SUMMARY OF SAFETY AND EFFECTIVNESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Stent, Carotid

Device Trade Name: Neuroguard IEP® 3-in-1 Carotid Stent and Post-Dilatation Balloon System with Integrated Embolic Protection (Neuroguard IEP® System)

Device Product code: NIM

Applicant's Name and Address: Contego Medical Inc.
3801 Lake Boone Trail, Suite 100
Raleigh, NC, 27607

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P240009

Date of FDA Notice of Approval: October 11, 2024

II. INDICATIONS FOR USE

The Neuroguard IEP 3-in-1 Carotid Stent and Post-Dilatation Balloon System with Integrated Embolic Protection is indicated for improving the carotid luminal diameter in subjects at high risk for adverse events from carotid endarterectomy who require carotid revascularization and meet the criteria outlined below:

- Patients with symptomatic stenosis of the common or internal carotid artery with ≥ 50% as determined by angiography using NASCET methodology OR
  Patients with asymptomatic stenosis of the common or internal carotid artery with ≥ 80% as determined by angiography using NASCET methodology;
- Patients with reference vessel diameters 4.0 – 8.0 mm.

This device is also indicated for post-dilation of the stent component with simultaneous capture and removal of embolic material. The Neuroguard IEP System should always be used in conjunction with an available primary distal embolic protection device as described in the IFU.

III. CONTRAINDICATIONS

The Neuroguard IEP 3-in-1 Carotid Stent and Post-Dilation Balloon System with Integrated Embolic Protection is contraindicated for use in:

- Patients in whom anticoagulant and/or antiplatelet therapy is contraindicated
- Patients with a known hypersensitivity to nickel-titanium

- Patients with severe vascular tortuosity or anatomy that would preclude the safe introduction of a guidewire, catheter, introducer sheath, delivery system or embolic protection device
- Patients with uncorrected bleeding disorders
- 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 Neuroguard IEP System labeling.

V. DEVICE DESCRIPTION

The Neuroguard IEP System consists of three main components:

- A self-expanding nickel-titanium (nitinol) stent
- A delivery catheter which includes a post-dilation balloon and activation handle
- Embolic protection filter that is integrated at the distal end of the delivery system

The stent is fabricated by laser cutting a nitinol tube and electropolishing the surface. The closed cell design is intended to provide an optimal balance of radial strength and flexibility. The stent design consists of concentric rings with cross-connectors. The stent is flared at both ends to facilitate adequate wall apposition in tortuous anatomy. On deployment, the stent self-expands to its unconstrained diameter and exerts a radial force on the luminal surface, helping to maintain the patency of the vessel.

The stent is available in four sizes and one configuration (**Figure 1** and **Table 1**). The nominal stent diameters are tapered at both the proximal and distal ends, with a larger taper at the proximal end to account for anatomical differences in reference vessel diameter when stenting from the common carotid artery to the internal carotid artery.

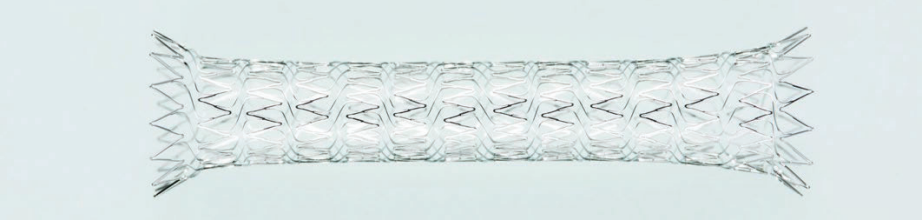


Figure 1. Neuroguard Stent

Table 1. Neuroguard IEP System Product Matrix

Model Number	Balloon OD (mm)	Catheter Length (cm)	Stent Diameter (mm)				Stent Length (mm)	Balloon Length (mm)	Filter Length (mm)	Filter diameter (mm)
			Proximal Tapered Diameter	Nominal Diameter	Distal Tapered Diameter	Flared Diameters – Proximal/Distal				
NG-0730-140-2	5	140	9	7	8	11	30	24	18	Adjustable up to 7mm
NG-0740-140-2	5	140	9	7	8	11	40	34		
NG-0630-140-2	5	140	8	6	7	11	30	24		
NG-0640-140-2	5	140	8	6	7	11	40	34		

The delivery system consists of a multi-lumen shaft with an inflatable semi-compliant angioplasty balloon at the distal end and a handle on the proximal end (**Figure 2**). Distal to the angioplasty balloon is an integrated filter in a collapsed state. The nitinol self-expanding stent is pre-loaded and centered on top of the angioplasty balloon. When introduced, the stent and filter are covered by an outer sheath. The balloon has radiopaque balloon markers located at both the proximal and distal shoulders of the balloon to indicate working length.

Figure 2. Neuroguard IEP System

An ergonomic activation handle is located at the proximal end of the Neuroguard IEP System (**Figure 3**). Expansion and collapse of the filter, as well as retraction of the outer sheath, is accomplished by manipulating the rotating knob and thumb wheel. The thumb wheel is connected to the proximal end of the outer sheath via a pull-wire, which wraps around the inner portion of the wheel when retracted. Following post-dilation of the stent, the rotating knob is rotated to collapse the filter.

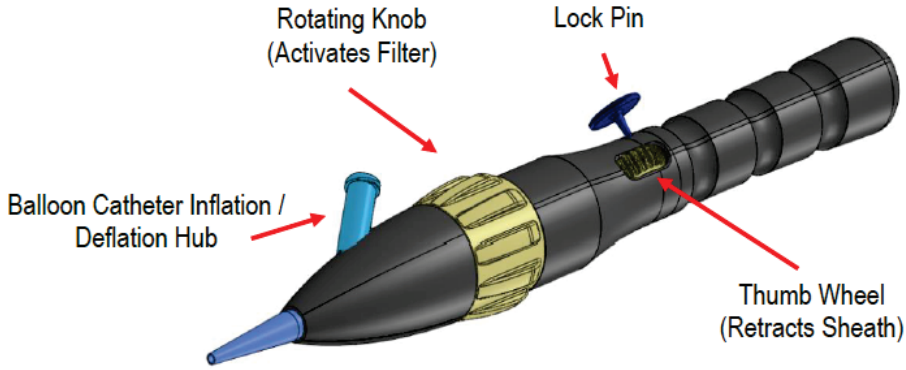


Figure 3. Neuroguard IEP System Handle

The embolic filter consists of a frame woven from nitinol wire and a polyurethane membrane with 40-micron (minimum) laser drilled pores attached to the distal end of the shaft (**Figure 4**). The filter is adjustable and identical for each Neuroguard IEP System size. The user can control the diameter of the filter to ensure optimal vessel wall apposition.

