of incoming stent wire are verified for conformance to the material specification, providing assurance that the mechanical and chemical properties of the stent material will be consistent.</p>
Stent Corrosion Resistance	<p>Corrosion can cause or contribute to premature stent failure.</p> <p>By-products may be toxic or cause other adverse biological and tissue responses.</p>	<p>Potential dynamic polarization testing of fine wire and WALLSTENT samples resulted in no observed pitting and high re-passivation potentials. Scanning electron microscopic examination of the surfaces of Carotid WALLSTENT Endoprostheses from accelerated durability testing as well as stent material coupons previously implanted in vivo at 750X magnification did not result in any evidence of fretting or galvanic corrosion. These results demonstrate that the Carotid WALLSTENT Endoprosthesis is resistant to corrosion and galvanically stable.</p>
<b>Stent Dimensional and Functional Attributes</b>		
Dimensional Verification	<p>Accurate stent dimensions assist in proper stent sizing and accurate placement.</p> <p>Stent dimensions affect the functional behavior of the stent.</p>	<p>The unconstrained stent diameter and length and the length of the stent when constrained on the delivery catheter were measured. The uniformity of stent expansion was also evaluated by measuring the stent diameter at multiple locations after deployment. The results show that these dimensions conform to the established device specifications.</p>
Percent Surface Area of Stent	<p>The area over which a stent contacts a vessel may affect the biological response of the vessel.</p> <p>The free area may influence tissue prolapse or ingrowth.</p>	<p>Data were derived through analytical modeling. The percent stent surface area did not vary significantly with stent length, nor did it vary more than 3% across all indicated stent diameters. These results for percent surface area met the device specifications.</p>
Foreshortening	<p>Foreshortening influences final stent length. Knowledge of foreshortening characteristics aids in proper stent length selection and proper placement.</p>	<p>An analytical model was used to calculate the percent foreshortening for the unconstrained diameter and the labeled/indicated implant diameters. The lengths of all stents at unconstrained and implanted diameters met the device specifications. These results demonstrate that the extent of foreshortening is acceptable and predictable.</p>
Stent Integrity	<p>Stent defect, whether a result of manufacturing flaws or subsequent damage, can contribute to clinical complications.</p>	<p>Data collected during 100% inspection of devices showed zero incidents of failure. No cracks, fractures, breaks or corrosion were detected via optical and SEM analysis on samples subjected to accelerated durability testing, indicating acceptable surface integrity.</p>
Radial Force	<p>Radial force characterizes the ability of the stent to</p>	<p>The radial force was calculated through analytical modeling and verified against</p>

In Vitro Test	Significance/ Relevant Functional Requirement	Summary of Tests/Results
	resist collapse under short-term or long-term external loads.	experimental test values. The analysis demonstrated that radial force was 1 - 4 N for all stent sizes at the labeled/indicated diameters, meeting the established acceptance criteria. The results demonstrate that the Carotid WALLSTENT Endoprosthesis possesses sufficient radial strength.
Stress and Fatigue Analysis	Stress analysis, combined with fatigue analysis and accelerated durability testing, provides an indication of device durability.	Stress characteristics of the stent under worst-case physiological loading conditions were predicted by means of analytical modeling. All stent sizes and labeled diameters displayed safety factors greater than 12, indicating sufficient safety margins within their respective safe stress regions under static and dynamic conditions.
Accelerated Durability Testing	Accelerated durability testing evaluates failure modes such as fretting, abrasion, and wear. This can help in the identification of device conditions and manufacturing not modeled using analytical or computational methods.	Stents representing worst-cases for fatigue life were subjected to 400 million pulsatile cycles at a frequency of 60Hz and magnitudes of 3.87 – 4.05% to simulate more than 10 years of equivalent implanted life. Following pulsatile fatigue testing, stents were examined with an optical microscope and with Scanning Electron Microscopy. No wire breaks were observed. Significant wear was observed between stent wires, specifically at the flared ends of the device. However, this amount of wear is believed to be due to the concentration of mechanical forces at these locations, which is not likely to occur in vivo. The tests results demonstrate satisfactory durability of the Carotid WALLSTENT Endoprosthesis under simulated pulsatile loading conditions.
Magnetic Resonance Imaging	MRI of patients with a stent may experience tissue damage resulting from: <ul style="list-style-type: none"> <li>- Heating of implant</li> <li>- Movement of implant</li> <li>- Inappropriate treatment resulting from imaging difficulties</li> </ul>	MRI compatibility of the Carotid WALLSTENT Endoprosthesis was evaluated at 3 Tesla with the exception of image artifact, which was evaluated at 1.5 Tesla. The maximum temperature rise for a single stent was 1.03°C and for overlapping stents was 1.72°C at an extrapolated whole body averaged specific absorption rate (SAR) of 2.0W/kg. The maximum magnetically induced angular deflection was 11°, equating to a displacement force of 0.046 mN. No magnetically induced torque was observed at any stent position. No imaging artifacts were observed. These results demonstrate that the Carotid WALLSTENT Endoprosthesis is sufficiently MRI compatible.
Radiopacity	Stent visibility using angiographic or radiographic imaging or	A qualitative indication of the visibility of the stent was examined during thirty (30) actual clinical procedures. Marker visibility was

In Vitro Test	Significance/ Relevant Functional Requirement	Summary of Tests/Results
	both generally assures proper stent placement and allows follow-up and secondary treatment.	rated "Excellent" in 18 cases; "Good" in 10 cases; and "Average" in 2 cases, indicating that the Carotid WALLSTENT Endoprosthesis is sufficiently visible under fluoroscopy.
Crush Resistance	Peripheral stents may experience external, non-cardiac focal, or distributed loads that could cause stent deformation and, possibly, adverse clinical consequence.	Analytical modeling demonstrates that the Carotid WALLSTENT Endoprosthesis will not incur permanent deformation or collapse under loads that may be encountered after implantation in the carotid artery. These results indicate that the Carotid WALLSTENT Endoprosthesis is resistant to crushing and permanent deformation.
Kink Resistance	Peripheral stents used in some anatomic locations bend during normal body motion, such as knee flexion. Bends could cause stent deformation and possible adverse clinical consequences.	Stent ends were bent to form a loop until a kink was observed, and the radius of this bend was determined. Kink radii of 0.5 – 1 mm were observed. These results demonstrate that the Carotid WALLSTENT Endoprosthesis is sufficiently resistant to kinking under clinical conditions.
<b>Delivery System Dimensional and Functional Attributes</b>		
Simulated Use	Safe and reliable delivery of the stent to the intended location according to the instruction for use without damage to the stent.	Samples were subjected to assessment of trackability/pushability, kink resistance, stent deployment/recapture, closing force without a stent, and freedom from leakage using a test apparatus simulating the appropriate vascular pathway. All devices were tracked to the target location without excessive buckling. All samples tracked across a 0.6" radius of curvature without kinking. Deployment, recapture, and closing forces were all below 15 N. No catheter leakage was observed within 30 seconds at 200 – 320 kPa pressure. The test results suggest acceptable performance of the stent delivery system.
Shelf Life	Safe and reliable delivery of the stent to the intended location according to the instruction for use without damage to the stent.	The delivery system tensile strength and delivery, deployment, and retraction characteristics of accelerated-aged samples, conditioned at 55°C for 164 days, were evaluated. The results confirm a product shelf life of 3.5 years (plus 1 month).
Catheter Bond Strength	Failure of bonds in the delivery catheter could lead to device failure and clinical complications.	Longitudinal tensile testing of key bonds in the Carotid WALLSTENT Endoprosthesis delivery system resulted in satisfactory tensile strength values for each bond. These results suggest that the Carotid WALLSTENT Endoprosthesis delivery system possesses adequate tensile strength.
Crossing Profile	Stent delivery system crossing profile influences the device's ability to cross	The crossing profile of the Carotid WALLSTENT Endoprosthesis system was measured by pulling the device through a

