SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Stent, Carotid Artery
Device Trade Name:	GORE Carotid Stent
Device Procode:	NIM
Applicant's Name and Address:	W.L. Gore & Associates, Inc. 4150 West Kiltie Lane Flagstaff, AZ 86005
Date(s) of Panel Recommendation:	None
Premarket Approval Application (PMA) Number:	P180010
Date of FDA Notice of Approval:	November 01, 2018

II. INDICATIONS FOR USE

The GORE Carotid Stent, used with the GORE Embolic Filter, is indicated for the treatment of carotid artery stenosis in patients deemed at high surgical risk for carotid endarterectomy (CEA) and who meet the criteria below.

- Patients with symptomatic carotid artery stenosis, ≥50%, as confirmed by ultrasound or angiography.
- Patients with asymptomatic carotid artery stenosis, ≥80%, as confirmed by ultrasound or angiography.
- Patients must have a Reference Vessel Diameter of 3.7 mm – 9.0 mm.

III. CONTRAINDICATIONS

The GORE Carotid Stent 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 the delivery catheter or embolic protection device.
- Patients with a known hypersensitivity to nickel-titanium.
- Patients with uncorrected bleeding disorders.
- Lesions in the ostium of the common carotid artery.
- Patients with known hypersensitivity to heparin, including those patients who have had a previous incident of Heparin-Induced Thrombocytopenia (HIT) type II.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the GORE Carotid Stent labeling.

V. DEVICE DESCRIPTION

The GORE Carotid Stent (GCS) is designed as a "hybrid" stent in that it incorporates open-cell and closed-cell stent features. The GCS is comprised of two sub-systems: a deployment catheter and a self-expanding, deployable stent. The stent integrates a proprietary stable, covalent end-point attached heparin, which is used to create the CBAS Heparin Surface. The device includes 18 part numbers with a diameter range from 5.0 to 10.0 mm, including tapered stents (6/8 mm, 7/9 mm, and 8/10 mm diameters), with lengths of 30 and 40 mm. **Table 1** summarizes the device sizes and delivery system compatibility.

Table 1. GORE Carotid Stent Sizing Summary

GORE Carotid Stent Catalogue Number	Stent Distal Inner Diameter (mm)	Stent Proximal Inner Diameter (mm)	Stent Length (mm)	Delivery System
GCS5530A	5	5	30	5 Fr
GCS5540A	5	5	40	
GCS6630A	6	6	30	
GCS6640A	6	6	40	
GCS7730A	7	7	30	
GCS7740A	7	7	40	
GCS8830A	8	8	30	
GCS8840A	8	8	40	
GCS6830A	6	8	30	
GCS6840A	6	8	40	
GCS9930A	9	9	30	6 Fr
GCS9940A	9	9	40	
GCS0030A	10	10	30	
GCS0040A	10	10	40	
GCS7930A	7	9	30	
GCS7940A	7	9	40	
GCS8030A	8	10	30	
GCS8040A	8	10	40	

A. Stent Component

The implantable stent portion of the GCS is constructed of a self-expanding, laser cut, nitinol (nickel-titanium alloy) stent frame comprising an "open cell" component of the device and with an expanded polytetrafluoroethylene (ePTFE) lattice comprising a "closed cell" component of the device, as shown in **Figure 1** below. The CBAS Heparin Surface is subsequently applied to all surfaces of the device prior to loading on the delivery system.

Figure 1. GORE Carotid Stent

B. Delivery System

The stent is delivered on the catheter-based delivery system. The stent is radially compressed and placed within a pullback sheath. The pullback sheath is mounted on a 5F or 6F introducer-sheath compatible delivery system as shown in **Figure 2**.

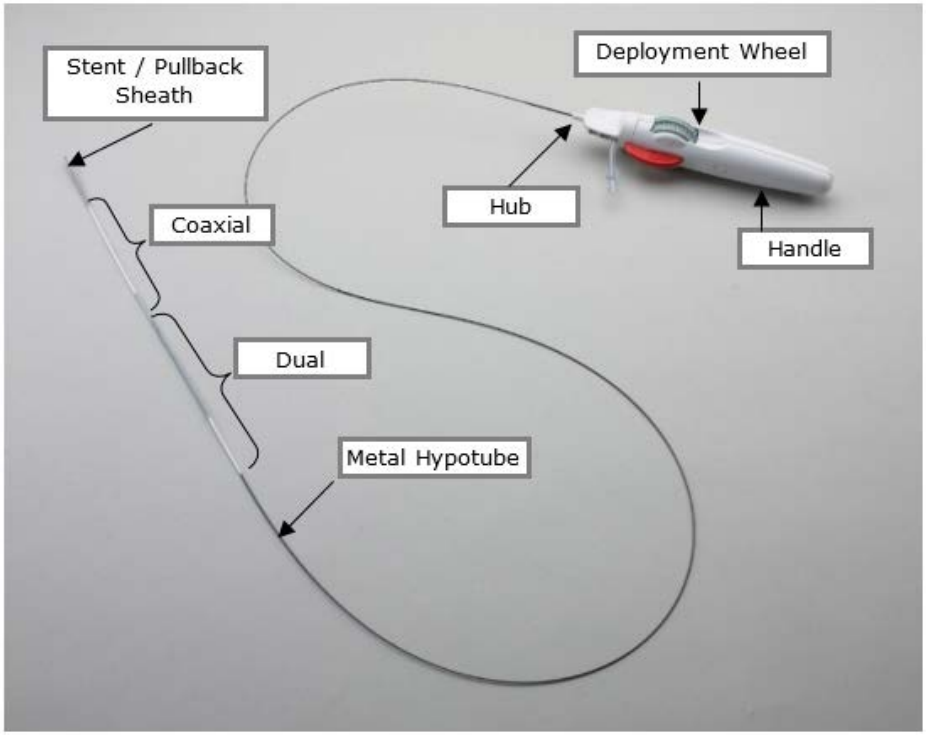

Figure 2. GCS Delivery System

C. Accessory Devices

The system packaging includes a 2.5cc syringe and luer adapter to facilitate system flushing from the hub (syringe only) and distal tip (syringe fitted with luer adapter).

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the correction of carotid artery disease. Alternate treatments for carotid artery disease are dependent on symptomatic status, patient anatomy and comorbidities, and degree of stenosis. Patients with less severe disease or symptoms are generally treated with medical management including antiplatelet and/or anticoagulant medicine, antihypertensive or antilipidemic drugs. Carotid endarterectomy and carotid artery stenting with other devices are more invasive alternative treatments, particularly with more severe disease. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The GCS is currently approved for use in the European Union, where the CE mark was obtained in April, 2014. These countries include the following: Austria, Belgium, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Italy, Luxembourg, Monaco, the Netherlands, Norway, Portugal, Spain, Sweden, Switzerland, and the United Kingdom.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Table 2 lists the potential adverse effects (e.g., complications) associated with the use of the device.

Table 2. List of Procedure and Device Related Potential Adverse Effects

Abrupt vessel closure
Allergic reactions to anti-platelet agents/contrast medium
Aneurysm
Angina/coronary ischemia
Arrhythmia
Arterial occlusion/thrombosis at puncture site or remote site
Arteriovenous fistula
Bacteremia or septicemia
Bleeding from anticoagulant or antiplatelet medications
Bradycardia/arrhythmia and other conduction disturbances
Cerebral edema
Cerebral hemorrhage
Cerebral ischemia / transient ischemic attack (TIA)

Congestive heart failure (CHF)
Death
Detachment and/or implantation of a component of the system
Drug reactions
Emboli, distal (air, device, tissue or thrombotic emboli)
Emergent or urgent endarterectomy or access vessel surgical or endovascular procedure
Fever
Filter thrombosis/occlusion
Groin hematoma, with or without surgical repair
Hemorrhage, with or without transfusion
Heparin induced thrombocytopenia (HIT)
Hyperperfusion syndrome
Hypotension/hypertension
Infection and pain at insertion site
Ischemia/infarction of tissue/organ
Myocardial infarction (MI)
Pain (head, neck)
Pseudoaneurysm, femoral
Renal failure/insufficiency
Restenosis of stented segment
Seizure
Severe unilateral headache
Stent/filter entanglement / damage
Stent embolization
Stent fracture
Stent malposition
Stent migration
Stent thrombosis / occlusion
Stroke/cerebrovascular accident (CVA) or other neurological complications (e.g. paralysis, paraplegia or aphasia)
Temporary or total occlusion of carotid artery or branch vessels
Tissue necrosis
Vascular access complications (e.g. bleeding, vessel damage, pseudoaneurysm and infection)
Vessel dissection, perforation, or rupture
Vessel spasm or recoil
Vessel thrombosis
Unstable angina pectoris

For the specific adverse events that occurred in the clinical study, please see Section X below.

IX. SUMMARY OF NONCLINICAL STUDIES

A. Biocompatibility Studies

Biocompatibility testing was conducted on the GCS in accordance with applicable Good Laboratory Practices (21 CFR §58) and ISO 10993-1: 2009, *Biological Evaluation of Medical Devices*. Tests were conducted separately on product manufactured, packaged and sterilized using materials and procedures intended for the marketed product for the delivery system and the stent.

The GCS delivery system is classified as an externally-communicating device in limited contact (< 24 hrs) with circulating blood. The stent is classified as an implant device in permanent contact (> 30 days) with blood. A summary of the biocompatibility testing conducted can be found in **Table 3** below.

Table 3. Summary of GORE Carotid Stent Biocompatibility Testing

Test Performed	Test Description	Stent	Delivery System	Results
Cytotoxicity	ISO MEM Elution Assay with L-929 Mouse Fibroblast Cells	X	X	Non-cytotoxic
Sensitization	ISO Guinea Pig Maximization	X	X	Non-sensitizing
Irritation	ISO Intracutaneous Reactivity	X	X	Non-irritating
Pyrogenicity	Material-Mediated Pyrogenicity	X	X	Non-pyrogenic
Acute Systemic Toxicity	ISO Systemic Toxicity Study	X	X	Non-toxic
Subchronic / Subacute Toxicity	14 Day Repeat Dose Intravascular and Intraperitoneal Toxicity Study	X	N/A	Non-toxic
Implantation	Subcutaneous Implantation Study – 4 Weeks	X	N/A	Non-irritant
Hemocompatibility	ASTM Hemolysis Study (Direct and Indirect Contact)	X	X	Non-hemolytic
	Complement Activation Assay (C3a and SC5b-9)	X	X	Not a complement activator
	In Vivo Thrombogenicity Study	X[a]	X	Non-thrombogenic
Genotoxicity	Bacterial Reverse Mutation (Ames) Assay	X	N/A	Non-mutagenic
	Mouse Lymphoma Assay	X	N/A	Non- clastogenic

[a] Evaluated as part of the animal studies outlined in Section C, below.

Stent thrombogenicity was evaluated as part of other *in vivo* studies conducted to evaluate safety and effectiveness of the device in a vascular implant location, as described in Section C below. These additional animal studies demonstrated a lack of significant thrombus formation when stents were implanted in a clinically-relevant vascular implant location.

The omission of chronic toxicity and carcinogenicity testing for the stent was supported by information regarding the starting materials, processing of the finished device compared to a marketed device, genotoxicity testing, the GLP animal study, and/or toxicity data from the literature.

The information provided demonstrates that the GCS is biocompatible.

B. *In Vitro* Engineering Testing

In vitro bench testing to support the GCS was developed based on the device risk assessment and is consistent with *FDA Non-Clinical Tests and Recommended Labeling of Intravascular Stents and Associated Delivery Systems*, April 18, 2010 and its addendum, *Select Updates for Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems*, August 30, 2013.

The relevant *in vitro* tests outlined in the guidance document and included in support of the GORE Carotid Stent devices are summarized in **Table 4** below.