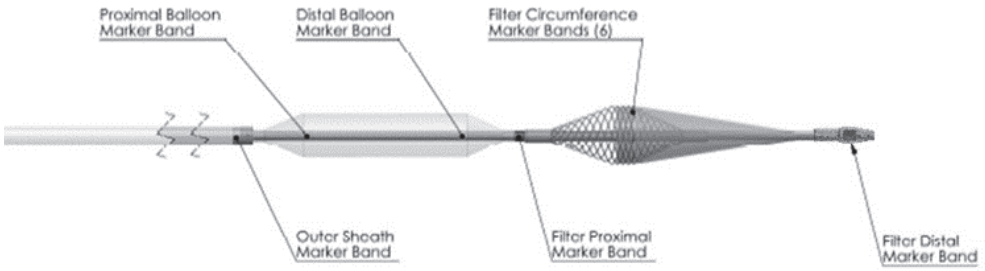


Figure 4. Neuroguard IEP System Balloon, Marker Bands and IEP Filter

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several alternative practices and procedures for the treatment of atherosclerotic disease of the carotid arteries which are dependent upon symptomatic status, patient anatomy and comorbidities, and degree of stenosis. Alternative treatments currently include lifestyle modification, endovascular intervention using FDA-approved carotid stents and embolic protection systems, carotid endarterectomy, transcarotid artery revascularization, optimal medical therapy, or a combination of these treatments. Stroke risk factor reduction is recommended through lifestyle modifications such as cessation of smoking and changes to diet and alcohol usage. Optimal medical therapy includes use of antiplatelet and/or anticoagulant medications (i.e., aspirin, clopidogrel or ticlopidine) as well as pharmaceutical treatment for hypertension and hyperlipidemia. The primary treatment used to prevent stroke in patients with carotid artery disease is surgical removal of the plaque from the stenotic artery by means of an endarterectomy. 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

CE Mark Certification of the Neuroguard IEP System was first issued on April 12, 2021. The device was introduced to markets outside of the United States as listed below.

- France
- Germany
- Italy
- Bulgaria
- Slovenia
- North Macedonia

The Neuroguard IEP System has not been withdrawn from any country for reasons relating to device safety and effectiveness.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Potential adverse effects (e.g., complications) may occur at any time during or after the procedure and include, but are not limited to:

- Angina
- Allergic reactions (including antiplatelet agents, contrast medium or stent materials)
- Aneurysm
- Arrhythmias
- Arterial occlusion/thrombosis at puncture site
- Bleeding from anticoagulant or antiplatelet medications
- Bradycardia
- Carotid artery Spasm
- Cerebral edema
- Cerebral hemorrhage
- Cerebral ischemia/transient ischemia attack
- Cardiac tamponade
- Cardiogenic shock
- Death
- Embolism
- Fever
- Groin hematoma, with or without surgical repair
- Heart failure
- Hematoma
- Hemorrhage
- Hypotension/hypertension
- Infection
- Ischemia/infarction of tissue/organ
- Myocardial infarction
- Pain and tenderness
- Pericardial effusion
- Pulmonary edema
- Femoral pseudoaneurysm
- Renal failure/insufficiency
- Respiratory failure
- Restenosis of the stented segment
- Seizure
- Severe unilateral headache
- Stroke/cerebrovascular accident (CVA)
- Total occlusion of carotid artery
- Vessel dissection, perforation, spasm or recoil
- Vessel trauma requiring surgical repair or intervention

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

IX. SUMMARY OF NON-CLINICAL STUDIES

A. Engineering Testing

A series of non-clinical laboratory studies were performed to ensure that the Neuroguard IEP System met the specified performance characteristics as defined via design inputs, published guidance documents and applicable international and domestic standards (**Table 2**).

Table 2. Summary of Non-clinical Engineering Bench Testing

Test	Description of Test	Specification/Acceptance Criteria	Results
Stent			
Material Characterization/ Composition	Measure the elemental composition of the stent tubing.	Material composition must comply with ASTM F2063, Wrought Nickel-Titanium Shape Memory Alloy for Medical Devices and Surgical Implants	Ensure material composition conforms to ASTM F2063/ASTM F2633.
Austenite Finish Transition Temperature	Determine the transformation temperature of the nitinol in accordance with ASTM 2082.	Stent comprises nitinol conforming to ASTM F2063; the austenite finish temperature of the electropolished stent is $8°C \geq A_f \leq 25°C$	The stent materials conform to applicable material standards
Finite Elemental Analysis	Use of mathematical modeling to understand the effects of physiologic loading on stent durability.	The stress and strain during loading and deployment	For characterization purposes only.
Accelerated fatigue Testing	Evaluate the integrity of the stent under cyclic radial loading in accordance with ASTM F2477	The devices tested must withstand the loading conditions with no fracture with 400 million cycles.	No complete segment breakage through 10 years of accelerated radial fatigue testing (400 million cycles).
Bending Fatigue	Must withstand physiological bending and torsional conditions in a carotid vessel for 10 years without breakage.	The devices tested must withstand the loading conditions with no fracture with 1 million cycles & 0 – 20° bend.	No complete segment breakage through 10 years of accelerated radial fatigue testing (1 million cycles).
Stent foreshortening	Evaluate dimensional changes that may occur when deploying a stent.	<27% based on commercially available carotid stents.	All test results passed the established acceptance criteria demonstrating an average length reduction of 15%.
Dimensional characterization Stent	Ability to access the intended location, accurately deploy, and appropriate sizing of the implant.	The stent recovers to its specified, unconstrained diameter and expanded stent length	The stent dimensions conform to applicable specifications.
Stent radial resistive Force	Characterize the stent's ability to withstand forces acting on it without experiencing excessive deformation, migration, or sustained collapse in accordance with ASTM 3067.	0.25 N/mm minimum	All test results passed the established acceptance criteria of 0.25 N/mm minimum.
Chronic Outward Force		0.45 N/mm maximum	All test results passed the established acceptance criteria 0.45 N/mm maximum