In Vitro Test	Significance/ Relevant Functional Requirement	Summary of Tests/Results
	lesions.	block with a known profile. The maximum stent system outer diameter was below 5.0 F for the 6 mm and 8 mm systems and below 5.9 for the 10 mm systems. These results demonstrate that the stent system possesses a sufficiently low crossing profile.

## 9.2 In Vivo Testing

Numerous acute and chronic animal studies, in a variety of vessel beds, have been conducted on the WALLSTENT product line. Historical information (1984 to 2003) includes studies conducted by the original designer and manufacturer of the WALLSTENT and preclinical animal data from the literature. The historical preclinical animal studies primarily focused on the inflammatory response, procedural techniques and the overall safety of the WALLSTENT in vivo. Even though a number of the historical studies were performed as long as 20 years ago, they remain relevant, as the stents evaluated in these studies are representative of the subject Carotid WALLSTENT Monorail Endoprosthesis in regards to design and materials.

Table 6 provides a summary of the key studies conducted by the original designer and manufacturer of the WALLSTENT. In general, the results from the WALLSTENT preclinical animal studies have demonstrated minimal inflammatory changes at the stent implant sites. Healing at the stent site is characterized by remodeling of the vessel wall, first thickening and then decreasing and ultimately forming a near normal vessel wall diameter.

The literature cites investigations of the WALLSTENT in animal models beginning in the early 1980's by Maass, Duboucher, Sigwart, and Rousseau. This preliminary research provided models to evaluate the foreign body and healing responses of the implanted stents. More recently, two articles were published evaluating different self-expanding stents, including the WALLSTENT, in the carotid arteries of a canine model. A summary of the historical and more recent literature references is provided in Table 7.

The abundance of historical information in combination with the animal studies

**Table 6. Summary of WALLSTENT® In Vivo Testing**

Study	<b>Protocol</b> <ul style="list-style-type: none"> <li>• # Animals</li> <li>• Follow-up</li> <li>• # WALLSTENTS</li> <li>• Implant Site(s)</li> </ul>	Relevant Findings
Endovascular WALLSTENT Prosthesis: Histologic and Morphologic Evaluation of Stent Deployment in the Canine Artery	<ul style="list-style-type: none"> <li>• 12 (canine)</li> <li>• 1, 3, 6, and 12 months</li> <li>• 12 WALLSTENTS</li> <li>• Femoral and popliteal arteries</li> </ul>	At 12 months, active inflammation was, for the most part, absent. No hemorrhage was found and intact endothelium was universally present.
Evaluation of the efficacy and arterial responses of an ePTFE-coated stent compared to the WALLSTENT	<ul style="list-style-type: none"> <li>• 8 (canine)</li> <li>• 30 and 60 days</li> <li>• 8 WALLSTENTS</li> <li>• Iliac/common femoral arteries</li> </ul>	All WALLSTENT devices were patent on explant; all iliac and one femoral coated stent were patent on explant.
Evaluation of the performance characteristics of a prototype abdominal aortic aneurysm endovascular prosthesis	<ul style="list-style-type: none"> <li>• 6 (ovine)</li> <li>• 4 weeks</li> <li>• 5 WALLSTENTS</li> <li>• Infrarenal abdominal aorta</li> </ul>	There was slight to moderate neointimal proliferation proximal to, within and distal to the aneurysms. Only 2 animals had substantial filling of the aneurysms around the WALLSTENT.
Evaluation of the safety, efficacy and tissue response of a PET-coated stent compared to the WALLSTENT	<ul style="list-style-type: none"> <li>• 13 (porcine)</li> <li>• 6-10 weeks</li> <li>• 5 WALLSTENTS</li> <li>• Transjugular intrahepatic portosystemic shunts</li> </ul>	The patency of the 2 stents proved equivalent; in contrast to the WALLSTENT, endothelialization of the luminal surface of the PET-coated stent occurred.
Performance evaluation of 2 prototype stents (PET, ePTFE) as compared to the WALLSTENT	<ul style="list-style-type: none"> <li>• 12 (canine)</li> <li>• 30, 90, and 180 days</li> <li>• 5 WALLSTENTS</li> <li>• Common iliac</li> </ul>	Minimal differences were noted between the 3 stents in any reactions within the tunica adventitia, the WALLSTENT resulted in the least diminution of luminal area, and the PET-coated stent caused the greatest inflammatory reaction. All WALLSTENT devices remained patent. No difficulties were noted during the placement of the WALLSTENT.

performed by the original manufacturer, as well as the recent literature references discussed above, provide a substantial body of evidence regarding the safety of the WALLSTENT in various vessel beds including the carotid artery. Therefore, no additional in vivo testing was conducted by Boston Scientific in support of this PMA.