Table 4. Summary of *in vitro* Test Results

Test	Purpose	Acceptance Criteria	Results
Material Composition	Document material composition and characterize the surface oxide of the nitinol frame component.	Characterize Nitinol stent frame via surface analysis.	The stent material conforms to the material specification, ASTM F2633, and ASTM F2063
Shape Memory & Superelasticity	Document the active austenitic finish transformation temperature (A_f) of the stent component.	Af must be ≤ body temperature.	Each lot of nitinol tubing used for the production of stents is tested for austenitic finish temperature (Af). The stent retains its specified size and shape by superelasticity.
Corrosion Resistance	The stent must resist corrosion following implantation.	The deployed stent must exhibit equivalent or superior breakdown potentials as compared to an appropriate reference device per ASTM F2129-15.	GCS devices exhibited statistically higher mean breakdown (Eb) potential than the reference device.
Nickel Elution	The stent must have acceptable levels of nickel elution.	The stent must not elute nickel beyond the acute and chronic tolerable intakes.	All stents meet the acceptance criteria for acute and chronic nickel elution.
Dimensional Verification (deployed length)	The stent must be within the dimensional specification when implanted.	Stents with a labeled length of 30 mm shall be ≥ 27.0 mm and ≤ 33.0 mm when deployed. Stents with a labeled length of 40 mm shall be ≥ 36.0 mm and ≤ 44.0 mm when deployed.	All measurements passed the applicable requirement for deployed length.
Dimensional Verification (deployed stent outer diameter)	The deployed stent outer diameter must be consistent with as-labeled diameter.	The deployed device must be the labeled device diameter ± 0.4 mm.	All measurements pass the applicable requirement for stent outer diameter.

Test	Purpose	Acceptance Criteria	Results
Percent Surface Area of Stent	Determine the ratio of the stent/vessel non-contact surface area to the vessel surface area at minimum, nominal, and maximum indicated vessel diameters.	Stents were characterized for information only.	The stent percent contact surface area was calculated and ranges from 29% to 47% depending on device diameter.
Foreshortening / Elongation	This test assesses the difference between crushed stent length and deployed stent length for the GCS.	Deployed stent length shall be ± 20% of the crushed stent length.	Foreshortening values range between 0.9% and 8.8% depending on labeled stent length.
Crushed Stent Length	This test assesses the crushed stent length for the GCS to provide a baseline for determination of foreshortening/elongation .	Length shall be ± 3 mm for 30mm devices and ± 4 mm for 40mm devices.	Crushed stent length values range between 31.6mm and 32.3mm for 30mm length and 40.8mm and 43.1mm for 40mm length devices.
Stent Integrity	To verify the stent has no clinically significant defects or flaws after deployment.	Frame fracture, percent delamination, and lattice breakage shall not be at a clinically relevant level, and there shall be no contamination.	All devices tested met established acceptance criteria.
Mechanical Integrity – Radial Outward Force	This test determines the radial pressure of the stent at its minimum and maximum indicated diameters.	The radial outward pressure must be sufficient to withstand clinically relevant forces.	All devices tested met established acceptance criteria.
Material Mechanical Properties	Characterize the stent materials mechanical properties to ensure they are acceptable for the intended use.	ASTM F2063	The stent material conforms to implant material standards ASTM F2063 for material properties.
Strain and Fatigue Analysis/Finite Element Analysis	To determine the location and magnitude of the maximum principal strains in the stents, under expected clinical use conditions, through the use of Finite Element Analysis (FEA).	Strains are calculated for: A) radial pulsatile loading conditions when deployed in vessels at maximum and minimum product specification diameters, B) radial compressions due to catheter loading C) flat plate compression and D) multi-modal loading conditions when subjected to pulsatile loading conditions that are combined with bending.	The location and magnitude of the maximum principle strains have been calculated and the strain states are below the endurance limit for the Nitinol material.

Test	Purpose	Acceptance Criteria	Results
Accelerated Durability Testing: Pulsatile	The purpose of this test is to evaluate the simulated 10 year durability of stents under expected clinical use conditions as it pertains to fatigue due to pulsatile motion.	The stent must exhibit a design life of at least 10 years through simulated physiological loading without failure that would compromise device function or patient safety.	All devices tested met established acceptance criteria.
Particulate Evaluation	This test evaluates particulation during simulated use.	The Finished Good shall not introduce clinically-relevant particulation during delivery, deployment, and retraction.	All devices were within the limits provided in USP <788>.
Magnetic Resonance Imaging Compatibility	To evaluate the MRI safety and compatibility of the stent.	The implant must not present additional risk to the patient when exposed to static magnetic field strengths of 1.5 and 3.0 Tesla.	The stent does not pose additional risk to patients and may be labeled MR Conditional.
Radiopacity	The purpose of this test is to demonstrate the ability of the stent and delivery system to be visualized adequately under fluoroscopy.	Units must be visible under fluoroscopy and comparable to a commercially available carotid stent and carotid stent system.	All samples were comparable to a commercially available carotid stent system and were all visible under digital radiographic imaging.
Crush Resistance	This test evaluates the ability of the GCS to recover its original size and shape from potential external, non-cardiac loads after removal of the load.	The stent must recover its desired shape after application and removal of external loads, deformation, or both.	The stent adequately recovers its diameter and length following deployment from the constrained profile.
Kink Resistance	This test determines the smallest radius of curvature the GCS can withstand without kinking, and demonstrates if the GCS recovers its original size and shape after testing.	The GCS shall not kink at bend radius ≤ 19mm.	All stents had kink radii below 19mm. All devices returned to original geometry after testing.
Dimensional Verification (Crossing Profile)	This test is to assess the diameter of the GCS delivery system with constrained stent.	The crossing profile for 5 Fr compatible delivery systems shall be ≤ 1.85 mm (0.073 in) diameter. The crossing profile for 6 Fr compatible delivery systems shall be ≤ 2.03 mm (0.080 in) diameter.	The delivery system and constrained stents met the acceptance criteria.
Dimensional Verification (Working Length)	Delivery catheter working length enables treatment of the intended site.	The delivery catheter working length must be 135 ± 3 cm.	The delivery catheter meets the acceptance criteria for working length.

Test	Purpose	Acceptance Criteria	Results
Delivery, Deployment, and Retraction	This test assesses the ability of the delivery system to: 1) access the target location; 2) deploy the stent; and 3) retract the delivery system without dislodging the stent.	The catheter delivery system must be able to reliably access target location, deploy the stent, and retract without dislodging the stent.	The catheter delivery system meets the established acceptance criteria.
Delivery, Deployment, and Retraction (Accessory Compatibility)	The system must be compatible with accessories typical of the procedure.	The system must be flushable with a syringe, compatible with 0.014" guidewires, pass through 5 Fr or 6 Fr introducer sheaths, and be compatible with embolic protection devices (GORE Embolic Filter).	The system is compatible with accessories that would be used in a typical clinical procedure.
Delivery Catheter Bond Strength	Evaluate the tensile strength of delivery catheter bonds.	The delivery catheter must maintain its function during access, deployment, and retraction per ISO 10555-1.	Tensile strengths for all delivery catheter samples across all bond locations pass the applicable acceptance criteria.
Delivery System Flexibility & Kink	To verify the catheter delivery system is able to reliably track through tortuous, clinically relevant anatomy and deliver the stent to its intended location.	The catheter delivery system must be able to reliably: • Access the target location. • Deploy the stent by withdrawing the tear tube. • Retract the intact catheter without dislodging the stent.	The catheter delivery system meets the established acceptance criteria.
Catheter Torque Strength	This test is to assess the torque strength of the catheter.	The catheter must be able to complete at least 1 full rotation without a kink in the body of the delivery system of failure of a bond.	The catheter delivery system meets the established acceptance criteria.
Coating Integrity	To characterize the CBAS Heparin Surface of the stent.	Stents were characterized for information only.	Based on the image analysis, the coating integrity of the CBAS Heparin Surface is maintained throughout aging, across device size configurations. There was no apparent gross heterogeneity in the presence or uniformity of the coating.
Heparin Surface Activity	To test that heparin surface activity of the CBAS Heparin Surface meets specification requirements throughout the stent shelf-life.	Must meet specification for heparin surface activity through the product shelf-life	The specification was met throughout the product shelf-life.

Test	Purpose	Acceptance Criteria	Results
Heparin Surface Concentration	To demonstrate the presence of heparin on the stent surface and characterize the mass of heparin present per unit area.	Testing must demonstrate the presence of heparin on the surface and characterize the mass of heparin present per unit area.	Results of heparin surface concentration testing met the established acceptance criteria.
Chemical Residuals	To test chemical residuals on the device surface related to the heparin coating process.	Must be acceptable within the bounds of established allowable limits.	Chemical residuals of the coated stent surface are within allowable limits.
Chandler Blood Loop Testing	To characterize the potential thrombogenicity of mechanically induced disruptions of the CBAS Heparin Surface of the stent.	Stents were characterized for information only.	The results of this evaluation did not identify, either grossly or with SEM, observable evidence of thrombus associated with any disruption. Additionally, no evidence of thrombus was observed on the surfaces of control CBAS Heparin Surface-coated GCS devices, which did not contain mechanically induced disruptions, and represents the final device design.

C. Animal Studies

The GCS was subjected to two GLP animal studies to evaluate the safety and performance of the device. The GLP *in vivo* animal studies demonstrated the safety and overall product performance of the GCS *in vivo* in a total of 14 porcine models. **Table 5** summarizes the results of the GLP studies conducted on finished, sterile devices.

Table 5. Summary Results of the GLP Animal Studies

Study Description	Study Overview	Purpose	Summary of Test Results
#2103SC GORE Carotid Stent **(GCS)**: A 24 hour *In Vivo* Compatibility Evaluation with the GORE Embolic Filter **(GEF)** and GORE Flow Reversal Systems **(GFRS)** in the Arterial Vasculature of the Porcine Model	-**GLP** -2 domestic swine -common carotid artery -24 hours -n=2 GCS/GEF -n=2 GCS/GFRS	Assess compatibility of the GCS with the GEF and GFRS	GCS is compatible with GEF and GFRS

Study Description	Study Overview	Purpose	Summary of Test Results
#2102SC GORE Carotid Stent **(GCS)**: An *In Vivo* Performance Evaluation in the Carotid Arteries of Swine	-**GLP** -12 Hanford mini-swine -common carotid artery -3, 30, 90 days -n=12 GCS -n=9 ACCULINK	Assess delivery/deployment, patency, integrity, and tissue response	-Delivery and deployment evaluations received **PASS** scores. -All GCS stents patent at each time point. -Four ACCULINKs migrated; three of four devices could not be analyzed. -Angiographic stenosis statistically similar between GCS and ACCULINK -All GCS stents intact at 90 days. -Tissue response biologically acceptable; GCS similar to ACCULINK for all histological parameters except vessel injury.

D. Sterilization, Packaging, and Shelf-Life

The GCS is sterilized by ethylene oxide. Validation of the sterilization method to ensure a Sterility Assurance Level (SAL) of 10^{-6} has been conducted in accordance with ISO 11135-1:2007 *Sterilization of health care products- Ethylene oxide-Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices*.

Packaging Validation demonstrated the ability of the packaging to protect the product and maintain a sterile barrier through shipping and shelf life. The device is packaged in a backer card, sealed in a foil-Tyvek primary pouch, and a poly-Tyvek secondary pouch. The packaged device is then placed in a carton.

A shelf life of 40 months has been established for the GCS based on product and package shelf life testing. Heparin stability testing was conducted to demonstrate that heparin surface activity and heparin surface concentration requirements will be met for the claimed 40-month shelf-life. The stability characteristics of the drug-related attributes of the GCS will continue to be monitored as part of an established on-going stability program.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study (SCAFFOLD) to establish a reasonable assurance of safety and effectiveness of carotid stenting with the GCS in patients at high risk for surgery with symptomatic carotid artery disease and ≥ 50% stenosis or asymptomatic disease and ≥ 80% stenosis by angiography under IDE #G110127. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

Patients were treated between August 6, 2013 and December 2, 2016. The database for this PMA reflected data collected through December 5, 2017 and included 312 patients at 35 investigational sites.