Test	Description of Test	Specification/Acceptance Criteria	Results
Crush resistance	Characterize ability of stent to recover its desired size and shape after application and removal of external loads.	The stent shall recover to its specified unconstrained diameter when released from a compressed state and will vary minimally over its length	All test results passed the established acceptance criteria of full recovery following stent compression.
Stent-free Area	Calculation performed to determine the localized ability of the stent to support the vessel.	70% minimum in a 5 mm vessel	Stent free area percentage was calculated for all diameters of the Neuroguard stent and met the specification of 70% stent free area.
Kink resistance - stent	Bend the tubing, containing the deployed stent, around successively tighter radii and observe when the stent kinks.	75° bend maximum without kinking	All test results passed the established acceptance criteria.
Conformability	Bend the tubing, containing the deployed stent, around successively tighter radii and observe the stent to determine if it is apposed to the tubing wall.	75° bend maximum with complete vessel apposition.	All test results passed the established acceptance criteria
Stent integrity	Evaluate stent surface after expansion to its unconstrained diameter for signs of damage.	Following expansion, the stent should be free of cracks, scratches and defects	All test results passed the established acceptance criteria.
Corrosion	Determine the general corrosion behavior as well as the susceptibility of the device to localized corrosion in accordance with ASTM F2129.	Eb – Er > 200mV, where Eb is the breakdown potential and Er is the resting potential.	Stent corrosion was evaluated by an established external laboratory. All devices met the product specification.
Magnetic Resonance Imaging (MRI) safety and compatibility	Characterize the movement, heating, and image artifacts that may arise from having the stent in a MRI environment.	The stent should meet the requirements of MR Conditional. Specifically, a patient with this device can be scanned safely in an MR system under the following conditions: • Static magnetic field of 1.5-Tesla and 3-Tesla, only • Maximum spatial gradient magnetic field of 4,000-Gauss/cm (40-T/m) • Maximum MR system reported whole body averaged specific absorption rate (SAR) of 2-W/kg or head SAR of 3.2-W/kg (Normal Operating Mode). Under the scan conditions defined, the Neuroguard stent is expected to produce a maximum temperature rise of 5°C after 15-minutes of continuous scanning (i.e., per pulse sequence). In non-clinical testing, the image artifact caused by the Neuroguard	MRI compatibility was evaluated by an established external laboratory. Meets requirements per F2213-06, ASTM F2052-15, ASTM 2182-11a and ASTM F2119-13

Test	Description of Test	Specification/Acceptance Criteria	Results
		stent extends approximately 3 mm from this device when imaged with a gradient echo pulse sequence and a 3-Tesla MR system. The artifact obscures the device lumen.	
Radiopacity	Determine the ability to visualize the stent using fluoroscopy to facilitate proper stent placement.	The stent must be visible under fluoroscopy	The results from testing demonstrated the stent has an acceptable level of radiopacity.
Delivery System			
Dimensional verification	Measure relevant component dimensions	The device dimensions should meet pre-established dimensional requirements.	The device dimensions conform to applicable specifications.
Trackability	Peak force required to advance catheter to target site and retract the device from a clinically relevant simulated use model.	1.0 lbf max	All devices tested met the product specification.
Filter performance	Evaluate the ability of the filter to deploy, the flow rate through the filter, and the efficiency at which the filter captures particulate.	The deployed filter shall capture no less than 80% of embolic particles greater than 125 microns. The deployed filter shall not obstruct flow more than 15% before capture of embolic particles.	All devices tested met the product specification.
Stent Deployment force	Measurement of peak force experienced during stent deployment at target site.	2.5 lbf. max	All systems tested met product specification with measured forces of ≤ 2.5 lbf.
Stent deployment accuracy	With the stent positioned at the target site, deploy the stent and measure the distance form the end of the stent to the target site.	The stent shall be deployed less than or equal to 4.0 mm from the intended deployment location.	All devices tested met the product specification.
Balloon inflation/deflation	Using a mixture of contrast media and water, measure the time required to inflate the device to rated burst pressure; pull a vacuum on the inflation device and measure the time required to deflate the balloon.	Less than10 seconds (inflation) and less than 20 seconds (deflation).	The inflation and deflation times met the product specifications.
Kink resistance – delivery catheter	Wrap the catheter shaft around successfully smaller radii mandrels until it kinks.	Will not kink at 0.5” bend radius or greater.	All test results passed the established acceptance criteria.
Tensile strength	Measure the ability of the bonds to withstand forces greater than those that may be experienced during clinical use.	The delivery system bonds will meet the minimum tensile strength noted on the device specifications.	All test results passed the established acceptance criteria.
Balloon compliance (nominal to RBP)	Measure the balloon outer diameter at nominal to rated burst pressures.	Nom Labeled OD ±10% @ 8 ATM (4.5 – 5.5 mm) Qtr. Size OD +10% Max @ 14 ATM (4.7 – 5.8 mm)	All test results passed the established acceptance criteria.
Rated burst pressure (in-stent)	Increase pressure until balloon reaches rated burst pressure.	14 atm minimum rated burst strength.	The test results passed the established acceptance criteria.
Balloon fatigue (in-stent)	Repeated inflations to rated burst pressure, with a 30 second dwell at	5 cycles to RBP without failure.	All devices tested met the product specification when

Test	Description of Test	Specification/Acceptance Criteria	Results
	RBP, to determine the number of times the device can be inflated and deflated without failure.		tested within an expanded stent.
Compatibility with commercial distal protection devices	Evaluate the compatibility of commercially available distal embolic filters with the Neuroguard IEP System in a clinically relevant model.	Integrated embolic filter must be compatible with commercial distal embolic filters.	Compatibility with the following embolic filters was evaluated using a simulated use model: • FilterWire EZ (Boston Scientific) • Emboshield NAV 6 (Abbott Vascular) • Spider FX (Medtronic) • Angioguard XP (Cordis)*

* Note that while compatibility with the Angioguard XP was evaluated in the bench testing, it was not used in any subjects in the clinical study. See Table 11 below for additional details on the distribution of primary distal embolic filters used in the clinical study.