**Table 7. Summary of Literature -WALLSTENT® In Vivo Testing**

Author (Year)	<b>Protocol</b> <ul style="list-style-type: none"> <li>• # Animals</li> <li>• Max. Follow-up</li> <li>• # Stents</li> <li>• Implant Site(s)</li> </ul>	Relevant Findings
Maass (1984)	<ul style="list-style-type: none"> <li>• 65 (canine) 5 (calf)</li> <li>• 24 months</li> <li>• 102 WALLSTENTS</li> <li>• Aorta</li> </ul>	Early in vivo studies using the WALLSTENT have provided extensive information on the healing response following stent implantation. Historical investigations have improved the physicians' ability to select the optimal vessels and stent sizes for stenting as well as demonstrate the importance of anticoagulant use.
Duboucher (1986) (unpublished report)	<ul style="list-style-type: none"> <li>• 6 (canine) 7 (sheep)</li> <li>• 3 months</li> <li>• 20 WALLSTENTS</li> <li>• Peripheral and coronary</li> </ul>	The early in vivo studies have also provided substantial evidence that the WALLSTENT induces minimal inflammatory change at the implant site. Following implantation, a series of vessel remodeling activities occur that result in reconstruction of the endothelial layer over the stent. During the first 4 to 6 weeks of this post-operative process, a gradual thickening of the vessel wall occurs. The wall eventually decreases in thickness and reaches a near normal level approximately 6 months post-implant.
Sigwart (1987)	<ul style="list-style-type: none"> <li>• 10 (canine)</li> <li>• 9 months</li> <li>• 15 WALLSTENTS</li> <li>• Peripheral and coronary</li> </ul>	These early in vivo studies also underscored the importance of anticoagulant therapy. Intra-operative doses of an anticoagulant (e.g., heparin) and an antiplatelet (e.g., aspirin), together with a similar post-operative drug protocol, appear to be important factors in preventing thrombotic sequelae.
Rousseau (1987)	<ul style="list-style-type: none"> <li>• 10 (sheep) 18 (canine)</li> <li>• 6 months</li> <li>• 47 WALLSTENTS</li> <li>• Iliac, femoral, axillary, renal, carotid, coronary</li> </ul>	No complications were noted during the implantation of the stents. At 4 months, all stents were widely patent and completely covered by endothelium. All stents showed similar low neointimal responses and the amount of neointimal hyperplasia did not differ between the normal-sized and oversized stents. The results of this study suggest that use of self-expanding stents in the carotid artery that are oversized by 30 to 40% appear to result in neointimal hyperplasia comparable to normal sized stents.
Rousseau (1989)	<ul style="list-style-type: none"> <li>• 34 (rabbit)</li> <li>• 6 months</li> <li>• 34 WALLSTENTS</li> <li>• Abdominal aorta</li> </ul>	At 6 months, there were no significant differences in residual luminal gains among the various stents. All patent stents had a smooth, glistening inner surface suggesting a complete covering of neointima. Histologic analysis of the neointima showed a uniform pattern of cellular and matrix contents in all four stent types. This study concluded that stent oversizing may be associated with acute vessel injury and thicker neointimal formation at 6 months. Other factors that affect neointimal hyperplasia may include stent material, design, and delivery systems. The luminal gains achieved from oversizing were offset by the neointimal response and all stents preserved arterial patency almost to the pre-stenting size.
Kirsch (2002)	<ul style="list-style-type: none"> <li>• 6 (canine)</li> <li>• 4 months</li> <li>• 8 WALLSTENTS and 16 stents from other manufacturers</li> <li>• Common carotid artery</li> </ul>	At 6 months, there were no significant differences in residual luminal gains among the various stents. All patent stents had a smooth, glistening inner surface suggesting a complete covering of neointima. Histologic analysis of the neointima showed a uniform pattern of cellular and matrix contents in all four stent types. This study concluded that stent oversizing may be associated with acute vessel injury and thicker neointimal formation at 6 months. Other factors that affect neointimal hyperplasia may include stent material, design, and delivery systems. The luminal gains achieved from oversizing were offset by the neointimal response and all stents preserved arterial patency almost to the pre-stenting size.
Cha (2003)	<ul style="list-style-type: none"> <li>• 11 (canine)</li> <li>• 6 months</li> <li>• 5 WALLSTENTS and 17 stents from other manufacturers</li> <li>• Common carotid artery</li> </ul>	At 6 months, there were no significant differences in residual luminal gains among the various stents. All patent stents had a smooth, glistening inner surface suggesting a complete covering of neointima. Histologic analysis of the neointima showed a uniform pattern of cellular and matrix contents in all four stent types. This study concluded that stent oversizing may be associated with acute vessel injury and thicker neointimal formation at 6 months. Other factors that affect neointimal hyperplasia may include stent material, design, and delivery systems. The luminal gains achieved from oversizing were offset by the neointimal response and all stents preserved arterial patency almost to the pre-stenting size.

### 9.3 Biocompatibility

The Carotid WALLSTENT Endoprosthesis was tested to determine the biocompatibility of the implantable stent and the delivery system. Biocompatibility testing was carried out according to the FDA Blue Book Memorandum #G95-1 dated July 1995 and entitled, 'Use of International Standard ISO 10993-1, Biological Evaluation of Medical Devices Part-1: Evaluation and Testing.' All tests were conducted on sterile, finished product and according to the requirements of Good Laboratory Practice for Nonclinical Laboratory Studies (21 CFR, Part 58). The sample size, surface area, sample preparation, and reference material comply with ISO 10993-12 (Biological evaluation of medical devices - Part 12: Sample preparation and reference materials).

Tests considered and performed on the device were appropriate according to the ISO 10993-1 (Biological Evaluation of Medical Devices – Part 1: Evaluation and Testing) classification of the device as an externally communicating device having contact with circulating blood for a limited exposure (<24 hours) (delivery system) and as an implant device with permanent blood contact (>30 days) (stent). In addition, testing for detectable latex according to ASTM D6499-03 (Standard Test Method for the Immunological Measurement of Antigenic Protein in Natural Rubber and its Products) was performed to comply with 21 CFR 801.437. Furthermore, testing was conducted to determine the presence of chemical residue according to USP <661> (Physicochemical Test for Plastics). Thrombogenicity, chronic toxicity, and carcinogenicity tests were not performed due to extensive clinical history of safe use and knowledge of the material as a non-health risk to the patient through exposure.

All testing yielded non-toxic and non-pyrogenic results. Therefore, the Carotid WALLSTENT Endoprosthesis is considered biocompatible for its intended use. In addition, the Carotid WALLSTENT Endoprosthesis contains no detectable latex and can be labeled accordingly.

Table 8 is a summary of biocompatibility testing and results.

**Table 8. Carotid WALLSTENT Endoprosthesis Biocompatibility Test Summary**

Name of Assay or Test	Test Build	Test Result
Cytotoxicity (MEM Elution)	Stent and Delivery System	Pass
Guinea Pig Maximization Sensitization Test	Stent and Delivery System	Pass
Intracutaneous Reactivity Test	Stent and Delivery System	Pass
Acute Systemic Injection Test	Stent and Delivery System	Pass
Material Mediated Rabbit Pyrogen	Stent and Delivery System	Pass
ASTM Hemolysis Assay	Stent and Delivery System	Pass
Partial Thromboplastin Time	Stent and Delivery System	Pass
Complement Activation	Stent and Delivery System	Pass
Subacute (14-Day) Intravenous Toxicity Study	Stent Only	Pass
Mouse Lymphoma Assay	Stent Only	Pass
Bacterial Mutagenicity/Ames Assay	Stent Only	Pass
ISO Intramuscular Implant Test	Stent Only	Pass
Latex Test (ASTM D6499-03)	Stent and Delivery System	Pass
USP Physicochemical Test for Plastics <USP 661>	Stent and Delivery System	Pass