The study evaluated the GCS for the treatment of carotid artery stenosis in patients at increased risk for adverse events from carotid endarterectomy. The study was a multicenter, single-arm, prospective study comparing the GCS to a performance goal developed from CEA outcomes used in performance goals for previous carotid stenting studies to evaluate the safety and effectiveness of the GCS for the treatment of carotid artery stenosis in similar patient populations.

The primary endpoint was the Major Adverse Event (MAE) rate, defined as a composite of death, stroke, or myocardial information (MI) through 30 days post-index procedure, and ipsilateral stroke from day 31 through 1 year. The endpoint was compared to a performance goal based on historical carotid stenting literature, reflecting an overall expected event rate derived from separate, weighted expected rates of adverse events in patients with anatomic versus co-morbid high-surgical-risk factors. All primary endpoint events were adjudicated and determined by the study Clinical Events Committee.

The Data Safety Monitoring Board (DSMB) reviewed all study safety data on a regular basis and advised on the continuing safety, validity and scientific merit of the study. Additionally, all vascular imaging required for the study was evaluated and analyzed by a core lab.

1. Clinical Inclusion and Exclusion Criteria

   Enrollment in the SCAFFOLD study was limited to patients who met the following inclusion criteria:

   General Inclusion Criteria

   - Patient is at least 18 years old at informed consent.
   - Patient is willing and capable of complying with all study protocol requirements, including specified follow-up period and can be contacted by telephone.
   - Patient is willing to provide written informed consent prior to enrollment in the study.
   - Patient has no childbearing potential, or is a non-lactating female of childbearing potential, practicing an acceptable method of birth control with a negative pregnancy test within 10 days of study procedure.
   - Patient is either:
     - Symptomatic with carotid stenosis ≥ 50% as determined by angiography using NASCET methodology.

        - Symptomatic is defined as amaurosis fugax ipsilateral to the carotid lesion; TIA or non-disabling stroke within 180 days of the procedure within the hemisphere supplied by the target vessel; or
    - Asymptomatic with carotid stenosis ≥ 80% as determined by angiography using NASCET methodology.
- Patient has a target lesion located at the carotid bifurcation and / or proximal ICA.
- Patient has a single de novo or restenotic (post-CEA) target lesion that can be covered by a single 40 mm stent.
- Patient has a stent landing zone diameter between 3.7 mm and 9.0 mm

High Risk Inclusion Criteria

For inclusion in the study, a patient must have qualified in **at least one** High-Risk condition, as shown below.

Anatomic Conditions:

- Patient has surgically inaccessible lesions at or above the level of C2 or below the clavicle
- Patient is status / post-radical head or neck surgery or radiation therapy
- Patient has spinal immobility of the neck
- Patient has the presence of tracheostomy stoma
- Patient has laryngeal palsy or laryngectomy
- Patient has contralateral laryngeal nerve paralysis
- Patient has restenosis after a previous CEA

Co-morbid Conditions:

- Patient is ≥ 75 years of age at time of enrollment
- Patient has NYHA Class III or IV congestive heart failure (CHF)
- Patient has chronic obstructive pulmonary disease (COPD) with FEV < 30%
- Patient has a left ventricular ejection fraction (LVEF) < 30%
- Patient has documented uncontrolled diabetes
- Patient has unstable angina with ECG changes
- Patient has had a recent myocardial infarction (≥ 72 hours, < 30 days)
- Patient has coronary artery disease with two or more vessels with ≥ 70% stenosis
- Patient has planned coronary artery bypass grafting (CABG) or valve replacement surgery between 31-60 days after the carotid artery stenting (CAS) procedure
- Patient has contralateral total occlusion of the internal carotid artery (ICA)

Patients were <u>not</u> permitted to enroll in the SCAFFOLD study if they met any of the following exclusion criteria:

General Exclusion Criteria:

- Patient has life expectancy of less than 1 year.
- Patient is experiencing (or has experienced) an evolving, acute, or recent disabling stroke.
- Patient has anticipated or potential sources of emboli (e.g. atrial fibrillation, known previously symptomatic patent foramen ovale (PFO), mechanical heart valve, or deep vein thrombosis (DVT) treated within 6-months).
- Patient has had an acute myocardial infarction within 72 hours prior to index procedure.
- Patient has had any major surgical procedure (i.e., intraabdominal or intrathoracic surgery or any surgery / interventional procedure involving cardiac or vascular system) within 30 days of the index procedure.
- Patient plans to have a major surgical procedure (i.e., intraabdominal or intrathoracic surgery or any surgery / interventional procedure involving cardiac or vascular system) within 30 days after index procedure.
- Patient has a history of major, disabling ipsilateral stroke with residual deficit that may confound the neurological subject assessments.
- Patient has known severe carotid stenosis contralateral to the target lesion requiring treatment within 30 days following the index procedure.
- Patient has a modified Rankin Scale of > 3 or has another neurological deficit, not due to stroke that may confound the neurological subject assessments.
- Patient has chronic renal insufficiency (serum creatinine ≥ 2.5 mg / dL).
- Patient has platelet count < 100,000 / μL.
- Patient has known sensitivity to heparin or previous incident of Heparin-Induced Thrombocytopenia (HIT) type II.
- Patient has contraindication to standard of care study medications, including antiplatelet therapy.
- Patient has known sensitivity to contrast media that cannot be adequately controlled with pre-medication.
- Patient has known bleeding diathesis or hypercoagulable state or refuses blood transfusions.
- Patient has intracranial pathology that, in the opinion of the investigator, makes the patient inappropriate for study participation (e.g. brain tumor, arteriovenous malformation (AVM), cerebral aneurysm) or would confound neurological evaluation.
- Patient had intracranial hemorrhage within the last 90 days.
- Patient is contraindicated for the GORE Embolic Filter per the criteria outlined in the IFU.
- Patient is currently enrolled in another investigational study protocol that has not completed its primary endpoint or that will confound the current study endpoints.
- Patients who are involved in the long-term surveillance of a clinical study are eligible.

Angiographic Exclusion Criteria:

- Patient has a total occlusion of the target carotid arteries (i.e., CCA or ICA).
- Patient has a previously placed arterial stent distal to or including the origin of the ipsilateral great vessel (includes a stent anywhere in the ICA, CCA or brachiocephalic artery).
- Patient has severe lesion calcification that may restrict the full deployment of the carotid stent.
- Patient has the presence of filling defect or thrombus in target vessel.
- Patient has occlusion or presence of "string sign" of the target vessel.
- Patient has carotid (intracranial) stenosis located distal to target stenosis that is more severe than target stenosis.
- Patient has ≥ 50% stenosis of the common carotid artery (CCA) proximal to the target lesion.
- Patient has known mobile plaque, thrombus, or excessive calcification in the aortic arch.
- Patient has aneurysmal carotid bifurcation on the ipsilateral side.
- Patient has tortuous anatomy or disease morphology which would prohibit the safe placement of guide catheter, sheaths, embolic protection systems or stent systems within the access or target vessel.

2. Follow-up Schedule

All patients were scheduled to return for follow-up examinations at 30 days (± 7 days), 6 months (± 14 days), 1 year (± 30 days), and 2 and 3 years (± 45 days) postoperatively, as shown in **Table 6** below. Adverse events and complications were recorded at all visits. To determine patient eligibility, a screening committee reviewed pre-operative angiography and/or computed tomography angiography (CTA), along with patient medical history, for assessment of entry criteria and approval prior to the study procedure.

The screening committee was comprised of an interdisciplinary team of study investigators with pertinent knowledge in carotid stenting, and operated under pre-specified procedures as outlined in the Screening Committee Charter. Prior to a patient being enrolled in the study, the investigational site received confirmation from the screening committee that the patient was eligible to be enrolled. Although patients may have been deemed eligible to be enrolled, it was still the responsibility of the investigator to assess all inclusion and exclusion criteria prior to enrollment.

The key timepoints are shown below in the tables summarizing the safety and effectiveness results.

Table 6: Schedule of Events

Procedure or Evaluation	Screening	Pre-procedure	Procedure/ Enrollment	Post-Procedure (prior to hospital discharge)	30 days (±7 days)	6 months (±14 days)	1 Year (±30 days)	2 & 3 Years (±45 days)	Unscheduled	Early Withdrawal
Informed Consent	X									
Demographics & Medical History	X									
Exam & Vital Signs[7]	X[6]			X	X	X	X	X	X[5]	X
NIH Stroke Scale[1]		X		X	X	X	X	X	X[5]	X
Modified Rankin Scale[6]	X				X	X	X	X	X[5]	X
CT Scan or MRI	X[2]									
Carotid Duplex Ultrasound	X[3]				X	X	X	X	X[5]	X
Cerebral Angiography			X						X[5]	
Screening angiogram or CTA	X									
Screening Committee review	X									
12-lead ECG[6]	X			X					X[5]	
Chemistry[6] (BUN, Creatinine)	X								X[5]	
Hematology[6] (CBC with Platelets)	X			X					X[5]	
Cardiac Enzymes (Troponin)		X		X					X[5]	
Pregnancy Test[4]		X								
Assess Concomitant Medications(antiplatelet or anticoagulant therapy)	X	X	X	X	X	X	X	X	X	X
Assess Adverse Events			X	X	X	X	X	X	X	X

[1] Neurological assessments by a physician certified in the administration of NIHSS or research personnel certified in the administration of NIHSS
[2] Required for symptomatic patients only within 180 days prior to index procedure
[3] Obtained within the 60 days preceding the index procedure
[4] Obtained within the 10 days preceding the index procedure. Pregnancy test (via urine or blood) required for females of childbearing potential
[5] To be done when clinically indicated
[6] May be obtained at either screening or pre-procedure visit
[7] Vital Signs include: Blood Pressure, Pulse, and respirations. Collection of height and weight will be done at screening. Temperature should be collected pre- and post- procedure at a minimum

3. Clinical Endpoints

The primary endpoint included a composite of major adverse events (MAE): death, any stroke, or myocardial infarction (MI) through 30 days post-index procedure and ipsilateral stroke between 31 days and 1 year. All primary endpoint events were adjudicated and determined by the study Clinical Events Committee.

Secondary endpoints included the following:

- Stent Technical Success: Successful deployment of a GCS.
- Embolic Protection Device (EPD) Technical Success: Device delivered, placed, and retrieved without requiring assisting interventional methods.
- Procedure Success: Successful GCS deployment, < 30% residual angiographic stenosis by visual assessment post-procedure in the target lesion and no in-hospital (pre-discharge) Major Adverse Event.
- 30-day Major Adverse Events: Composite of death, any stroke, or myocardial infarction through 30 days post-index procedure
- In-stent Restenosis: Measured as percent stenosis at follow-up evaluation within the stented lesion or within 5 mm proximal or distal to the stent. Additionally, will assess percent of subjects with stenosis ≥ 50% by ultrasound and ≥ 80% by angiographic evaluation.
- Target Lesion Revascularization (TLR): any clinically driven revascularization procedure of the original treatment site, including angioplasty, stenting, endarterectomy, or thrombolysis, performed to open or increase the luminal diameter inside or within 5 mm of the previously treated lesion.

B. Accountability of PMA Cohort

At the time of database lock, of 312 patients enrolled in the PMA study, 100% (312) patients were available for analysis at the completion of the study, the 1-year post-operative visit.

After the first 100 subjects were enrolled, the screening committee retrospectively reviewed anatomical criteria from angiograms and MR/CT; 38 subjects were deemed ineligible by this review. The most commonly occurring reasons for ineligibility were that the subject did not meet the inclusion criterion of having a target lesion located at the carotid bifurcation and/or proximal ICA, met the angiographic exclusion criteria of having severe lesion calcification that may restrict the full deployment of the carotid stent or tortuous anatomy or disease morphology which would prohibit the safe placement of guide catheter, sheaths, embolic protection systems or stent systems within the access or target vessel, or did not meet the specified high risk exclusion criteria of having surgically inaccessible lesions at or above the level of c2 or below the clavicle. An additional 9 subjects were enrolled in the study and subsequently found to have an inclusion or exclusion eligibility criteria deviation. The most commonly occurring reasons for ineligibility among these 9 subjects were that the subject was enrolled with a history of atrial fibrillation (a general exclusion criterion for the study) or with an asymptomatic stenosis of < 80%. A total of 47 subjects were deemed ineligible for

inclusion in the study; 265 patients were treated per protocol, and study results will be presented for these subjects below. The intent-to-treat cohort of all 312 subjects enrolled in the study, regardless of the final eligibility determination, was also analyzed; results were consistent with the per-protocol cohort.