B. Biocompatibility

The Neuroguard IEP System was evaluated for biocompatibility in accordance with applicable subparts of ISO 10993, "*Biological evaluation of medical devices*" and FDA guidance document, "*Use of International Standard ISO 10993-1, "Biological evaluation of medical devices Part 1: Evaluation and testing within a risk management process,*" issued on September 4, 2020.

Table 3: Biocompatibility

Test	Purpose	Results
Stent		
Chemical characterization & toxicological risk assessment	Chemical assessments, including extractables and leachables studies for medical devices combined with an evaluation of the results of the chemical characterization focused on the risk of the device and the nature of patient contact to determine safety.	Based on the evaluation of exhaustive extractables of the Neuroguard stent, no compounds above the Analytical Evaluation Threshold (AET) were detected. The results of the toxicological risk assessment support a conclusion that the identified extractable chemicals pose a tolerable risk and low toxicity to patients.
Cytotoxicity Qualitative (Medium Eluate Method Test – MEM)	Cytotoxicity testing is designed to evaluate the general toxicity of medical devices.	Pass; non-cytotoxic
Sensitization (Kligman Maximization Test)	Sensitization Testing is used for the determination of sensitizing activity of medical devices. These tests are assessing the potential of a material or product to cause a delayed hyper-sensitivity reaction.	Pass; Non-sensitizing No reaction at the challenge (0% sensitization) following an induction phase.
Irritation – Intracutaneous Reactivity (Rabbit Intracutaneous Reactivity Test)	Irritation tests can be used to determine if a material will cause local irritation in the skin, mucosal, or ocular tissues	Pass; Non-irritating The test article sites did not have a significantly greater biological reaction than the sites injected with the control article.

Acute Systemic Toxicity: Systemic Injection (Mouse Systemic Injection Test)	Acute Systemic Injection testing provides general information on health hazards likely to arise from an acute exposure from a medical device	Pass; systemically non-toxic The test article did not induce a significantly greater biological reaction than the control extracts.
Acute Systemic Toxicity: Material Mediated Pyrogen (Rabbit Pyrogen Test – Material Mediated)	Material Mediated Pyrogen testing evaluates the ability a substance in/on a medical device to produce a pyrogenic response	Pass; Non-pyrogenic All rabbits treated with either the test article or negative control had a temperature increase of 0.0ºC
Subacute Toxicity/subchronic Toxicity	Subacute and subchronic Toxicity Test is used to discover the effects a material with repeat exposure would have on a patient, including any compound toxicity effects.	Pass; no evidence of toxicity during chronic animal study.
Genotoxicity (In Vitro Ames Plate Incorporation Test and Spot Test)	The Ames Mutagenicity test is used to determine the potential mutagenic activity of an extract from a medical device	All five bacterial strains were found to be non-mutagenic using both the activated and non-activated systems as compared to the corresponding negative controls. Non-mutagenic.
Genotoxicity (In Vitro Chromosomal Aberration in Mouse Lymphoma)	The Chromosomal Aberration test is used to screen medical devices to determine if they cause structural chromosomal aberrations in Chinese Hamster Ovary (CHO) cells.	The number of test article induced chromosomal aberrations per cell were within limits of the negative control using both the activated and non-activated systems. The test article was determined to be non-genotoxic.
Implantation (Chronic animal implantation)	Determine if the test article causes a local tissue response after 26 weeks implantation	Pass; Significant gross changes were not observed in any test or control article as viewed from the adventitial surface at both timepoints; carotid arterial segments proximal and distal to the implantation sites were also grossly normal in each animal at both timepoints;
Complement Activation SC5b-9	Evaluates the device's potential to activate the SC5b-9 complement system	Pass; Test article response was similar to the predicate and negative control.
Hemolysis (Direct) (ASTM Blood Compatibility Test – Hemolysis Assay)	Hemolysis testing is designed to determine the hemolytic properties of a medical device materials that have direct or indirect blood contact	Pass; Non-hemolytic There were no significant differences between the test article extract and negative control article results.
Hemolysis (Indirect) (ASTM Blood Compatibility Test – Hemolysis Assay)	Hemolysis testing is designed to determine the hemolytic properties of a medical device materials that have direct or indirect blood contact	Pass; Non-hemolytic There were no significant differences between the test article extract and negative control article results.
Haemocompatibility (Thrombogenicity Test)	*In Vivo* Thrombogenicity test determines a comparative thrombo-resistant for medical devices that are intended for blood contact	The test article was evaluated using an animal model (swine) designed to mimic the clinical application of the device. The results of animal testing demonstrated suitable device thromboresistance.
Delivery System		
Cytotoxicity Qualitative (Medium Eluate Method Test – MEM)	Determine the potential for the test article to cause cytotoxicity	Pass; non-cytotoxic
Sensitization (Kligman Maximization Test)	Sensitization Testing is used for the determination of sensitizing activity of medical devices. These tests are assessing the potential of a material or product to cause a delayed hyper-sensitivity reaction.	Pass; Non-sensitizing No reaction at the challenge (0% sensitization) following an induction phase.