#### 9.4 Sterilization

The Carotid WALLSTENT Endoprosthesis is sterilized by gamma radiation. Sterilization qualification conforms to the guidelines in the following standards:

- ISO/TR 13409, Sterilization of health care products – Radiation Sterilization – Substantiation of 25 kGy as a sterilization dose for small or infrequent production batches
- Sterilization validation AAMI Method 3

- ANSI/AAMI/ISO 11137, Sterilization of health care products—Requirements for validation and routine control—Radiation sterilization
- ISO/AAMI TIR 27, Sterilization of health care products—Radiation sterilization—Substantiation of 25 kGy as a sterilization dose,  $VD_{max}$  method

Pyrogenicity testing is performed according to the 1987 FDA document, "Guideline on Validation of the Limulus Amebocyte Lysate Test as an End-Product Endotoxin Test for Human and Animal Parenteral Drugs, Biological Products, and Medical Devices," and pyrogen levels of the end product must fall below the lower limits specified therein.

## 9.5 Packaging Verification and Shelf Life

The Carotid WALLSTENT Endoprosthesis packaging verification and a 3.5-year shelf life study were successfully completed using qualified test methods based on the following standards:

- ISTA 2A: Performance Test for Packaged-Products Weighing 150 lbs (68 kg) or Less
- ISTA 2E: Performance Test for Elongated Packaged-Products for Parcel Delivery System Shipment
- ASTM F 1980-02: Standard Guide for Accelerated Aging of Sterile Medical Device Packages
- ASTM F 1886-98: Standard Test Method for Determining Integrity of Seals for Medical Packaging by Visual Inspection
- ASTM F 88-00: Standard Test Method for Seal Strength of Flexible Barrier Materials
- ASTM F 1140-00: Standard Test Methods for Internal Pressurization Failure Resistance of Unrestrained Packages for Medical Applications
- ASTM F 1929-98: Standard Test Method for Detecting Seal Leaks in Porous Medical Packaging by Dye Penetration

## 9.6 Product Shelf Life

A 3.5-year product shelf life was established, based on accelerated aging studies.

## 10. Summary of Clinical Studies

BEACH, (Boston Scientific EPI: A Carotid Stenting Trial for High-Risk Surgical Patients), was a prospective, single-arm, multi-center trial to evaluate the safety and efficacy of the Carotid WALLSTENT Endoprosthesis in conjunction with the FilterWire EX<sup>®</sup>/FilterWire EZ<sup>™</sup> Embolic Protection System to treat surgical high-risk, symptomatic ( $\geq 50\%$  stenosis) and asymptomatic ( $\geq 80\%$  stenosis) patients with disease in the carotid artery. A trial design utilizing a roll-in phase for initial clinical experience was employed in the study. In addition, a bilateral registry was included for patients presenting with bilateral carotid artery disease requiring treatment. A total of 747 patients were enrolled

at 47 centers involving 49 clinical sites in the United States, including 189 roll-in patients, 480 pivotal patients and 78 bilateral registry patients. This trial is summarized in Table 9.

**Table 9. Overview of BEACH Trial Study Design**

<p><b>Product Evaluated:</b> Carotid WALLSTENT Endoprosthesis and FilterWire EX<sup>®</sup> / FilterWire EZ<sup>™</sup> System</p>
<p><b>Sample Size for Pivotal Patients:</b> 480  <b>Number of Centers:</b> 47  <b>One-Year Primary Endpoint:</b>          Non Q-wave MI to 24 hours          Death, Stroke, Q-wave MI through 30 days          Ipsilateral Stroke, neurological death 31-360 days  <b>Secondary Endpoints:</b></p> <ul style="list-style-type: none"> <li>- FilterWire EX<sup>®</sup> / FilterWire EZ<sup>™</sup> System Technical Success<sup>1</sup></li> <li>- Carotid WALLSTENT Endoprosthesis Technical Success<sup>2</sup></li> <li>- System Technical Success<sup>3</sup></li> <li>- Angiographic Success<sup>4</sup></li> <li>- Procedure Success<sup>5</sup></li> <li>- 30-Day Clinical Success<sup>6</sup></li> <li>- Peri-Procedural Morbidity and Mortality<sup>7</sup></li> <li>- Peri-Procedural Overall Morbidity<sup>8</sup></li> <li>- One-Year Clinical Success<sup>9</sup></li> <li>- Late Stroke, TIA and Death<sup>10</sup></li> </ul> <p><b>Study Hypothesis:</b> Non-inferiority to historical control  <b>Patient Follow-up:</b></p> <ul style="list-style-type: none"> <li>- Neurological assessment by independent neurologist</li> <li>- Creatine kinase (CK)/ creatine kinase MB (CKMB) to 24 hours</li> <li>- ECG: discharge and 30 days</li> <li>- Carotid ultrasound: discharge, 30 days, 6 months and 1 year to 5 years</li> <li>- AEs: discharge, 30 days, 6 months, 1 year to 5 years</li> </ul>

<sup>1</sup>FilterWire EX/FilterWire EZ System successfully delivered and deployed beyond the target lesion and successfully retrieved after completion of the stent placement. Calculated based on the number of FilterWire<sup>®</sup> System uses attempted.

<sup>2</sup>Deployment of the Carotid WALLSTENT Endoprosthesis at the intended location and successful retrieval of the delivery catheter after stent placement. Calculated based on the number of stent implantations attempted.

<sup>3</sup>Includes FilterWire System technical success combined with Carotid WALLSTENT Endoprosthesis technical success. Calculated based on the number of system placement attempts.

<sup>4</sup>System technical success with a residual diameter stenosis ≤30% immediately after post-dilatation as determined by angiographic core lab. Based on number of patients on whom a procedure is attempted.

<sup>5</sup>Includes system technical success and angiographic success without death, stroke and MI (Q-wave and non Q-wave) immediately following the index procedure. Based on number of patients attempted to be treated.

<sup>6</sup>Procedure success without any death, stroke or MI (Q-wave) up to and including 30 days post procedure. Based on number of patients on whom a procedure is attempted.

<sup>7</sup>Non Q-wave MI through 24 hours post procedure and death, stroke and Q-wave MI through 30 days post procedure.

<sup>8</sup>Morbidity occurring up to and including 30 days after the index procedure, including complications associated with routine catheterization, e.g., infection, hematoma, etc.

<sup>9</sup>Defined as a patent vessel by Duplex Ultrasound (as assessed by core laboratory to be <50% stenosis and confirmed by angiogram in patients that develop symptoms post procedurally) combined with freedom from interim target vessel revascularization and ipsilateral stroke or death up to and including one-year. One-year clinical success was based on the number of patients treated. One-year clinical success includes late ipsilateral stroke and death (31-360 days) and repeat revascularization.