Of the 265 per-protocol subjects, two hundred thirty-five (235) subjects have completed the 1-year study interval, 1 subject evaluation was pending and later determined to be missed, 14 visits were missed and 15 subjects discontinued prematurely. A summary of subject disposition is presented in **Table 7**.

Table 7. Subject Disposition

All Per-Protocol Subjects (N=265)	**Pre-Discharge**	**30 Days[1]**	**6 Months**	**1 Year**
Discontinued Prior to Interval	NA	1	5	10
Not Reached Start of Interval	NA	0	0	0
Evaluation Not Expected[2]	0	0	0	0
Available for Follow-up[3]	265	264	260	255
With Follow-up Evaluation	265 (100.0%)	261 (98.9%)	247 (95.0%)	235 (92.2%)
In Protocol Window	247 (93.2%)	225 (85.2%)	192 (73.8%)	204 (80.0%)
Outside Protocol Window	18 (6.8%)	36 (13.6%)	55 (21.2%)	31 (12.2%)
Pending Evaluation	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.4%)
Without Evaluation	0 (0.0%)	3 (1.1%)	13 (5.0%)	19 (7.5%)
Discontinued in Interval	0 (0.0%)	0 (0.0%)	1 (0.4%)	5 (2.0%)
Missed Visit	0 (0.0%)	3 (1.1%)	12 (4.6%)	14 (5.5%)

Percentages use Subjects Available for Interval Follow-up as the denominator.
NA = Not Applicable
[1] Follow-up windows are: 30 Days (30±7 days) 6 Months (180±14 days) 1 Year (365±30 days) and 2 and 3 Years (730 and 1095 ±45 days).
[2] For technical failures, follow-up at 30 days is the only evaluation expected.
[3] Subjects Available for Interval Follow-up is equal to Total Number of Subjects minus Subjects Discontinued Prior to Interval, Subjects Not Reached Start of Interval, and Evaluation Not Expected.

C. Study Population Demographics and Baseline Parameters

One hundred seventy-six (176) men and 89 women with a median age of 74 years (range 45 to 92) were enrolled in the study. Subject demographics are summarized in **Table 8**. The demographics of the study population are typical for a carotid artery stenting study performed in the US.

Table 8. Subject Demographics

All Per-Protocol Subjects	
Number of Subjects	265
Sex at Birth	N = 265
Male	176 (66.4%)
Female	89 (33.6%)
Ethnicity	N = 263
Hispanic or Latino	5 (1.9%)
Not Hispanic or Latino	258 (98.1%)
Race	N = 265
American Indian or Alaska Native	1 (0.4%)
Asian	2 (0.8%)
Black	7 (2.6%)
White	253 (95.5%)
Hawaiian	0 (0.0%)
Other Race	3 (1.1%)
Age at Procedure (years)	N = 265
Mean (Std Dev)	73.1 (8.8)
Median	74.4
(Min, Max)	(45.8, 92.8)

1. Subject Medical History

   A summary of subject medical history is provided in **Table 9**. A total of 33 subjects (12.5%) were reported to be symptomatic, 249 (94%) were reported as having hypertension and 107 (40%) were reported as having a history of diabetes.

Table 9. Subject Medical History

All Per-Protocol Subjects (N = 265)	
Carotid Disease and Symptoms	
Previous carotid disease	47.2% (125/265)
Etiology of current carotid disease	N = 265
Atherosclerosis	207 (78.1%)
Radiation	9 (3.4%)
Restenosis	43 (16.2%)
Other	1 (0.4%)
Unknown	5 (1.9%)
Symptomatic	12.5% (33/265)
Evidence of non-carotid morphology	6.1% (2/33)
History of ischemic stroke	18.1% (48/265)
Location of most recent ischemic stroke	N = 43

All Per-Protocol Subjects (N = 265)	
Ipsilateral	27 (62.8%)
Contralateral	16 (37.2%)
History of TIA	15.1% (40/265)
Location of most recent TIA	N = 33
Ipsilateral	25 (75.8%)
Contralateral	8 (24.2%)
Ipsilateral Amaurosis Fugax or TMB	3.4% (9/265)
Endarterectomy	29.8% (79/265)
Location of most recent endarterectomy	N = 79
Ipsilateral	53 (67.1%)
Contralateral	26 (32.9%)
Vascular and Cardiovascular History	
Coronary artery disease	62.6% (166/265)
Peripheral vascular disease	37.0% (98/265)
Myocardial infarction	26.8% (71/265)
Previous Cardiovascular Intervention	
PCI	38.1% (101/265)
Aortic / mitral valve surgery	3.8% (10/265)
CABG	27.2% (72/265)
Radiotherapy in cerebral circulation	3.8% (10/265)
General Medical History	
Diabetes Mellitus	40.4% (107/265)
Hypertension	94.0% (249/265)
Cigarette Smoking	N = 265
Current or stopped < 12 Months ago	67 (25.3%)
Previous (stopped > 12 Months ago)	139 (52.5%)
Never	59 (22.3%)

2. Procedure Characteristics

Procedure characteristics are summarized in **Table 10** below. The mean lesion length was 20 mm. The mean target lesion percent stenosis was 84.9%.

Table 10. Procedure Characteristics

All Per-Protocol Subjects (N = 265)	
Angiography performed	100.0% (265/265)
Bovine Arch	15.8% (42/265)
Pre-procedure ECA < 50% stenosis	51.7% (137/265)
Pre-dilation required before EPD deploy	5.7% (15/265)
Pre-dilation required before stent deploy	79.6% (211/265)
Post-dilation performed after stent deploy	92.5% (245/265)
Target Lesion Side	N = 265
Right	144 (54.3%)

All Per-Protocol Subjects (N = 265)	
Left	121 (45.7%)
Arch Type	N = 265
Type I	133 (50.2%)
Type II	120 (45.3%)
Type III	12 (4.5%)
Arterial Access Site	N = 265
Left femoral	15 (5.7%)
Right femoral	244 (92.1%)
Other	6 (2.3%)
Target Lesion Location	N = 265
ICA	235 (88.7%)
Bifurcation	30 (11.3%)
Target vessel reference diameter (mm)	N = 265
Mean (Std Dev)	5.6 (1.0)
Median	5.5
(Min, Max)	(3.7, 9.0)
Target lesion length (mm)	N = 265
Mean (Std Dev)	20.0 (9.0)
Median	20.0
(Min, Max)	(1.0, 40.0)
Target lesion % stenosis	N = 265
Mean (Std Dev)	84.9 (6.3)
Median	85.0
(Min, Max)	(50.0, 99.0)

3. Procedure Outcomes

A summary of procedure outcomes is provided in **Table 11**. All study devices (100%) were successfully delivered to the target lesion with a mean residual stenosis of 11.8% at the completion of the study procedure.

Table 11. Procedure Outcomes

All Per-Protocol Subjects (N = 265)	
Gore Carotid Stent attempted	100.0% (265/265)
Gore Embolic Filter successfully used	94.7% (251/265)
Additional EPD used	4.5% (12/265)
Gore Carotid Stent successfully implanted	100.0% (265/265)
Other stent implanted	0.8% (2/265)
More than one stent implanted	3.0% (8/265)

All Per-Protocol Subjects (N = 265)	
Gore Embolic Filter total dwell time (minutes)	N = 251
Mean (Std Dev)	14.2 (9.3)
Median	11.0
(Min, Max)	(1.0, 60.0)
Post-procedure target lesion % stenosis	N = 265
Mean (Std Dev)	11.8 (9.5)
Median	10.0
(Min, Max)	(0.0, 42.0)
Contrast volume (cc)	N = 265
Mean (Std Dev)	124.2 (62.2)
Median	120.0
(Min, Max)	(15.0, 400.0)
Total fluoroscopy time (minutes)	N = 263
Mean (Std Dev)	16.9 (9.5)
Median	14.5
(Min, Max)	(3.8, 60.0)
Total procedure time (minutes)	N = 265
Mean (Std Dev)	53.7 (23.5)
Median	50.0
(Min, Max)	(17.0, 148.0)
Total hospital time (days)	N = 265
Mean (Std Dev)	1 (1)
Median	1
(Min, Max)	(1, 13)

D. Safety and Effectiveness Results

1. Safety and Effectiveness Results

The primary analysis of safety and effectiveness was based on the per-protocol cohort of 265 patients with 244 patients with evaluable endpoint information through 1 year. The primary study endpoint was defined as a composite of Major Adverse Events (MAEs) defined as death, any stroke, or myocardial infarction (MI) through 30 days post-index procedure, and ipsilateral stroke between 31 days and 1 year. Eight (8) subjects (3.0%) had one or more MAEs through 30 days post-index procedure. Of those MAEs, four (1.5%) were due to myocardial infarction, three (1.1%) were due to major stroke, and one (0.4%) was due to death resulting from pulseless electrical activity at day 15. Three subjects (1.2%) had ipsilateral stroke between 31 days and 1 year post-index procedure. All three of the strokes reported were ischemic and minor with one

occurring at day 50, one at day 249 and one at day 276 post-index procedure. **Table 12** lists the MAEs through 30 days post-index procedure and ipsilateral stroke between 31 days and 1 year.

Table 12. Major Adverse Events through 30 Days and 1 year

All Per-Protocol Subjects (N=265)		**95% CI[3]**
Subjects Evaluable for 30-Day MAE[1]	264 (99.6%)	
Not Evaluable for 30-Day MAE	1 (0.4%)	
Unsuccessful Procedure	0 (0.0%)	
Discontinued Early	0 (0.0%)	
Missing or Insufficient Follow-up	1 (0.4%)	
Subjects With One or More 30-Day MAE	8 (3.0%)	[1.3%, 5.9%]
Death	1 (0.4%)	[0.0%, 2.1%]
Myocardial Infarction	4 (1.5%)	[0.4%, 3.8%]
Q-Wave MI	0 (0.0%)	[0.0%, 1.4%]
Non-Q-Wave MI	4 (1.5%)	[0.4%, 3.8%]
Stroke	3 (1.1%)	[0.2%, 3.3%]
Major Stroke	3 (1.1%)	[0.2%, 3.3%]
Ischemic Stroke	2 (0.8%)	[0.1%, 2.7%]
Ipsilateral	2 (0.8%)	[0.1%, 2.7%]
Non-ipsilateral	0 (0.0%)	[0.0%, 1.4%]
Hemorrhagic Stroke	1 (0.4%)	[0.0%, 2.1%]
Ipsilateral	1 (0.4%)	[0.0%, 2.1%]
Non-ipsilateral	0 (0.0%)	[0.0%, 1.4%]
Minor Stroke	0 (0.0%)	[0.0%, 1.4%]
Ischemic Stroke	0 (0.0%)	[0.0%, 1.4%]
Ipsilateral	0 (0.0%)	[0.0%, 1.4%]
Non-ipsilateral	0 (0.0%)	[0.0%, 1.4%]
Hemorrhagic Stroke	0 (0.0%)	[0.0%, 1.4%]
Ipsilateral	0 (0.0%)	[0.0%, 1.4%]
Non-ipsilateral	0 (0.0%)	[0.0%, 1.4%]
Subjects Evaluable for 1-year MAE[2]	244 (92.1%)	
Not Evaluable for 1-year MAE	21 (7.9%)	
Unsuccessful Procedure	0 (0.0%)	
Discontinued Early	6 (2.3%)	
Missing or Insufficient Follow-up	15 (5.7%)	
Subjects With One or More 1-year MAE	11 (4.5%)	[2.3%, 7.9%]
30-Day MAE	8 (3.3%)	[1.4%, 6.4%]
Ipsilateral Stroke (31-365 Days)	3 (1.2%)	[0.3%, 3.6%]

[1] Experienced MAE within 30 days or MAE-free with at least 23 days clinical follow-up

[2] Experienced 30-Day MAE or 31-365-day ipsilateral stroke, or MAE-free with at least 335 days clinical follow-up
[3] Clopper-Pearson exact confidence interval

The overall weighted MAE proportion was 4.5%, which was identical within rounding error to the overall unweighted proportion of 4.5% (11/244). The 95.1% one-sided upper confidence limit (UCL) for the weighted MAE proportion was 8.5%, which is substantially lower than the pre-specified weighted performance goal of 16.9%, leading to the conclusion of acceptable performance of the test device on the basis of 1-year MAE. The corresponding binomial test versus the 16.9% performance goal produced a significant one-sided $p < 0.00001$.