Irritation – Intracutaneous Reactivity (Rabbit Intracutaneous Reactivity Test)	Irritation tests can be used to determine if a material will cause local irritation in the skin, mucosal, or ocular tissues	Pass; Non-irritating The test article sites did not have a significantly greater biological reaction than the sites injected with the control article.
Acute Systemic Toxicity: Systemic Injection (Mouse Systemic Injection Test)	Acute Systemic Injection testing provides general information on health hazards likely to arise from an acute exposure from a medical device	Pass; systemically non-toxic The test article did not induce a significantly greater biological reaction than the control extracts.
Acute Systemic Toxicity: Material Mediated Pyrogen (Rabbit Pyrogen Test – Material Mediated)	Material Mediated Pyrogen testing evaluates the ability a substance in/on a medical device to produce a pyrogenic response	Pass; Non-pyrogenic All rabbits treated with either the test article or negative control had a temperature increase of 0.0ºC
Partial Thromboplastin Time (PTT)	Partial Thromboplastin Time (PTT) testing is a general screening test for the detection of coagulation abnormalities in the intrinsic pathway	Pass: Test article had a significantly shorter clotting time than the negative control (polypropylene pellets); the positive control (glass beads) had a significantly shorter clotting time than the negative control; the plasma control had a similar clotting time to the negative control
Complement Activation SC5b-9	Evaluates the device's potential to activate the SC5b-9 complement system	Pass; Test article response was similar to the predicate and negative control.
Hemolysis (Direct) (ASTM Blood Compatibility Test – Hemolysis Assay)	Hemolysis testing is designed to determine the hemolytic properties of a medical device materials that have direct or indirect blood contact	Pass; Non-hemolytic There were no significant differences between the test article extract and negative control article results.
Hemolysis (Indirect) (ASTM Blood Compatibility Test – Hemolysis Assay)	Hemolysis testing is designed to determine the hemolytic properties of a medical device materials that have direct or indirect blood contact	Pass; Non-hemolytic There were no significant differences between the test article extract and negative control article results.
Haemocompatibility (Thrombogenicity Test)	In Vivo Thrombogenicity test determines a comparative thrombo-resistant for medical devices that are intended for blood contact	The test article was evaluated using an animal model (swine) designed to mimic the clinical application of the device. The results of animal testing demonstrated suitable device thromboresistance.

C. Animal Studies

A porcine animal study evaluating 30-day acute and 6-month chronic outcomes was conducted in accordance with Good Laboratory Practice (GLP) regulations as set forth in 21 CFR 58 to demonstrate the pre-clinical safety and performance of the Neuroguard IEP System.

The objective of the chronic study was to evaluate acute performance of the stent, stent delivery system, embolic filter and post-dilation balloon. Properties such as device trackability, ease of maneuverability, stent placement accuracy, radiopacity, and other performance characteristics were evaluated. For the filter element, the reliability of deployment and retrieval of the filter, radiopacity, and an assessment of the effects the filter pore size on blood flow or thrombogenicity were reviewed. Basic balloon characteristics

such as inflation/deflation time were also noted. Recorded observations are presented in **Table 4** below.

In addition, the study provided chronic performance data of the Neuroguard stent. This included angiographic assessment and histopathological analysis of the vascular and downstream tissue response to implantation such as healing response, endothelialization and stent patency as compared with a legally marketed control stent. Study success and acceptance criteria are shown in **Table 5**.

Table 4. Summary of Animal Testing

Study Objective	Device Size (mm) and Samples (N)	Implant Duration; Number of Animals	Results
In vivo assessment of acute performance of the Neuroguard IEP System	6mm x 30 mm stent, (N=8)	Acute 1 animal	The study demonstrated acceptable performance of the Neuroguard IEP System.
In vivo assessment of acute performance of the Neuroguard IEP System and biological response to the stent after 1 month and 6 months	6mm x 30 mm stent, (N=20) 7mm x 40 mm stent, (N=2) Control Article: XACT Carotid Stent System 8 x 20 mm (N=2)	Chronic 1 month & 6 months 6 animals at each time point (12 total)	The mechanical characteristics of the Neuroguard IEP System allow accurate and safe placement in the carotid arteries. The stent component of the Neuroguard IEP System and associated filter system were well tolerated and safe based on tissue response at 1 month and 6 months.

Table 5. In Vivo Success and Acceptance Criteria

Criteria	Outcome
The mechanical characteristics (trackability, pushability and torquability) of the Neuroguard IEP System are sufficient to allow accurate and safe placement in the carotid arteries.	Pass
The radiopaque elements of the catheter, balloon and filter allow for sufficient visibility on fluoroscopy.	Pass
The system is capable of accurately deploying the stent in the target location.	Pass
The filter can be opened and closed in the desired position and conforms to the vessel wall.	Pass
The pore size of the filter does not obstruct flow or cause thrombosis within the filter based on post-procedural filter analysis.	Pass
Animals are free from angiographically or clinically relevant (as established by the attending veterinarian and pathologist) subacute device-associated adverse events.	Pass
Acceptable angiographic outcomes including Score 3 TICI post procedure and term.	Pass
Acceptable (for species and lab) clinical chemistry values as determined by the attending veterinarian.	Pass
Overall mild regional or downstream inflammatory responses, absence of device-associated regional or downstream thrombus.	Pass

Following harvest, tissues were submitted for histological processing and the resulting slides were evaluated via light microscopy by an independent pathologist. The carotid arteries of the healthy swine model implanted with the Neuroguard IEP System and the control stent were evaluated, in addition to the downstream tissue response.

The stent component of the Neuroguard IEP System and associated filter system were well tolerated, safe and appeared comparable to the control stent based on local and dependent tissue response in the healthy swine model at 30 days and 6 months.

D. Sterilization

The Neuroguard IEP System is a single-use device that is sterilized with ethylene oxide gas and distributed sterile to the end user. Sterilization and validation have been conducted in accordance with AAMI/ANSI/ISO *11135-1:2014 "Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for the Development, Validation, and Routine Control of Ethylene Oxide Sterilization Process for Medical Devices* to ensure a Sterility Assurance Level (SAL) of 10^{-6}.