<sup>10</sup>Defined as the incidence of any stroke (major or minor), TIA or death occurring after 30 days and up to and including one-year post procedure. Major stroke: a new focal ischemic neurological deficit of abrupt onset, which is present after 7 days and increases the National Institutes of Health (NIH) Stroke Scale by  $\geq 4$ . Minor stroke: a new focal ischemic neurological deficit of abrupt onset, lasting >24 hours and increases the NIH Stroke Scale by  $\leq 3$ . TIA: a focal ischemic neurological deficit of abrupt onset and of presumed vascular etiology that resolves completely within 24 hours of onset.

The BEACH trial was designed to show equivalence (non-inferiority) of the major adverse event rate at one year between carotid stenting and a historical control. The historical control was established based on a review of the current literature related to outcomes from carotid endarterectomy and medical therapy, which represent the standard of care. The major adverse event rate at one year for these patients was determined from the literature. Because this rate differed depending on the nature of a patient's risk factors, a weighted objective performance criterion (OPC) was used. A criterion of 15% for patients who had comorbidity risk factors and a criterion of 11% for patients who had anatomical risk factors were selected. A spread of 4% for the "delta" definition of equivalency was selected. This value represents the maximum allowable difference between the BEACH study outcome and the OPC.

$$\text{Weighted OPC} = (\% \text{ Comorbid} \times 15\%) + (\% \text{ Anatomic} \times 11\%)$$

Enrollment percentages in each category were 41.2% (197/478) in the comorbid group and 58.8% (281/478) in the anatomic group; therefore, the weighted OPC for BEACH was 12.6%. Note that 59 patients included in the comorbid group presented with both comorbid and anatomic risk factors.

$$12.6\% = (41.2\% \times 15\%) + (58.8\% \times 11\%)$$

Based on the weighted OPC of 12.6% and the pre-specified delta of 4%, the threshold for claiming non-inferiority to CEA was 16.6%, i.e., the one-sided upper 95% confidence limit of the primary endpoint must be <16.6% to conclude non-inferiority.

The protocol required regular patient follow-up by the treating physician and follow-up neurological assessments by an independent neurologist. Core laboratories provided independent assessments for angiographic, ultrasound, ECG and CT/MRI testing. Monitors reviewed all safety data to ensure appropriate reporting of adverse events. A Clinical Events Committee (CEC) adjudicated suspected primary endpoint events. A Data Safety Monitoring Board reviewed 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, with discrete lesions in the common carotid artery (CCA), internal carotid artery (ICA) or carotid bifurcation. Patients had to be at high-risk for surgical intervention; both symptomatic ( $\geq 50\%$  stenosis) and asymptomatic ( $\geq 80\%$  stenosis) patients were eligible.

The key inclusion criteria included the following:

- Symptomatic: Carotid stenosis of  $\geq 50\%$  via angiography with cerebral or retinal TIA or ischemic stroke symptoms determined to have occurred ipsilateral to the target lesion and to be reasonably attributable to the lesion within 180 days of the stenting procedure
- Asymptomatic: Carotid stenosis of  $\geq 80\%$  via angiography without cerebral or retinal TIA or ischemic stroke symptoms within 180 days of the stenting procedure
- Patient had to meet at least ONE High-Risk Category as follows:

Anatomical High-Risk Conditions:

ONE (1) criterion qualifies

1. Surgically inaccessible lesions at or above the second cervical vertebra or below the clavicle
2. Previous neck or head radiation therapy or surgery that included the area of stenosis/repair or ipsilateral radical neck dissection for cancer
3. Spinal immobility of the neck due to cervical arthritis or other cervical disorders
4. Restenosis after a previous or unsuccessful attempt of CEA ( $\geq 50\%$  symptomatic,  $\geq 80\%$  asymptomatic) at least 31 days prior to enrollment if arteriotomy was performed
5. Presence of laryngeal palsy or laryngectomy
6. Presence of a tracheostoma
7. Contralateral total occlusion with a qualifying lesion on the ipsilateral side (Note: Applies to roll-in and pivotal groups only)
8. Bilateral carotid artery disease (Note: Patients with Bilateral disease were placed in the Bilateral Registry provided that both ipsilateral and contralateral arteries required treatment at the time of enrollment.)

Comorbid High-Risk Conditions:

CLASS I [ONE (1) criterion qualifies]

1. Congestive heart failure (New York Heart Association (NYHA) Class III/IV)
2. Unstable angina (Canadian Cardiovascular Society (CCS) Class III/IV)
3. Requirement for staged and scheduled coronary artery bypass graft (CABG) or valve replacement post carotid index procedure (Note: The staged procedure must occur  $>30$  days post index procedure.)
4. Chronic Obstructive Pulmonary Disease (COPD) manifested with a forced expired volume (FEV)  $\leq 30\%$
5. Known severe left ventricular ejection fraction (LVEF  $\leq 30\%$ )

CLASS II [TWO (2) criteria qualifies]

1. Age  $\geq$  75 years
2. Recent MI (Q-wave and or non Q-wave)  $>$ 72 hours and  $\leq$ 30 days, with any elevation in CK-MB greater than the local laboratory upper limit of normal values
3. Two or more major diseased coronary arteries with  $\geq$ 70% stenosis at the time of index procedure in patients with a history of angina
4. Requirement for staged and scheduled peripheral vascular surgery or other major surgeries [e.g., abdominal aortic aneurysm (AAA)] post carotid index procedure

**Specific Inclusion Criteria for the Carotid WALLSTENT Endoprosthesis and FilterWire EZ™ System**

1. The target lesion had to have been in the CCA, ICA, or carotid bifurcation.
2. The target arterial segment to be stented must have a diameter  $\geq$ 4.0 mm and  $\leq$ 9.0 mm.
3. Vessel diameter distal to the target lesion must be  $\geq$ 3.5 mm and  $\leq$ 5.5 mm as an optimal “landing zone” for placement of the FilterWire EZ System with visual angiographic recommendations.

**10.2 Description of Patients Evaluated**

Table 10 summarizes patient follow-up at the endpoint evaluation time points of 30 days, 6 months, and 12 months. Patients were considered to have been evaluated if they had physician contact as evidenced by at least one of the following at the given time point: office visit, neurologic evaluation, AE log, stroke scales, event forms such as Repeat Carotid Angiography Form, SAE Notification Form, Subsequent Hospitalization Form, Vascular Event Form, Neurological Event Form, etc.