2. Secondary Effectiveness Endpoint Results

As described above, secondary endpoints were capture to evaluate performance of the stent and EPD. Results are shown in **Tables 13-15**. Technical success, as defined as successful deployment of the GCS and successful delivery, placement, and retrieval of the EPD, was for the stent and EPD were 100% and 94.7% respectively. Procedure Success as defined by successful stent deployment, < 30% residual angiographic stenosis by visual assessment post-procedure in the target lesion and no in-hospital MAEs was 94.3%.

Table 13. Secondary Endpoints

All Per-Protocol Subjects (N=265)	
Stent Technical Success[1]	100.0% (265/265)
Stent Technical Failure	0.0% (0/265)
EPD Technical Success[2]	94.7% (251/265)
EPD Technical Failure	5.3% (14/265)
Procedure Success[3]	94.3% (250/265)
Procedure Failure	5.7% (15/265)
Stent Technical Failure	0.0% (0/265)
≥30% Residual Stenosis	4.2% (11/265)
In-hospital MAE	1.5% (4/265)

[1] Successful deployment of a GORE Carotid Stent
[2] GORE Embolic Filter delivered, placed, and retrieved without requiring assisting interventional methods
[3] Stent Technical Success, < 30% residual stenosis and no in-hospital MAE

Kaplan-Meier estimated for in-stent restenosis as measured as percent stenosis (≥ 50% by ultrasound and ≥ 80% by angiographic evaluation) at follow-up evaluation within the stented lesion or within 5 mm proximal or distal to the stent are shown in **Table 14**.

Table 14. Kaplan-Meier Estimates of Probability of Restenosis

Time from Procedure (Months)	At Risk at Start of Interval	Events During Interval (Cumulative)	Censored During Interval (Cumulative)	Probability of Restenosis	95% C.I.
All Per-Protocol Subjects (N=265)					
0	265	0 (0)	0 (0)	0.0%	(0.0%, 0.0%)
1	265	0 (0)	5 (5)	0.0%	(0.0%, 0.0%)
6	260	0 (0)	11 (16)	0.0%	(0.0%, 0.0%)
12	249	4 (4)	104 (120)	1.8%	(0.7%, 4.7%)
Time defined as time from index procedure to restenosis, or last follow-up if censored. Event defined as restenosis (≥80% diameter stenosis by core lab angiographic analysis).					

Five subjects underwent a clinically-driven TLR, including angioplasty, stenting, endarterectomy, or thrombolysis, performed to open or increase the luminal diameter inside or within 5 mm of the previously treated lesion, as described in **Table 15**.

Table 15. Freedom from Clinically Driven Target Lesion Revascularization (TLR) Kaplan-Meier Estimates of Probability of Freedom from Clinically Driven TLR

Time from Procedure (Months)	At Risk at Start of Interval	Events During Interval (Cumulative)	Censored During Interval (Cumulative)	Probability of Freedom from Clinically Driven TLR	95% C.I.
All Per-Protocol Subjects (N=265)					
0	265	0 (0)	0 (0)	100.0%	(100.0%, 100.0%)
1	265	0 (0)	5 (5)	100.0%	(100.0%, 100.0%)
6	260	0 (0)	11 (16)	100.0%	(100.0%, 100.0%)
12	249	5 (5)	103 (119)	97.8%	(94.8%, 99.1%)
Time defined as time from index procedure to first clinically driven TLR, or last follow-up if censored. Event defined as any clinically driven target lesion revascularization. Clinically driven defined as core lab angiographic diameter stenosis ≥80%, or diameter stenosis ≥50% with clinical symptoms.					

3. Adverse Events

Adverse events (AEs) were defined as any untoward medical occurrences (that the investigator feels were reportable events) experienced by a subject whether device related or not. Adverse Device Effects were defined as any adverse events related to the use of an investigational medical device. Serious Adverse Events were defined as any events that:

- led to death
- led to serious deterioration in the health of a subject that:
- resulted in a life threatening illness or injury
- resulted in a permanent impairment of a body structure or a body function

- required inpatient hospitalization or prolongation of existing hospitalization
- resulted in medical or surgical intervention to prevent permanent impairment to a body structure or a body function
- led to fetal distress, fetal death or a congenital abnormality or birth defect

i. Adverse Events through the 30-Day Follow-Up

Of 265 subjects, one hundred ten (110) subjects (41.5%) experienced an adverse event through the 30-day follow-up period. Of those subjects, one (0.4%) experienced a stent-related adverse event due to internal carotid partial in-stent thrombus at day 4 post-index procedure and was treated with medication and hospitalization. Sixty-seven (67) subjects (25.3%) experienced one or more procedure-related events. The majority of those events (7.5%) were due to minor episodes of hypotension. Four (4) subjects (1.5%) experienced one or more medication-related events as a result of the antiplatelet therapy regimen required during their participation in the study. Eight (8) subjects (3%) experienced one or more disease-related events; 53 subjects (20%) experienced one or more unrelated events; 14 subjects (5.3%) experienced one or more events of unknown study relationship; and no subjects experienced EPD-related events. **Tables 16 and 17** below summarize all adverse events through the 30-day follow-up by seriousness of event.

Table 16. Adverse Events through 30-Day Follow-Up by Study Relationship and Seriousness

	Seriousness of Event		
All Per-Protocol Subjects (N=265)	**Non-Serious**	**Serious[1]**	**Overall**
Subjects with Coded Adverse Events	90 (34.0%)	37 (14.0%) [3]	110 (41.5%)
Stent Related	0 (0.0%)	1 (0.4%)	1 (0.4%)
EPD Related	0 (0.0%)	0 (0.0%)	0 (0.0%)
Procedure Related	54 (20.4%)	18 (6.8%)	67 (25.3%)
Medication Related	3 (1.1%)	1 (0.4%)	4 (1.5%)
Disease Related	7 (2.6%)	1 (0.4%)	8 (3.0%)
Not Related	42 (15.8%)	16 (6.0%) [3]	53 (20.0%)
Relationship Unknown	9 (3.4%)	6 (2.3%)	14 (5.3%)

[1]Number of subject deaths related to a serious adverse event are presented in [ ].

Table 17. Adverse Events through 30-Day Follow-Up by MedDRA SOC, Preferred Term, and Seriousness

	Seriousness of Event		
All Per-Protocol Subjects (N=265)	**Non-Serious**	**Serious**	**Overall**
Subjects with Coded Adverse Events	90 (34.0%)	37 (14.0%)	110 (41.5%)
Vascular disorders	27 (10.2%)	7 (2.6%)	33 (12.5%)
Hypotension	17 (6.4%)	6 (2.3%)	23 (8.7%)

	Seriousness of Event		
All Per-Protocol Subjects (N=265)	**Non-Serious**	**Serious**	**Overall**
Hypertension	7 (2.6%)	-	7 (2.6%)
Haematoma	2 (0.8%)	-	2 (0.8%)
Deep vein thrombosis	1 (0.4%)	-	1 (0.4%)
Orthostatic hypotension	-	1 (0.4%)	1 (0.4%)
Peripheral artery stenosis	1 (0.4%)	-	1 (0.4%)
Thrombosis	1 (0.4%)	-	1 (0.4%)
Nervous system disorders	19 (7.2%)	9 (3.4%)	26 (9.8%)
Headache	10 (3.8%)	1 (0.4%)	11 (4.2%)
Carotid artery dissection	1 (0.4%)	1 (0.4%)	2 (0.8%)
Cerebrovascular accident	-	2 (0.8%)	2 (0.8%)
Dizziness	2 (0.8%)	-	2 (0.8%)
Hypoaesthesia	2 (0.8%)	-	2 (0.8%)
Seizure	-	2 (0.8%)	2 (0.8%)
Syncope	2 (0.8%)	-	2 (0.8%)
Transient ischaemic attack	-	2 (0.8%)	2 (0.8%)
Aphasia	1 (0.4%)	-	1 (0.4%)
Ataxia	-	1 (0.4%)	1 (0.4%)
Carpal tunnel syndrome	1 (0.4%)	-	1 (0.4%)
Haemorrhage intracranial	-	1 (0.4%)	1 (0.4%)
Hemiparesis	1 (0.4%)	-	1 (0.4%)
Presyncope	1 (0.4%)	-	1 (0.4%)
Visual field defect	1 (0.4%)	-	1 (0.4%)
Injury, poisoning and procedural complications	21 (7.9%)	4 (1.5%)	25 (9.4%)
Incision site haemorrhage	8 (3.0%)	-	8 (3.0%)
Incision site haematoma	4 (1.5%)	-	4 (1.5%)
Procedural hypotension	2 (0.8%)	1 (0.4%)	3 (1.1%)
Vascular pseudoaneurysm	1 (0.4%)	1 (0.4%)	2 (0.8%)
Anaemia postoperative	-	1 (0.4%)	1 (0.4%)
Autonomic dysreflexia	-	1 (0.4%)	1 (0.4%)
Incision site complication	1 (0.4%)	-	1 (0.4%)
Incision site oedema	1 (0.4%)	-	1 (0.4%)
Incision site pain	1 (0.4%)	-	1 (0.4%)
Laceration	1 (0.4%)	-	1 (0.4%)
Limb injury	1 (0.4%)	-	1 (0.4%)
Muscle strain	1 (0.4%)	-	1 (0.4%)
Wound	1 (0.4%)	-	1 (0.4%)
Cardiac disorders	13 (4.9%)	7 (2.6%)	19 (7.2%)
Bradycardia	8 (3.0%)	1 (0.4%)	8 (3.0%)
Angina pectoris	3 (1.1%)	2 (0.8%)	5 (1.9%)
Pulseless electrical activity	-	2 (0.8%)	2 (0.8%)
Acute myocardial infarction	-	1 (0.4%)	1 (0.4%)
Angina unstable	1 (0.4%)	-	1 (0.4%)
Cardiomyopathy	-	1 (0.4%)	1 (0.4%)