E. Packaging and Shelf Life

The packaging qualification and device verification testing was performed for the Neuroguard IEP System at baseline and on product accelerated aged to 24 months. The packaging validation included a visual assessment, gross leak detection (bubble test), and seal tensile strength testing to demonstrate that the packaging system was able to maintain a sterile barrier after exposure to temperature, distribution conditioning, and accelerated aging. A shelf life of 24 months has been established based on product and packaging shelf-life testing.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of the Neuroguard IEP System in human subjects for the treatment of carotid artery stenosis at elevated risk for adverse events following carotid endarterectomy (CEA).

This study was performed in centers located within the United States (US) and outside of the US (OUS) under IDE # G200007 in accordance with Good Clinical Practice guidelines, ISO 14155, 21 CFR 812, as well as local regulations and applicable regulatory requirements. Data from this clinical study are the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

Subjects were treated between June 12, 2020 and November 10, 2022. The database for this PMA reflected data collected through the last follow up visit on October 31, 2023 and included 305 subjects enrolled at 32 sites. Two hundred thirty-nine (239) subjects (78.36%) enrolled at 23 US sites and 66 subjects (21.64%) enrolled at 9 OUS sites.

The study was a prospective, multi-center single-arm study designed to evaluate the safety and effectiveness of the Neuroguard IEP System for the treatment of carotid artery stenosis in subjects at elevated risk for adverse events following CEA.

The evaluation of safety and effectiveness was performed through a primary endpoint of Major Adverse Event (MAE), defined as death, all stroke and myocardial infarction (MI) within 30 days of the index carotid stenting procedure plus ipsilateral stroke through 12 months of the procedure compared to a pre-specified weighted performance goal (PG). The PG was set at 13.8% and was established based on data from four prior non-randomized carotid stent pivotal Investigational Device Exemption (IDE) studies that had a similar primary composite endpoint and applying weights for anatomic (30%) and co-morbid (70%) high-risk CEA conditions.

Secondary endpoints included procedural success, technical success, clinically-driven target lesion revascularization (CD-TLR), in-stent restenosis (ISR), major stroke, minor stroke, and neurological death. Procedural success was defined as a successful Neuroguard stent implantation with ≤ 50% residual angiographic stenosis of the target lesion as determined by the angiographic core lab. Technical success was defined as successful deployment of the Neuroguard stent in the targeted treatment location with a residual diameter stenosis ≤ 50% immediately after post-dilation as determined by the angiographic core lab, and successful delivery and deployment of the Neuroguard IEP System filter beyond the target lesion and retrieval after completion of the stent placement, and successful post-dilation of the Neuroguard stent with the integrated angioplasty balloon, and lastly, successful removal of the delivery system.

CD-TLR was defined as any revascularization procedure of the original treatment site associated with narrowing of > 80% as determined by the angiographic core lab within 12 months of the index-procedure. ISR was defined as > 70% narrowing observed within the Neuroguard stent as per core lab ultrasound analysis through 12 months, 24 months, and 36 months. Major stroke at 30 days, minor stroke at 30 days and neurological death through 12 months were also evaluated as secondary endpoints.

The primary endpoint was assessed based on 90% power to test the primary hypothesis at a one-sided 5% alpha level using a weighted Z-test. Secondary endpoints were descriptive only, with no formal statistical hypotheses tested. However, proportions and confidence intervals were produced for technical success, procedure success, CD-TLR through 12 months, ISR through 12 months, major stroke through 30 days, minor stroke through 30 days and neurological death through 12 months.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the PERFORMANCE II Clinical study was limited to subjects who met the following inclusion and none of the exclusion criteria:

General Inclusion Criteria:

- Male and non-pregnant, non-breastfeeding female subjects whose age is ≥ 20 and ≤ 80 years.

- Patient is willing and capable of complying with all study protocol requirements, including the specified follow-up visits and could be contacted by telephone.
- Patient or his/her authorized legal representative must sign a written informed consent form that has been approved by the local governing Institutional Review Board (IRB)/Ethics Committee (EC) of the respective clinical site.
- Patient is diagnosed with carotid artery stenosis treatable with carotid artery stenting and is considered a high operative risk for CEA.
- Patient is diagnosed with either:
    a. Symptomatic carotid artery stenosis ≥ 50% as determined by angiography using NASCET methodology. Symptomatic subjects are defined as having stroke, transient ischemic attack (TIA) ipsilateral in the hemisphere supplied by the target vessel carotid lesions or ipsilateral transient monocular blindness (amaurosis fugax) within 180 days of the procedure; or
    b. Asymptomatic carotid artery stenosis ≥ 80% as determined by angiography using NASCET methodology.
- Patient has a modified Rankin Score of ≤ 2 at the time of informed consent.
- Females of child-bearing potential must have a negative pregnancy test within 24 hours of the index procedure.
- Patient is willing and able to take dual antiplatelet therapy for a minimum of 30 days following the index procedure.

Angiographic Inclusion Criteria:

- Target lesion located at the carotid bifurcation and/or proximal internal carotid artery (ICA).
- Single *de novo* or restenotic (post carotid endarterectomy (CEA) target lesion or severe tandem lesions that can be covered by a single Neuroguard stent.
- Target lesion length is ≤ 20 mm (for 30 mm stents) or is ≤ 30 mm for 40 mm stents).
- Index vessel diameter (segment covered by the mid-portion of the stent) is between 4.0 mm and 6.0 mm at the site of target lesion.
- Distal vessel diameter at the site of the Neuroguard IEP System filter deployment is between 4.0 mm and 7.0 mm.
- Distal common carotid artery diameter (segment covered by the proximal portion of the stent) is between 4.0 mm and 8.0 mm.
- Sufficient landing zone exists in the cervical internal carotid artery distal to the target lesion to allow for the safe and successful deployment of both the primary embolic protection filter and the Neuroguard IEP System filter.