**Table 10. BEACH Patient Follow-up**

	<b>Pivotal (N=480)</b>
Primary Analysis Sample (intent-to-treat)	480
30-day Follow-up Evaluation Completed	466
6-month Follow-up Evaluation Completed	435
12-month Follow-up Evaluation Completed	418
12-month Follow-up Evaluation not Completed	62
Death	36
Lost to Follow-up	10
Missed Visit	16
Patients with Ultrasound Data Pre-Procedure	455
Patients with Ultrasound Data at 30 Days	443
Patients with Ultrasound Data at 6 Months	417
Patients with Ultrasound Data at 12 Months	395

Baseline demographics and lesion characteristics for the study are presented in Table 11. All reported angiographic data on the treated lesions are based on measurements obtained by the centralized angiographic core laboratory.

**Table 11. Baseline Patient Demographics**

<b>Demographic and Medical History</b>	<b>Value</b>	<b>95% Confidence Interval (CI)</b>
<b>Age (years)</b>		
Mean±Standard Deviation (SD) (N)	70.9±9.3 (480)	[70.0, 71.7]
Range (min, max)	(41.0, 92.0)	
<b>Gender</b>		
Male	65.2% (313/480)	[60.8%, 69.5%]
<b>History</b>		
Diabetes mellitus	33.8% (162/480)	[29.5%, 38.2%]
Hypertension	89.4% (429/480)	[86.3%, 92.0%]
Hyperlipidemia	86.5% (415/480)	[83.1%, 89.4%]
Current or history of smoking	74.6% (358/480)	[70.4%, 78.4%]
Number of Symptomatic Patients	23.3% (112/480)	[19.6%, 27.4%]
<b>Baseline Lesion Characteristics</b>		
Calcification	48.8% (234/480)	[44.2%, 53.3%]
<b>Lesion Length (mm)</b>		
Mean±SD (N)	15.13±7.25 (480)	[14.48, 15.78]
Range (min, max)	(2.46, 57.60)	
<b>Minimal Lumen Diameter (MLD, mm)</b>		
Mean ± SD (N)	1.33±0.58 (480)	[1.27, 1.38]
Range (min, max)	(0.12, 3.51)	
<b>Percent Diameter Stenosis (%DS)</b>		
Mean ± SD (N)	71.61±10.71 (480)	[70.65, 72.58]
Range (min, max)	(36.75, 96.52)	
<b>High-Risk Inclusion Criteria</b>		
<b>Anatomic High-Risk Conditions (One Criterion Qualifies)</b>		
Surgically inaccessible lesions		9.2% (44/480)
Previous head/neck radiation therapy or radical neck surgery		10.8% (52/480)
Spinal immobility		7.3% (35/480)
Restenosis after previous, or unsuccessful attempt, of CEA		34.2% (164/480)
Presence of laryngeal palsy or laryngectomy		1.0% (5/480)
Presence of tracheostoma		2.1% (10/480)
Contralateral total occlusion		18.1% (87/480)
<b>Comorbid Conditions - Class I (One Criterion Qualifies)</b>		
Congestive heart failure (NYHA Class III/IV)		11.7% (56/480)
Unstable angina (CCS Class III/IV)		12.5% (60/480)
Requirement for CABG or valve replacement		6.5% (31/480)
COPD manifested with a forced expired volume (FEV ≤30%)		2.3% (11/480)
Known severe left ventricular ejection fraction (LVEF ≤30%)		12.1% (58/480)
<b>Comorbid Conditions - Class II (Two Criteria Qualifies)</b>		
Age ≥75 years old		39.0% (187/480)
Recent MI (Q-wave and/or non Q-wave) ≥72 hours and ≤30 days		1.3% (6/480)
Two or more major diseased coronary arteries with ≥70% stenosis		21.7% (104/480)
Requirement for peripheral vascular or other major surgery		2.9% (14/480)

### 10.3 Results

The primary endpoint for the BEACH trial was one-year morbidity and mortality defined as the cumulative incidence of any non Q-wave myocardial infarction within the 24 hours following carotid stenting, peri-procedural ( $\leq 30$  days) death, stroke, Q-wave myocardial infarction, and late ipsilateral stroke or death due to neurologic events from 31 to 360 days. Table 12 presents the primary and secondary endpoints for the trial. The 1-year Major Adverse Event rate was 8.8%. Rates for each contributor to the composite rate are presented along with the endpoints in Table 12.

The trial utilized the FilterWire EX<sup>®</sup> and the FilterWire EZ<sup>™</sup> embolic protection devices. One hundred ninety-five (195) patients were enrolled using the FilterWire EX System and 285 patients were enrolled using the FilterWire EZ System. Poolability analysis was conducted to determine baseline homogeneity. No significant differences between the groups were found. In addition, a group difference on peri-procedural outcome analysis was performed. There was no evidence found against pooling the FilterWire EX and FilterWire EZ System groups for purposes of estimating the treatment effect on one-year morbidity and mortality.

The primary objective of the BEACH trial was met. The observed one-year morbidity and mortality rate of 8.8% with an upper confidence limit of 11.3% fell well below 16.6%, the predefined weighted OPC + delta, demonstrating that carotid stenting with the Carotid WALLSTENT Endoprosthesis and the FilterWire<sup>®</sup> Embolic Protection System is non-inferior to surgical treatment for carotid artery disease in patients who were at high risk for CEA.

**Table 12. Clinical Results Through 360 Days Follow-up**

Primary Endpoint Measures	Pivotal (N=480)	95% CI <sup>1</sup>
One-Year Morbidity and Mortality	8.8% (39/445)	[11.3%]
Non Q-wave MI (Through 24 hours)	0.9% (4/445)	[0.3%, 2.3%]
Death, Stroke, Q-wave MI (Through 30 days)	5.2% (23/445)	[3.3%, 7.7%]
Death	1.6% (7/445)	[0.6%, 3.2%]
Neurologic	0.4% (2/445)	[0.1%, 1.6%]
Cardiac	0.7% (3/445)	[0.1%, 2.0%]
General	0.4% (2/445)	[0.1%, 1.6%]
Stroke	4.3% (19/445)	[2.6%, 6.6%]
Ipsilateral <sup>2</sup>	3.1% (14/445)	[1.7%, 5.2%]
Major Ischemic	1.1% (5/445)	[0.4%, 2.6%]
Minor Ischemic	1.8% (8/445)	[0.8%, 3.5%]
Hemorrhagic (excludes Subarachnoid Hemorrhages)	0.2% (1/445)	[0.0%, 1.3%]
Contralateral	1.1% (5/445)	[0.4%, 2.6%]
Major Ischemic	0.0% (0/445)	[0.0%, 0.8%]
Minor Ischemic	0.7% (3/445)	[0.1%, 2.0%]