	Seriousness of Event		
All Per-Protocol Subjects (N=265)	**Non-Serious**	**Serious**	**Overall**
Sinus arrest	1 (0.4%)	-	1 (0.4%)
General disorders and administration site conditions	11 (4.2%)	4 (1.5%)	14 (5.3%)
Fatigue	3 (1.1%)	-	3 (1.1%)
Adverse drug reaction	2 (0.8%)	-	2 (0.8%)
Oedema peripheral	2 (0.8%)	-	2 (0.8%)
Asthenia	1 (0.4%)	-	1 (0.4%)
Chest discomfort	1 (0.4%)	-	1 (0.4%)
Chest pain	-	1 (0.4%)	1 (0.4%)
Chills	1 (0.4%)	-	1 (0.4%)
Gait disturbance	-	1 (0.4%)	1 (0.4%)
Non-cardiac chest pain	-	1 (0.4%)	1 (0.4%)
Pain	1 (0.4%)	-	1 (0.4%)
Peripheral swelling	1 (0.4%)	-	1 (0.4%)
Pyrexia	1 (0.4%)	-	1 (0.4%)
Swelling	1 (0.4%)	-	1 (0.4%)
Vascular stent thrombosis	-	1 (0.4%)	1 (0.4%)
Infections and infestations	10 (3.8%)	4 (1.5%)	14 (5.3%)
Urinary tract infection	4 (1.5%)	3 (1.1%)	7 (2.6%)
Groin infection	2 (0.8%)	-	2 (0.8%)
Cellulitis	1 (0.4%)	-	1 (0.4%)
Kidney infection	1 (0.4%)	-	1 (0.4%)
Laryngitis	1 (0.4%)	-	1 (0.4%)
Nasopharyngitis	1 (0.4%)	-	1 (0.4%)
Pneumonia	-	1 (0.4%)	1 (0.4%)
Respiratory tract infection	1 (0.4%)	-	1 (0.4%)
Sinusitis	1 (0.4%)	-	1 (0.4%)
Musculoskeletal and connective tissue disorders	8 (3.0%)	1 (0.4%)	9 (3.4%)
Pain in jaw	2 (0.8%)	-	2 (0.8%)
Arthralgia	1 (0.4%)	-	1 (0.4%)
Back pain	1 (0.4%)	-	1 (0.4%)
Lumbar spinal stenosis	-	1 (0.4%)	1 (0.4%)
Muscular weakness	1 (0.4%)	-	1 (0.4%)
Musculoskeletal discomfort	1 (0.4%)	-	1 (0.4%)
Myalgia	1 (0.4%)	-	1 (0.4%)
Neck pain	1 (0.4%)	-	1 (0.4%)
Pain in extremity	1 (0.4%)	-	1 (0.4%)
Gastrointestinal disorders	4 (1.5%)	4 (1.5%)	8 (3.0%)
Nausea	3 (1.1%)	-	3 (1.1%)
Gastrointestinal haemorrhage	-	2 (0.8%)	2 (0.8%)
Constipation	1 (0.4%)	-	1 (0.4%)
Intestinal obstruction	-	1 (0.4%)	1 (0.4%)
Odynophagia	1 (0.4%)	-	1 (0.4%)

	Seriousness of Event		
All Per-Protocol Subjects (N=265)	**Non-Serious**	**Serious**	**Overall**
Retroperitoneal haemorrhage	-	1 (0.4%)	1 (0.4%)
Vomiting	1 (0.4%)	-	1 (0.4%)
Respiratory, thoracic and mediastinal disorders	6 (2.3%)	3 (1.1%)	8 (3.0%)
Dyspnoea	2 (0.8%)	-	2 (0.8%)
Chronic obstructive pulmonary disease	-	1 (0.4%)	1 (0.4%)
Cough	1 (0.4%)	-	1 (0.4%)
Dyspnoea exertional	1 (0.4%)	-	1 (0.4%)
Hypoxia	-	1 (0.4%)	1 (0.4%)
Pulmonary mass	1 (0.4%)	1 (0.4%)	1 (0.4%)
Respiratory failure	-	1 (0.4%)	1 (0.4%)
Sleep apnoea syndrome	1 (0.4%)	-	1 (0.4%)
Blood and lymphatic system disorders	4 (1.5%)	2 (0.8%)	6 (2.3%)
Anaemia	4 (1.5%)	2 (0.8%)	6 (2.3%)
Thrombocytopenia	1 (0.4%)	-	1 (0.4%)
Renal and urinary disorders	4 (1.5%)	2 (0.8%)	6 (2.3%)
Chronic kidney disease	1 (0.4%)	1 (0.4%)	2 (0.8%)
Urinary retention	2 (0.8%)	-	2 (0.8%)
Nephrolithiasis	-	1 (0.4%)	1 (0.4%)
Neurogenic bladder	1 (0.4%)	-	1 (0.4%)
Investigations	4 (1.5%)	1 (0.4%)	5 (1.9%)
Blood pressure decreased	2 (0.8%)	-	2 (0.8%)
Blood creatinine increased	-	1 (0.4%)	1 (0.4%)
Body temperature decreased	1 (0.4%)	-	1 (0.4%)
Weight decreased	1 (0.4%)	-	1 (0.4%)
Eye disorders	3 (1.1%)	1 (0.4%)	4 (1.5%)
Vision blurred	2 (0.8%)	-	2 (0.8%)
Conjunctival haemorrhage	1 (0.4%)	-	1 (0.4%)
Diplopia	-	1 (0.4%)	1 (0.4%)
Metabolism and nutrition disorders	3 (1.1%)	-	3 (1.1%)
Hyperglycaemia	2 (0.8%)	-	2 (0.8%)
Hypoglycaemia	1 (0.4%)	-	1 (0.4%)
Psychiatric disorders	2 (0.8%)	-	2 (0.8%)
Depression	1 (0.4%)	-	1 (0.4%)
Insomnia	1 (0.4%)	-	1 (0.4%)
Mental status changes	1 (0.4%)	-	1 (0.4%)
Immune system disorders	1 (0.4%)	-	1 (0.4%)
Contrast media reaction	1 (0.4%)	-	1 (0.4%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	-	1 (0.4%)	1 (0.4%)
Pancreatic carcinoma	-	1 (0.4%)	1 (0.4%)

ii. Adverse Events through 1-Year Follow-Up

One hundred eighty-six (186) subjects (70.2%) experienced an adverse event through the 1-year follow-up period. Of those subjects, 13 (4.9%) experienced one or more stent-related adverse events:

- Thirteen (13) device-related events were due to in-stent carotid artery restenosis treated with revascularization.
- One (1) device-related event was due to internal carotid partial in-stent thrombus treated with medication and hospitalization.
- One (1) device-related event was an asymptomatic occluded carotid stent with no treatment given.
- One (1) device-related event was for questionable carotid stent fracture reported by the site during revascularization of the in-stent carotid artery restenosis.

Sixty-seven (67) subjects (25.3%) experienced one or more procedure-related events. The majority of those events (7.5%) were due to minor episodes of hypotension. Seven (7) subjects (2.6%) experienced one or more medication-related events as a result of the antiplatelet therapy regimen required during their participation in the study. Twenty-seven (27) subjects (10.2%) experienced one or more disease-related events; 145 subjects (54.7%) experienced one or more unrelated events; 18 subjects (6.8%) experienced one or more events of unknown study relationship; and no subjects experienced EPD-related events. **Tables 18 and 19** summarize all adverse events through the 1-year follow-up by seriousness of event.

Table 18. Adverse Events through 1-Year Follow-Up by Study Relationship and Seriousness

	Seriousness of Event		
All Per-Protocol Subjects (N=265)	**Non-Serious**	**Serious[1]**	**Overall**
Subjects with Coded Adverse Events	148 (55.8%)	104 (39.2%) [12]	186 (70.2%)
Stent Related	2 (0.8%)	11 (4.2%)	13 (4.9%)
EPD Related	0 (0.0%)	0 (0.0%)	0 (0.0%)
Procedure Related	54 (20.4%)	18 (6.8%)	67 (25.3%)
Medication Related	5 (1.9%)	2 (0.8%)	7 (2.6%)
Disease Related	15 (5.7%)	13 (4.9%)	27 (10.2%)
Not Related	109 (41.1%)	79 (29.8%) [12]	145 (54.7%)
Relationship Unknown	13 (4.9%)	6 (2.3%)	18 (6.8%)

[1]Number of subject deaths related to a serious adverse event are presented in [ ].

Table 19. Adverse Events through 1-Year Follow-Up by MedDRA SOC, Preferred Term, and Seriousness

	Seriousness of Event		
All Per-Protocol Subjects (N=265)	**Non-Serious**	**Serious**	**Overall**
Subjects with Coded Adverse Events	148 (55.8%)	104 (39.2%)	186 (70.2%)
Nervous system disorders	39 (14.7%)	32 (12.1%)	66 (24.9%)
Headache	14 (5.3%)	1 (0.4%)	15 (5.7%)
Carotid artery stenosis	1 (0.4%)	9 (3.4%)	10 (3.8%)
Dizziness	8 (3.0%)	2 (0.8%)	10 (3.8%)
Cerebrovascular accident	-	6 (2.3%)	6 (2.3%)
Hypoaesthesia	4 (1.5%)	1 (0.4%)	5 (1.9%)
Syncope	5 (1.9%)	-	5 (1.9%)
Transient ischaemic attack	-	4 (1.5%)	4 (1.5%)
Amnesia	2 (0.8%)	-	2 (0.8%)
Carotid artery dissection	1 (0.4%)	1 (0.4%)	2 (0.8%)
Carpal tunnel syndrome	1 (0.4%)	1 (0.4%)	2 (0.8%)
Hemiparesis	1 (0.4%)	1 (0.4%)	2 (0.8%)
Presyncope	1 (0.4%)	1 (0.4%)	2 (0.8%)
Seizure	-	2 (0.8%)	2 (0.8%)
Aphasia	1 (0.4%)	-	1 (0.4%)
Ataxia	-	1 (0.4%)	1 (0.4%)
Balance disorder	1 (0.4%)	-	1 (0.4%)
Cerebral artery stenosis	1 (0.4%)	-	1 (0.4%)
Cervical radiculopathy	1 (0.4%)	-	1 (0.4%)
Dementia Alzheimer's type	-	1 (0.4%)	1 (0.4%)
Diabetic neuropathy	1 (0.4%)	-	1 (0.4%)
Dysgraphia	1 (0.4%)	-	1 (0.4%)
Encephalopathy	-	1 (0.4%)	1 (0.4%)
Generalised tonic-clonic seizure	-	1 (0.4%)	1 (0.4%)
Haemorrhage intracranial	-	1 (0.4%)	1 (0.4%)
Ischaemic stroke	-	1 (0.4%)	1 (0.4%)
Nerve compression	1 (0.4%)	-	1 (0.4%)
Parkinson's disease	-	1 (0.4%)	1 (0.4%)
Post herpetic neuralgia	1 (0.4%)	-	1 (0.4%)
Radiculopathy	1 (0.4%)	-	1 (0.4%)
Tremor	1 (0.4%)	-	1 (0.4%)
Vertebral artery stenosis	1 (0.4%)	-	1 (0.4%)
Visual field defect	1 (0.4%)	-	1 (0.4%)
Vascular disorders	46 (17.4%)	18 (6.8%)	61 (23.0%)
Hypotension	24 (9.1%)	9 (3.4%)	33 (12.5%)

	Seriousness of Event		
All Per-Protocol Subjects (N=265)	**Non-Serious**	**Serious**	**Overall**
Hypertension	9 (3.4%)	-	9 (3.4%)
Haematoma	5 (1.9%)	-	5 (1.9%)
Aortic aneurysm	1 (0.4%)	3 (1.1%)	4 (1.5%)
Intermittent claudication	2 (0.8%)	2 (0.8%)	4 (1.5%)
Aortic stenosis	-	2 (0.8%)	2 (0.8%)
Deep vein thrombosis	2 (0.8%)	-	2 (0.8%)
Orthostatic hypotension	1 (0.4%)	1 (0.4%)	2 (0.8%)
Peripheral arterial occlusive disease	2 (0.8%)	-	2 (0.8%)
Peripheral artery occlusion	2 (0.8%)	-	2 (0.8%)
Aortic aneurysm rupture	-	1 (0.4%)	1 (0.4%)
Labile hypertension	1 (0.4%)	-	1 (0.4%)
Peripheral artery stenosis	1 (0.4%)	-	1 (0.4%)
Peripheral vascular disorder	1 (0.4%)	-	1 (0.4%)
Subclavian artery thrombosis	-	1 (0.4%)	1 (0.4%)
Thrombosis	1 (0.4%)	-	1 (0.4%)
Infections and infestations	35 (13.2%)	19 (7.2%)	49 (18.5%)
Urinary tract infection	14 (5.3%)	3 (1.1%)	17 (6.4%)
Pneumonia	2 (0.8%)	10 (3.8%)	12 (4.5%)
Bronchitis	4 (1.5%)	1 (0.4%)	5 (1.9%)
Cellulitis	2 (0.8%)	2 (0.8%)	4 (1.5%)
Sinusitis	4 (1.5%)	-	4 (1.5%)
Influenza	3 (1.1%)	-	3 (1.1%)
Diverticulitis	1 (0.4%)	1 (0.4%)	2 (0.8%)
Groin infection	2 (0.8%)	-	2 (0.8%)
Herpes zoster	2 (0.8%)	-	2 (0.8%)
Sepsis	-	2 (0.8%)	2 (0.8%)
Upper respiratory tract infection	2 (0.8%)	-	2 (0.8%)
Acute sinusitis	1 (0.4%)	-	1 (0.4%)
Appendicitis	-	1 (0.4%)	1 (0.4%)
Ear infection	1 (0.4%)	-	1 (0.4%)
Helicobacter gastritis	1 (0.4%)	-	1 (0.4%)
Kidney infection	1 (0.4%)	-	1 (0.4%)
Laryngitis	1 (0.4%)	-	1 (0.4%)
Localised infection	1 (0.4%)	-	1 (0.4%)
Nasopharyngitis	1 (0.4%)	-	1 (0.4%)
Osteomyelitis	-	1 (0.4%)	1 (0.4%)
Otitis media	1 (0.4%)	-	1 (0.4%)
Prostate infection	1 (0.4%)	-	1 (0.4%)
Respiratory tract infection	1 (0.4%)	-	1 (0.4%)