In addition, patients had to meet at least one of the significant anatomic or comorbid high-risk conditions listed below for inclusion in the study. Patients at high risk for CEA were defined as having significant physiological comorbidities and/or anatomic risk factors and would be poor candidates for CEA in the opinion of a physician.

High Anatomic Risk for CEA Conditions:

- Target lesion is located at or above C2 (level of the jaw) or below the clavicle.
- Inability to extend the head due to cervical arthritic or other cervical disorders.
- History of radiation treatment to the neck or radical neck dissection.
- Prior head and neck surgery in the region of the carotid artery.
- Spinal immobility of the neck.
- Tracheostomy or tracheostoma.
- Hostile neck or surgical inaccessible lesion.
- Laryngeal palsy or laryngectomy.
- Severe tandem lesions (total length must be ≤ 30 mm and must be covered with one stent).
- Occlusion of contralateral common carotid artery (CCA) or ICA.

High Co-Morbid Risk Conditions for CEA:

- Patient is ≥ 70 years of age (maximum 80 years) at the time of enrollment.
- NYHA Class III or IV congestive heart failure (CHF).
- Chronic obstructive pulmonary disease (COPD) with FEV1 < 50 or on intermittent or chronic oxygen therapy.
- Left ventricular ejection fraction (LVEF) ≤ 35%.
- Unstable angina.
- History of recent myocardial infarction (MI) (between 14 days and 6 weeks prior to the index procedure).
- Coronary artery disease with two or more vessels with ≥ 70% stenosis.
- Planned coronary artery bypass grafting (CABG) or valve replacement surgery between 31- and 60 days following carotid artery stenting (CAS) procedure.
- Peripheral vascular surgery or abdominal aortic aneurysm repair is required and planned between 31- and 60 days following CAS procedure.
- Contralateral laryngeal nerve paralysis.
- Restenosis following prior carotid endarterectomy (CEA).

General Exclusion Criteria:

- Life expectancy of less than 1 year, cancer with metastatic spread, undergoing active chemotherapy treatment, or currently requiring an organ transplantation.
- An evolving, acute stroke.
- Anticipated or potential sources of emboli including left ventricular aneurysm, severe cardiomyopathy, aortic or mitral mechanical heart valve, severe calcific aortic stenosis (valve area < 1.0 cm^2), endocarditis, moderate to severe mitral stenosis, known previously symptomatic patent foramen ovale (PFO), left atrial thrombus, any intracardiac mass or DVT or PE treated within the past 12 months.
- History of paroxysmal atrial flutter or atrial fibrillation requiring chronic anticoagulation.
- History of atrial flutter or chronic atrial fibrillation.
- Anticoagulation with Phenprocoumon (Marcumar®), warfarin, direct thrombin inhibitor, or anti-Xa agents within 14 days of the index procedure.

- Acute febrile illness (temperature ≥ 100.4 °F or 38° C) or active infection.
- Subjects with presumptive or confirmed SARS-CoV2/COVID-19 infection.
  - A SARS-CoV2/COVID-19 exposure and symptomology screening must be conducted for all subjects. If one or more of the screening questions is yes, a COVID-19 test must be performed with a negative result in order for the patient to be eligible.
  - Note: If a subject has confirmed SARS-CoV-2/COVID-19 infection (SARS-CoV2/COVID-19 +), eligibility may be re-established 21 days following diagnosis if infection is asymptomatic and 21 days following resolution of symptoms if infection is symptomatic.
- Acute myocardial infarction (MI) < 14 days prior to index procedure.
- Any major surgical procedure (i.e., intraabdominal or intrathoracic surgery or any surgery / interventional procedure involving cardiac or vascular system) within 30 days prior to or following the index procedure.
- History of major disabling stroke with substantial residual disability (modified Rankin score ≥ 3).
- Other neurological deficit not due to stroke that may confound the neurological assessments.
- Dementia considered other than mild.
- Known severe carotid stenosis or complete occlusion contralateral to the target lesion requiring treatment within 30 days of the index procedure.
- Known hypersensitivity to nitinol or its components (e.g., nickel, titanium).
- History of intracranial hemorrhage within 90 days prior to the index procedure.
- History of GI bleed within 30 days prior to the index procedure
- Chronic renal insufficiency (serum creatinine ≥ 2.5 ml/dL or estimated GFR < 30 cc/min) or end stage renal disease on hemodialysis.
- Any condition that precludes proper angiographic assessment or makes percutaneous arterial access unsafe (e.g., severe hepatic impairment, malignant hypertension, morbid obesity).
- Known hypersensitivity to contrast media that cannot be adequately premedicated.
- Hemoglobin (Hgb) < 8 gm/dL, platelet count < 100,000, INR > 1.5 (irreversible), or heparin-induced thrombocytopenia.
- History or current indication of bleeding diathesis or coagulopathy including thrombocytopenia or an inability to receive heparin in amounts sufficient to maintain an activated clot time (ACT) at ≥ 250 seconds.
- Contraindication to standard of care study medications, including antiplatelet therapy or aspirin.
- Previously enrolled in this study or currently enrolled in another interventional device or drug study that has not yet reached the primary endpoint.
- Potential for subject non-compliance with protocol-required follow up or antiplatelet medication.