Hemorrhagic (excludes Subarachnoid Hemorrhages)	0.4% (2/445)	[0.1%, 1.6%]
Subarachnoid Hemorrhagic	0.0% (0/445)	[0.0%, 0.8%]
Q-wave MI	0.2% (1/445)	[0.0%, 1.3%]
Neurologic Death, Ipsilateral Stroke (31 days through 360 days)	3.1% (14/445)	[1.7%, 5.2%]
Neurologic Death	1.6% (7/445)	[0.6%, 3.2%]
Ipsilateral Stroke	2.5% (11/445)	[1.2%, 4.4%]
Major Ischemic	1.3% (6/445)	[0.5%, 2.9%]
Minor Ischemic	0.4% (2/445)	[0.1%, 1.6%]
Hemorrhagic (excludes Subarachnoid Hemorrhages)	0.7% (3/445)	[0.1%, 2.0%]
Freedom from 1-Year Morbidity and Mortality – Kaplan-Meier Estimate	91.8%	[89.1%, 94.5%]

Secondary Endpoint Measures	Pivotal (N=480)	95% CI
FilterWire EX <sup>®</sup> and FilterWire EZ <sup>™</sup> System Technical Success <sup>3</sup>	97.1% (475/489)	[95.2%,98.4%]
Carotid WALLSTENT Endoprosthesis Technical Success <sup>4</sup>	94.1% (475/505)	[91.6%,96.0%]
System Technical Success <sup>5</sup>	98.3% (469/477)	[96.7%,99.3%]
Angiographic Success <sup>6</sup>	90.8% (433/477)	[87.8%,93.2%]
Procedure Success <sup>7</sup>	87.8% (419/477)	[84.6%,90.6%]
30-Day Clinical Success <sup>8</sup>	85.5% (406/475)	[82.0%,88.5%]
Peri-Procedural Morbidity and Mortality <sup>9</sup>	5.4% (26/478)	[3.6%,7.9%]
Peri-Procedural Overall Morbidity <sup>10</sup>	68.7% (329/479)	[64.3%,72.8%]
One-Year Clinical Success <sup>11</sup>	69.7% (292/419)	[65.0%,74.1%]
Late Death, Stroke and TIA (31 days through 360 days) <sup>12</sup>	10.7% (49/458)	[8.0%,13.9%]
<b>Post-procedure In-lesion Minimal Lumen Diameter (mm):</b> Mean ± SD (N) Range (min, max)	3.90±0.79 (480) (0.8, 7.2)	[3.83, 3.97]
<b>Post-procedure In-lesion Percent Diameter Stenosis:</b> Mean ± SD (N) Range (min, max)	16.5%±11.5% (480) (-27.7%, 90.6%)	[15.5%, 17.5%]
<b>Target Lesion Revascularization (TLR) Rate (Through 360 days)<sup>13</sup></b>	4.7% (20/429)	[2.9%, 7.1%]
<b>Carotid Duplex Ultrasound ICA/CCA Ratio:</b> Pre-Procedure Post-Procedure at 1 month at 6 months at 12 months	5.3±3.1 (420) 1.4±0.5 (438) 1.4±0.5 (434) 1.9±1.2 (397) 1.9±1.1 (362)	[5.0, 5.6] [1.4, 1.5] [1.4, 1.5] [1.8, 2.0] [1.8, 2.0]

Numbers are % (count/sample size) or %. The number of patients evaluated is less than 480 for some parameters due to patient unavailability.

<sup>1</sup>One-sided 95% upper confidence limit is presented for one-year morbidity and mortality.

<sup>2</sup>Patient 42-014 was originally denoted to have suffered a minor ipsilateral stroke 27 days post-procedure. This event was sent back to the CEC for additional review after the CT/MRI core lab provided a review of films made available to them. Based upon the core lab report, the CEC adjudicated the event as a TIA.

<sup>3</sup>FilterWire EX<sup>®</sup>/FilterWire EZ<sup>™</sup> System successfully delivered and deployed beyond the target lesion and successfully retrieved after completion of the stent placement. Calculated based on the number of FilterWire<sup>®</sup> System uses attempted.

<sup>4</sup>Deployment of Carotid WALLSTENT Endoprosthesis at the intended location and successful retrieval of the delivery catheter after stent placement. Calculated based on the number of stent implantations attempted. Three patients did not have a Carotid WALLSTENT Endoprosthesis implantation attempted.

<sup>5</sup>Includes FilterWire System technical success combined with Carotid WALLSTENT Endoprosthesis technical success. Calculated based on the number of system placement attempts.

<sup>6</sup>System technical success with a residual diameter stenosis  $\leq 30\%$  immediately after post-dilatation as determined by angiographic core lab. Based on number of patients on whom a procedure is attempted.

<sup>7</sup>Includes system technical success and angiographic success without death, stroke and MI (Q-wave and non Q-wave) immediately following the index procedure. Based on number of patients attempted to be treated.

<sup>8</sup>Procedure success without any death, stroke or MI (Q-wave) up to and including 30 days post procedure. Based on number of patients on whom a procedure is attempted.

<sup>9</sup>Non Q-wave MI through 24 hours post procedure and death, stroke and Q-wave MI through 30 days post procedure.

<sup>10</sup>Morbidity occurring up to and including 30 days after the index procedure, including complications associated with routine catheterization, e.g., infection, hematoma, etc.

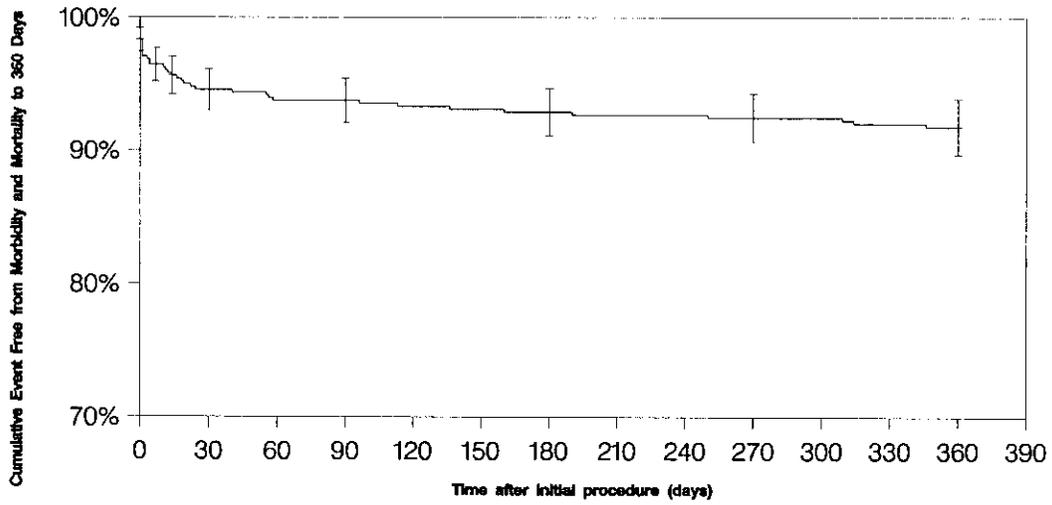
<sup>11</sup>Defined as a patent vessel by Duplex Ultrasound (as assessed by core laboratory to be  $< 50\%$  stenosis and confirmed by angiogram in patients that develop symptoms post procedurally) combined with freedom from interim target vessel revascularization and ipsilateral stroke or death up to and including one-year. One-year clinical success was based on the number of patients treated. One-year clinical success includes late ipsilateral stroke and death (31-360 days) and repeat revascularization.