	Seriousness of Event		
All Per-Protocol Subjects (N=265)	**Non-Serious**	**Serious**	**Overall**
Septic shock	-	1 (0.4%)	1 (0.4%)
Staphylococcal bacteraemia	1 (0.4%)	-	1 (0.4%)
Tuberculosis	1 (0.4%)	-	1 (0.4%)
Injury, poisoning and procedural complications	36 (13.6%)	10 (3.8%)	43 (16.2%)
Incision site haemorrhage	8 (3.0%)	-	8 (3.0%)
Laceration	6 (2.3%)	-	6 (2.3%)
Incision site haematoma	5 (1.9%)	-	5 (1.9%)
Procedural hypotension	2 (0.8%)	1 (0.4%)	3 (1.1%)
Carotid artery restenosis	1 (0.4%)	1 (0.4%)	2 (0.8%)
Fall	1 (0.4%)	1 (0.4%)	2 (0.8%)
Vascular pseudoaneurysm	1 (0.4%)	1 (0.4%)	2 (0.8%)
Anaemia postoperative	-	1 (0.4%)	1 (0.4%)
Ankle fracture	1 (0.4%)	-	1 (0.4%)
Autonomic dysreflexia	-	1 (0.4%)	1 (0.4%)
Comminuted fracture	-	1 (0.4%)	1 (0.4%)
Contusion	1 (0.4%)	-	1 (0.4%)
Extradural haematoma	-	1 (0.4%)	1 (0.4%)
Hand fracture	1 (0.4%)	-	1 (0.4%)
Head injury	1 (0.4%)	-	1 (0.4%)
Incision site complication	1 (0.4%)	-	1 (0.4%)
Incision site oedema	1 (0.4%)	-	1 (0.4%)
Incision site pain	1 (0.4%)	-	1 (0.4%)
Joint injury	-	1 (0.4%)	1 (0.4%)
Ligament rupture	1 (0.4%)	-	1 (0.4%)
Limb injury	1 (0.4%)	-	1 (0.4%)
Muscle strain	1 (0.4%)	-	1 (0.4%)
Skin abrasion	1 (0.4%)	-	1 (0.4%)
Subdural haematoma	-	1 (0.4%)	1 (0.4%)
Tendon injury	1 (0.4%)	-	1 (0.4%)
Upper limb fracture	1 (0.4%)	-	1 (0.4%)
Wound	1 (0.4%)	-	1 (0.4%)
Cardiac disorders	26 (9.8%)	21 (7.9%)	40 (15.1%)
Angina pectoris	5 (1.9%)	5 (1.9%)	10 (3.8%)
Bradycardia	9 (3.4%)	1 (0.4%)	9 (3.4%)
Acute myocardial infarction	2 (0.8%)	4 (1.5%)	6 (2.3%)
Coronary artery disease	1 (0.4%)	5 (1.9%)	6 (2.3%)
Atrial fibrillation	3 (1.1%)	1 (0.4%)	4 (1.5%)
Cardiac failure congestive	1 (0.4%)	2 (0.8%)	3 (1.1%)

	Seriousness of Event		
All Per-Protocol Subjects (N=265)	**Non-Serious**	**Serious**	**Overall**
Pulseless electrical activity	-	2 (0.8%)	2 (0.8%)
Sinus tachycardia	1 (0.4%)	1 (0.4%)	2 (0.8%)
Tachycardia	2 (0.8%)	-	2 (0.8%)
Angina unstable	1 (0.4%)	-	1 (0.4%)
Atrial flutter	1 (0.4%)	-	1 (0.4%)
Atrial tachycardia	-	1 (0.4%)	1 (0.4%)
Cardiac flutter	1 (0.4%)	-	1 (0.4%)
Cardiomyopathy	-	1 (0.4%)	1 (0.4%)
Left ventricular failure	-	1 (0.4%)	1 (0.4%)
Palpitations	1 (0.4%)	-	1 (0.4%)
Sinus arrest	1 (0.4%)	-	1 (0.4%)
Sinus bradycardia	1 (0.4%)	-	1 (0.4%)
Ventricular tachycardia	-	1 (0.4%)	1 (0.4%)
General disorders and administration site conditions	22 (8.3%)	16 (6.0%)	36 (13.6%)
Vascular stent restenosis	2 (0.8%)	10 (3.8%)	12 (4.5%)
Fatigue	6 (2.3%)	-	6 (2.3%)
Adverse drug reaction	2 (0.8%)	2 (0.8%)	4 (1.5%)
Non-cardiac chest pain	2 (0.8%)	2 (0.8%)	4 (1.5%)
Peripheral swelling	4 (1.5%)	-	4 (1.5%)
Asthenia	2 (0.8%)	-	2 (0.8%)
Gait disturbance	1 (0.4%)	1 (0.4%)	2 (0.8%)
Oedema peripheral	2 (0.8%)	-	2 (0.8%)
Pyrexia	2 (0.8%)	-	2 (0.8%)
Chest discomfort	1 (0.4%)	-	1 (0.4%)
Chest pain	-	1 (0.4%)	1 (0.4%)
Chills	1 (0.4%)	-	1 (0.4%)
Pain	1 (0.4%)	-	1 (0.4%)
Swelling	1 (0.4%)	-	1 (0.4%)
Vascular stent occlusion	1 (0.4%)	-	1 (0.4%)
Vascular stent thrombosis	-	1 (0.4%)	1 (0.4%)
Respiratory, thoracic and mediastinal disorders	21 (7.9%)	14 (5.3%)	32 (12.1%)
Dyspnoea	9 (3.4%)	-	9 (3.4%)
Chronic obstructive pulmonary disease	2 (0.8%)	3 (1.1%)	5 (1.9%)
Dyspnoea exertional	3 (1.1%)	1 (0.4%)	4 (1.5%)
Respiratory failure	-	4 (1.5%)	4 (1.5%)
Hypoxia	1 (0.4%)	2 (0.8%)	3 (1.1%)
Pulmonary mass	2 (0.8%)	2 (0.8%)	3 (1.1%)
Acute respiratory failure	1 (0.4%)	1 (0.4%)	2 (0.8%)

	Seriousness of Event		
All Per-Protocol Subjects (N=265)	**Non-Serious**	**Serious**	**Overall**
Haemoptysis	1 (0.4%)	1 (0.4%)	2 (0.8%)
Aspiration	1 (0.4%)	-	1 (0.4%)
Cough	1 (0.4%)	-	1 (0.4%)
Pleural effusion	1 (0.4%)	-	1 (0.4%)
Pneumonia aspiration	-	1 (0.4%)	1 (0.4%)
Respiratory tract congestion	1 (0.4%)	-	1 (0.4%)
Sleep apnoea syndrome	1 (0.4%)	-	1 (0.4%)
Throat irritation	1 (0.4%)	-	1 (0.4%)
Gastrointestinal disorders	17 (6.4%)	11 (4.2%)	28 (10.6%)
Nausea	5 (1.9%)	-	5 (1.9%)
Gastrointestinal haemorrhage	-	4 (1.5%)	4 (1.5%)
Abdominal pain	2 (0.8%)	1 (0.4%)	3 (1.1%)
Constipation	3 (1.1%)	-	3 (1.1%)
Dysphagia	3 (1.1%)	-	3 (1.1%)
Large intestine polyp	2 (0.8%)	1 (0.4%)	3 (1.1%)
Vomiting	3 (1.1%)	-	3 (1.1%)
Gastritis	2 (0.8%)	-	2 (0.8%)
Haematemesis	1 (0.4%)	1 (0.4%)	2 (0.8%)
Intestinal obstruction	-	1 (0.4%)	1 (0.4%)
Odynophagia	1 (0.4%)	-	1 (0.4%)
Oesophageal varices haemorrhage	-	1 (0.4%)	1 (0.4%)
Oesophagitis	1 (0.4%)	-	1 (0.4%)
Retroperitoneal haemorrhage	-	1 (0.4%)	1 (0.4%)
Small intestinal obstruction	-	1 (0.4%)	1 (0.4%)
Tongue disorder	1 (0.4%)	-	1 (0.4%)
Musculoskeletal and connective tissue disorders	22 (8.3%)	9 (3.4%)	28 (10.6%)
Arthralgia	5 (1.9%)	-	5 (1.9%)
Pain in extremity	5 (1.9%)	-	5 (1.9%)
Back pain	4 (1.5%)	-	4 (1.5%)
Muscular weakness	2 (0.8%)	-	2 (0.8%)
Musculoskeletal chest pain	1 (0.4%)	1 (0.4%)	2 (0.8%)
Musculoskeletal discomfort	2 (0.8%)	-	2 (0.8%)
Musculoskeletal pain	2 (0.8%)	-	2 (0.8%)
Osteoarthritis	-	2 (0.8%)	2 (0.8%)
Pain in jaw	2 (0.8%)	-	2 (0.8%)
Synovial cyst	1 (0.4%)	1 (0.4%)	2 (0.8%)
Arthritis	-	1 (0.4%)	1 (0.4%)
Bursitis	1 (0.4%)	-	1 (0.4%)

	Seriousness of Event		
All Per-Protocol Subjects (N=265)	**Non-Serious**	**Serious**	**Overall**
Chondrocalcinosis pyrophosphate	-	1 (0.4%)	1 (0.4%)
Flank pain	1 (0.4%)	-	1 (0.4%)
Limb discomfort	1 (0.4%)	-	1 (0.4%)
Lumbar spinal stenosis	-	1 (0.4%)	1 (0.4%)
Myalgia	1 (0.4%)	-	1 (0.4%)
Neck pain	1 (0.4%)	-	1 (0.4%)
Osteonecrosis	1 (0.4%)	1 (0.4%)	1 (0.4%)
Spinal column stenosis	1 (0.4%)	-	1 (0.4%)
Spinal osteoarthritis	-	1 (0.4%)	1 (0.4%)
Renal and urinary disorders	14 (5.3%)	5 (1.9%)	19 (7.2%)
Urinary retention	6 (2.3%)	-	6 (2.3%)
Chronic kidney disease	2 (0.8%)	1 (0.4%)	3 (1.1%)
Renal artery stenosis	-	2 (0.8%)	2 (0.8%)
Acute kidney injury	-	1 (0.4%)	1 (0.4%)
Dysuria	1 (0.4%)	-	1 (0.4%)
Haematuria	1 (0.4%)	-	1 (0.4%)
Micturition urgency	1 (0.4%)	-	1 (0.4%)
Nephrolithiasis	-	1 (0.4%)	1 (0.4%)
Neurogenic bladder	1 (0.4%)	-	1 (0.4%)
Nocturia	1 (0.4%)	-	1 (0.4%)
Pollakiuria	1 (0.4%)	-	1 (0.4%)
Renal cyst	1 (0.4%)	-	1 (0.4%)
Renal failure	1 (0.4%)	-	1 (0.4%)
Urinary incontinence	1 (0.4%)	-	1 (0.4%)
Blood and lymphatic system disorders	8 (3.0%)	5 (1.9%)	12 (4.5%)
Anaemia	6 (2.3%)	4 (1.5%)	10 (3.8%)
Disseminated intravascular coagulation	-	1 (0.4%)	1 (0.4%)
Heparin-induced thrombocytopenia	1 (0.4%)	-	1 (0.4%)
Iron deficiency anaemia	1 (0.4%)	-	1 (0.4%)
Thrombocytopenia	1 (0.4%)	-	1 (0.4%)
Metabolism and nutrition disorders	11 (4.2%)	1 (0.4%)	12 (4.5%)
Dehydration	2 (0.8%)	-	2 (0.8%)
Hyperglycaemia	2 (0.8%)	-	2 (0.8%)
Metabolic acidosis	1 (0.4%)	1 (0.4%)	2 (0.8%)
Abnormal loss of weight	1 (0.4%)	-	1 (0.4%)
Diabetes mellitus	1 (0.4%)	-	1 (0.4%)
Diabetes mellitus inadequate control	1 (0.4%)	-	1 (0.4%)
Hypoglycaemia	1 (0.4%)	-	1 (0.4%)
Type 2 diabetes mellitus	1 (0.4%)	-	1 (0.4%)