<sup>12</sup>Defined as the incidence of any stroke (major or minor), TIA or death occurring after 30 days and up to and including one-year post procedure. Major stroke: a new focal ischemic neurological deficit of abrupt onset, which is present after 7 days and increases the NIH Stroke Scale by  $\geq 4$ . Minor stroke: a new focal ischemic neurological deficit of abrupt onset, lasting  $> 24$  hours and increases the NIH Stroke Scale by  $\leq 3$ . TIA: a focal ischemic neurological deficit of abrupt onset and of presumed vascular etiology that resolves completely within 24 hours of onset.

<sup>13</sup>Defined as any surgical or percutaneous attempt to revascularize the target lesion after the initial treatment. The target lesion is defined as the stented segment including 0.5 cm at the proximal and distal margins of the stented segment.

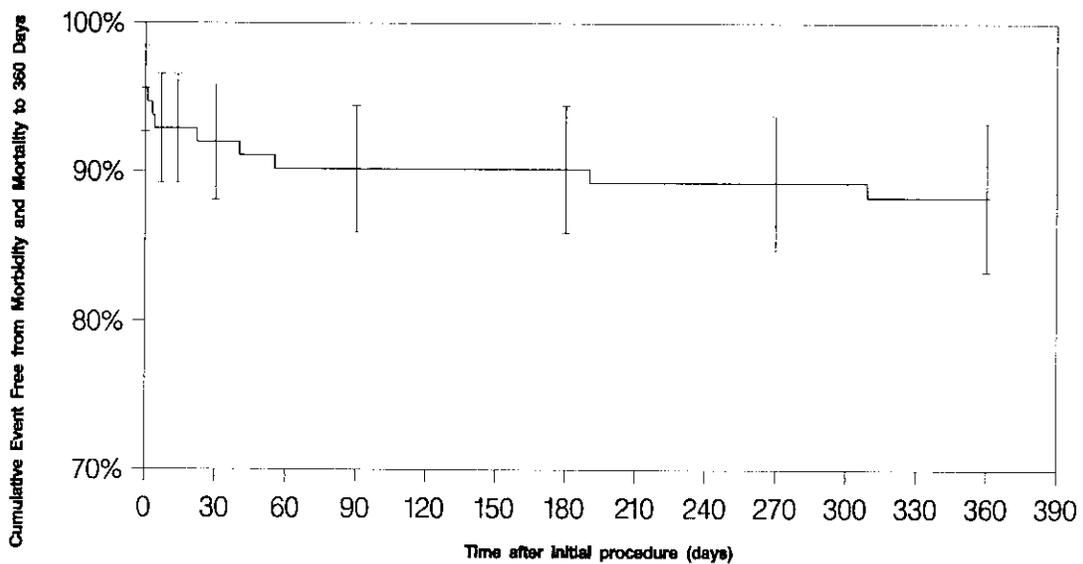
The Kaplan-Meier curve through 360 days for all pivotal patients is presented in Figure 2. As can be seen, most major adverse events occur within 30 days with acceptable adverse event rates within one year.

**Figure 2. All Pivotal Patients, Freedom from Morbidity and Mortality through 360 Days**

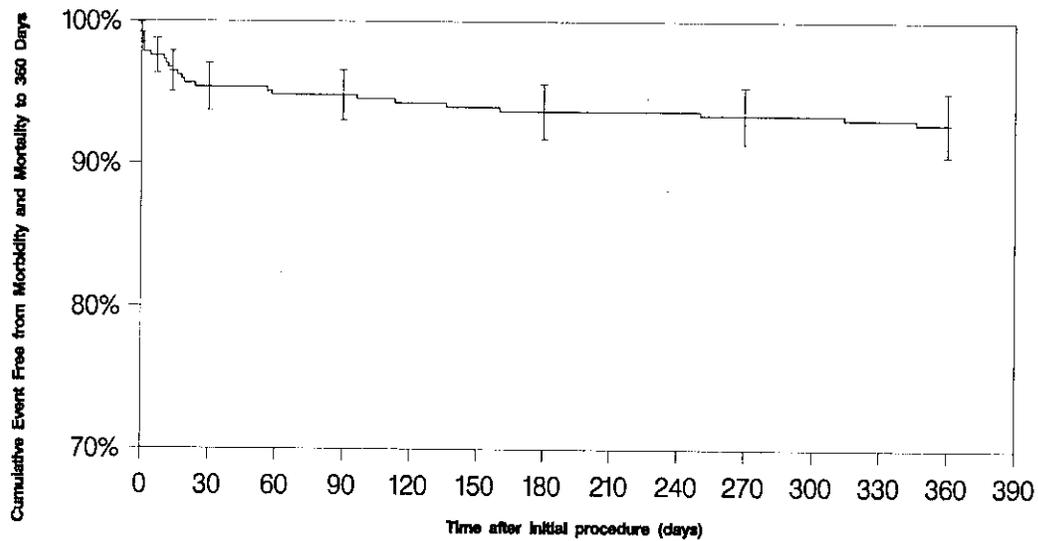


Figures 3 and 4 present the Kaplan-Meier curves through 360 days for symptomatic and asymptomatic patients, respectively.

**Figure 3. Symptomatic Patients, Freedom from Morbidity and Mortality through 360 Days**



**Figure 4. Asymptomatic Patients, Freedom from Morbidity and Mortality through 360 Days**



## **11. Conclusions Drawn From Studies**

Data from pre-clinical studies performed on the Carotid WALLSTENT Endoprosthesis demonstrate that the device meets or exceeds the performance specifications. Results from the multi-center BEACH Clinical Trial demonstrate that the Carotid WALLSTENT Endoprosthesis, used in conjunction with embolic protection, is a safe and effective treatment for carotid artery disease in the patient population studied. The combined preclinical and clinical results provide valid scientific evidence and reasonable assurance that the Carotid WALLSTENT Endoprosthesis is safe and effective when used in accordance with its labeling.

## **12. 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. CDRH Decision**

FDA issued an approval order on October 23, 2008.

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

**14. Approval Specifications:**

**14.1 Directions for Use:** See product labeling.

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

**14.3 Post-approval Requirements and Restrictions:** See approval order. A post-approval study involving use of the device according to its approved indications is required to obtain data related to the adequacy of the device training program, detection of rare adverse events, and applicability of the clinical study data to the real-world patient population.