	Seriousness of Event		
All Per-Protocol Subjects (N=265)	**Non-Serious**	**Serious**	**Overall**
Vitamin B12 deficiency	1 (0.4%)	-	1 (0.4%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	5 (1.9%)	5 (1.9%)	10 (3.8%)
Adenosquamous cell lung cancer stage III	-	1 (0.4%)	1 (0.4%)
Colon cancer	-	1 (0.4%)	1 (0.4%)
Essential thrombocythaemia	1 (0.4%)	-	1 (0.4%)
Lung neoplasm malignant	-	1 (0.4%)	1 (0.4%)
Myelodysplastic syndrome	1 (0.4%)	-	1 (0.4%)
Pancreatic carcinoma	-	1 (0.4%)	1 (0.4%)
Seborrhoeic keratosis	1 (0.4%)	-	1 (0.4%)
Skin cancer	1 (0.4%)	-	1 (0.4%)
Squamous cell carcinoma of lung	-	1 (0.4%)	1 (0.4%)
Squamous cell carcinoma of skin	1 (0.4%)	-	1 (0.4%)
Eye disorders	8 (3.0%)	1 (0.4%)	9 (3.4%)
Diplopia	1 (0.4%)	1 (0.4%)	2 (0.8%)
Vision blurred	2 (0.8%)	-	2 (0.8%)
Amaurosis fugax	1 (0.4%)	-	1 (0.4%)
Blindness transient	1 (0.4%)	-	1 (0.4%)
Cataract	1 (0.4%)	-	1 (0.4%)
Conjunctival haemorrhage	1 (0.4%)	-	1 (0.4%)
Visual impairment	1 (0.4%)	-	1 (0.4%)
Investigations	8 (3.0%)	1 (0.4%)	9 (3.4%)
Blood pressure decreased	2 (0.8%)	-	2 (0.8%)
Blood creatinine increased	-	1 (0.4%)	1 (0.4%)
Blood glucose increased	1 (0.4%)	-	1 (0.4%)
Body temperature decreased	1 (0.4%)	-	1 (0.4%)
Cardiac murmur	1 (0.4%)	-	1 (0.4%)
Ejection fraction decreased	1 (0.4%)	-	1 (0.4%)
Weight decreased	1 (0.4%)	-	1 (0.4%)
Weight increased	1 (0.4%)	-	1 (0.4%)
Psychiatric disorders	8 (3.0%)	-	8 (3.0%)
Mental status changes	3 (1.1%)	-	3 (1.1%)
Confusional state	2 (0.8%)	-	2 (0.8%)
Depression	2 (0.8%)	-	2 (0.8%)
Anxiety	1 (0.4%)	-	1 (0.4%)
Disorientation	1 (0.4%)	-	1 (0.4%)
Insomnia	1 (0.4%)	-	1 (0.4%)
Libido decreased	1 (0.4%)	-	1 (0.4%)
Mania	1 (0.4%)	-	1 (0.4%)

	Seriousness of Event		
All Per-Protocol Subjects (N=265)	**Non-Serious**	**Serious**	**Overall**
Ear and labyrinth disorders	3 (1.1%)	-	3 (1.1%)
Tinnitus	2 (0.8%)	-	2 (0.8%)
Cerumen impaction	1 (0.4%)	-	1 (0.4%)
Vertigo positional	1 (0.4%)	-	1 (0.4%)
Hepatobiliary disorders	1 (0.4%)	2 (0.8%)	3 (1.1%)
Cholecystitis	-	1 (0.4%)	1 (0.4%)
Cholelithiasis	1 (0.4%)	-	1 (0.4%)
Hepatic cirrhosis	-	1 (0.4%)	1 (0.4%)
Skin and subcutaneous tissue disorders	3 (1.1%)	-	3 (1.1%)
Actinic keratosis	1 (0.4%)	-	1 (0.4%)
Dermatitis	1 (0.4%)	-	1 (0.4%)
Erythema	1 (0.4%)	-	1 (0.4%)
Seborrhoeic dermatitis	1 (0.4%)	-	1 (0.4%)
Product issues	-	2 (0.8%)	2 (0.8%)
Device breakage	-	1 (0.4%)	1 (0.4%)
Device malfunction	-	1 (0.4%)	1 (0.4%)
Congenital, familial and genetic disorders	1 (0.4%)	-	1 (0.4%)
Gastrointestinal arteriovenous malformation	1 (0.4%)	-	1 (0.4%)
Endocrine disorders	1 (0.4%)	-	1 (0.4%)
Hypothyroidism	1 (0.4%)	-	1 (0.4%)
Immune system disorders	1 (0.4%)	-	1 (0.4%)
Contrast media reaction	1 (0.4%)	-	1 (0.4%)
Surgical and medical procedures	1 (0.4%)	-	1 (0.4%)
Toe amputation	1 (0.4%)	-	1 (0.4%)

The DSMB reviewed adverse events on a quarterly basis and considered these to be in line with subject age and co-morbid conditions.

iii. Unanticipated Adverse Device Effects (UADEs)

There have been no reported UADEs in this study. In addition, there is no new adverse information that may affect the risk analysis of the device.

4. Subgroup Analyses

Analyses to evaluate possible primary endpoint differences in the per-protocol population for protocol specified baseline subgroups suggest that 1-year MAE is similar between subgroups defined for age, sex, and race, although the study was not specifically powered to detect such differences.

Table 20 below summarizes the results of these subgroup analyses. The MAE proportions and statistical tests are unweighted (i.e. not weighted by anatomic and comorbid high risk status) in order to avoid sparseness issues in the age and race subgroups, and the p-values are nominal, i.e. not adjusted for multiplicity.

The age subgroups were defined by the threshold for comorbid high risk (75 years or older connotes comorbid high risk). Age was also analyzed as a continuous variable in a logistic regression model and, consistent with the contingency table analyses below, resulted in a nonsignificant effect: odds ratio of 1.023 with 95% CI [0.951, 1.099] and Wald chi-square p=0.55.

The race subgroups were defined as white only (answered yes to white and no to all other race types) and any non-white (answered yes to one or more of the other race types, regardless of answer to white type). Among the 244 per-protocol subjects evaluable for 1-year MAE, 13 subjects reported a non-white race, and none of these 13 subjects reported MAE.

Table 20. Per Protocol 1-Year MAE Subgroup Analyses

Subgroup	1-Year MAE[1]	95% CI[2]	Subgroups P-Value[3]	Performance Goal P-Value[4]
Overall	4.5% (11/244)	[2.3%, 7.9%]	NA	<0.0001
Age				
<75	3.9% (5/127)	[1.3%, 9.0%]	0.76	<0.0001
≥75	5.1% (6/117)	[1.9%, 10.8%]		0.0003
Sex				
Male	3.8% (6/159)	[1.4%, 8.0%]	0.52	<0.0001
Female	5.9% (5/85)	[1.9%, 13.2%]		0.0034
Race				
White Only	4.8% (11/231)	[2.4%, 8.4%]	1.00	<0.0001
Any Non-white	0.0% (0/13)	[0.0%, 24.7%]		0.052

[1] Unweighted
[2] Two-sided exact from Clopper-Pearson method
[3] Two-sided from Fisher's exact test; not adjusted for multiplicity
[4] One-sided from binomial test vs. 16.9% performance goal using unweighted standard error under H_0; not adjusted for multiplicity

5. Pediatric Extrapolation

In this premarket application, existing clinical data were not leveraged to support approval of a pediatric patient population.

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included

five(5) investigators who had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: 0
- Significant payment of other sorts: 5
- Proprietary interest in the product tested held by the investigator: 0
- Significant equity interest held by investigator in sponsor of covered study: 0

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. The information provided does not raise any questions about the reliability of the data.

XI. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(3) 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.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Safety and Effectiveness Conclusions

The risks of the device are based on non-clinical laboratory and animal studies as well as data collected in a clinical study conducted to support PMA approval as described above. Non-clinical testing performed during the design and development of the GCS system confirmed the product design characteristics, specifications, and intended use. The non-clinical engineering testing conducted on the stent and delivery system demonstrated that the performance characteristics met the product specifications. The biocompatibility and in vivo animal testing demonstrated that the acute and chronic in vivo performance characteristics of the Gore Carotid Stent system provide reasonable assurance of safety and acceptability for clinical use. The test results obtained from the sterilization testing demonstrated that the product can be adequately sterilized and is acceptable for clinical use. The shelf life testing has established acceptable performance for a labeled shelf life up to 40 months.

The primary composite endpoint of the clinical study was a composite of MAEs defined as death, any stroke, or myocardial infarction (MI) through 30 days post-index procedure, and ipsilateral stroke between 31 days and 1 year. The proportion of subjects with a primary endpoint event was 4.5%, with a 95.1% 1-sided upper confidence limit of 8.5%, which was significantly less than the 16.9% performance goal ($p<0.00001$). The secondary endpoint of technical success was 100%. The rate of in stent restenosis and clinically driven TLR were 1.8% and 2.2%, respectively. These results indicate that the GCS met its primary endpoint for treatment of carotid artery disease and is a durable treatment option for up to one year. There were no unanticipated adverse events in the study.

B. Benefit-Risk Determination

The probable benefits of the device are also based on data collected in a clinical study conducted to support PMA approval as described above. Other bare metal stents are currently being used for this treatment. The GCS offers similar benefits that stenting with a bare metal open-cell or closed-cell stent offers over alternative treatments to stenting. The SCAFFOLD trial has established the safety and effectivenss of the GCS, and the results are in alignment with other approved carotid stents. In conclusion, given the available information, the data support that for the treatment of carotid artery stenosis in patients deemed at high surgical risk for carotid endarterectomy, the overall benefits of using the GCS outweigh the overall risks.

1. Patient Perspectives

   This submission did not include specific information on patient perspectives for this device.

C. Overall Conclusions

The clinical and non-clinical data in this application support a reasonable assurance that the device is safe and effective when used in accordance with the indications for use. The clinical study met the pre-specified primary endpoint. Therefore, it is reasonable to conclude that the benefits of use of the device for the target population outweigh the risk of illness or injury when used as indicated in accordance with the labeling and Instructions for Use (IFU).

XIII. CDRH DECISION

CDRH issued an approval order on November 01,2018. The final conditions of approval cited in the approval order are described below.

Post-Approval Study – SCAFFOLD Continued Follow-Up Study. This study should be conducted per protocol GCS 10-08, Amendment 3 (dated October 22, 2014). This study is a prospective, multi-center follow-up of the SCAFFOLD pivotal study (G110127) that treated 312 subjects from 30 investigational sites. It will evaluate the long-term safety and effectiveness of the GORE Carotid Stent. All 290 remaining subjects, active at the end of the 12-month evaluation, will continue to be followed annually through 36 months. Follow-up at the 2- and 3-year timepoints will include the following: exam and vital signs, NIH Stroke Scale, Modified Rankin Scale, carotid duplex ultrasound, an assessment of concomitant medications (antiplatelet or anticoagulant therapy), and an assessment of adverse events.

The applicant’s manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XIV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

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

Post-approval Requirements and Restrictions: See approval order.