Angiographic Exclusion Criteria:

- Total occlusion of the target carotid artery.
- Previously placed stent in the ipsilateral carotid artery.
- Severe calcification or vascular tortuosity of the target vessel that may preclude or make difficult the safe introduction of the sheath, guiding catheter, distal filter, Neuroguard stent, or integrated filter. Excessive circumferential calcification of the target lesion is defined as > 3 mm of thickness of calcification seen in orthogonal views on fluoroscopy. Severe vascular tortuosity is defined as 2 or more bends of 90 degrees or more within 4 cm of the target lesion.
- Qualitative characteristics of stenosis and stenosis-length of carotid bifurcation (common carotid) and/or ipsilateral external carotid artery, that preclude or make difficult the safe introduction of the sheath.
- Angulation or tortuosity (≥ 90 degree) of the innominate and common carotid artery (CCA) that precludes safe, expeditious sheath placement or that will transmit a severe loop to the internal carotid after sheath placement.
- Angiographic evidence of a mobile filling defect or fresh thrombus in the target carotid artery.
- Presence of "string sign" of the target lesion (a sub-totally occluded, long segment of the true lumen of the artery with markedly reduced contrast flow).
- Non-atherosclerotic carotid stenosis (e.g., dissection, fibromuscular dysplasia).
- Proximal/ostial CCA, innominate artery stenosis, or intracranial artery stenosis located distal to the target stenosis that is more severe than the target stenosis.
- Patient in whom percutaneous vascular access is not possible, including severe tortuosity or stenosis that requires additional endovascular procedures or that prevents safe and expeditious access.
- Patient with intracranial pathology, that in the opinion of the investigator, makes the patient inappropriate for study participation (e.g., arteriovenous malformation, brain tumor, microangiopathy or large vessel cerebral vascular disease, etc.) or that would confound the neurological evaluation.
- Known mobile plaque or thrombus in the aortic arch.
- Type III aortic arch.
- Angiographic, CT, MR or ultrasound evidence of severe atherosclerosis, tortuosity or angulation of the aortic arch or origin of the innominate or common carotid arteries that would preclude or make difficult safe passage of the sheath and other endovascular devices to the target artery as needed for carotid stenting.

2. Follow-up Schedule

All patients were scheduled to return for follow-up examinations at 30 days, 6 months, and 12 months, with annual follow-up continuing at 24 and 36 months post-procedure. Adverse events and complications were recorded at all visits through 12 months post-procedure. The key timepoints are shown below in **Table 6** summarizing safety and effectiveness.

Table 6. PERFORMANCE II Study Subject Follow-up

Assessment	Follow Up					
	30 Days (± 7 d)	6 months (± 30 d)	12 months (± 30 d)	24 months (± 45 d)	36 months (± 45 d)	Unscheduled Visit
Informed Consent						
Medical History, Demographics						
Physical exam						
Modified Rankin Scale (mRS)	X	X	X	X	X	X[2]
National Institutes of Health Stroke Scale (NIHSS)	X	X	X	X	X	X[2]
Head CT or Brain MRI						X[2]
Carotid duplex ultrasound		X	X	X	X	X[2]
Catheter based angiography, 3D CTA or 3D MRA showing the internal, common carotid arteries and aortic arch						X[3]
Index Procedure						
12-lead ECG	X					X[1]
Cardiac Biomarkers (troponin or CK Total, CK-MB)						X[1]
Pregnancy test						
CBC, Serum creatinine (Cr), BUN, potassium						
Dual antiplatelet therapy assessment	X	X	X	X	X	X
Concomitant medications	X	X	X	X	X	X
SARS-CoV-2/COVID-19 test						X[4]
AE assessment	X	X	X	X	X	X

1. Performed only if clinically indicated.
2. Neurological examination, modified Rankin Scale (mRS), and National Institutes of Health Stroke Scale (NIHSS) was performed if an unscheduled visit was due to a neurological event.
3. Performed if carotid re-intervention / revascularization was required.
4. A SARS-CoV-2/COVID-19 test was conducted for all serious adverse events.

3. Clinical Endpoints

The primary safety and effectiveness endpoint was defined as a composite of 30-day rate of Major Adverse Event (MAE), defined as death, all stroke and myocardial infarction (MI) within 30 days of the index carotid stenting procedure plus ipsilateral stroke through 12 months of the procedure.

The null hypothesis is that the true primary endpoint rate in subjects treated with the Neuroguard IEP System is greater than or equal to the PG that represents acceptable performance for subjects treated with CAS who are at high risk for complications if treated with CEA and stratified by comorbid and anatomic high-risk cohorts. The alternate hypothesis is that the rate is less than the PG. Symbolically, the null and alternative hypotheses are:

$$H0: w1\pi1 + w2\pi2 \geqslant PG$$

$$H1: w1\pi1 + w2\pi2 < PG$$

where w1 and w2 are pre-specified weight constants and π1 and π2 are the primary endpoint proportions for comorbid and anatomic risk cohorts as specified further below.
Using the following weighted Z-test, if the Z-score for the primary endpoint event rate is greater than 1.645, the null hypothesis is rejected, and the study goal is met:

$$Z = (PG - (w_1\hat{\pi}_1 + w_2\hat{\pi}_2)/\sqrt{var(w_1\hat{\pi}_1 + w_2\hat{\pi}_2)}$$

where

$$var(w_1\hat{\pi}_1 + w_2\hat{\pi}_2) = w_1^2\, PG_1(1 - PG_1)/n_1 + w_2^2\, PG_2(1 - PG_2)/n_2$$

and

- PG=13.8%
- PG_1 (comorbid)=15%
- PG_2 (anatomic)=11%
- w_1=weight of comorbid subpopulation equal to its actual frequency
- w_2=weight of anatomic subpopulation equal to its actual frequency
- $\hat{\pi}_1$=proportion of primary endpoint event in comorbid subpopulation
- $\hat{\pi}_2$=proportion of primary endpoint event in anatomic subpopulation
- n_1=number of evaluable patients in comorbid subpopulation
- n_2=number of evaluable patients in anatomic subpopulation

Secondary endpoints included the following:

- Procedural success, defined as successful Neuroguard stent implantation with ≤ 50% residual angiographic stenosis of the target lesion as determined by the angiographic core lab;
- Technical Success, defined as successful deployment of the Neuroguard stent in the targeted treatment location with ≤ 50% residual angiographic restenosis immediately after post-dilation as determined by the angiographic core lab, successful delivery and deployment of the Neuroguard IEP System filter beyond the target lesion with retrieval after completion of the stent placement, successful post-dilation of the Neuroguard stent with the integrated angioplasty balloon, and successful removal of the delivery system;
- Clinically-Driven Target Lesion Revascularization (CD-TLR), defined as any revascularization procedure of the original treatment site associated with narrowing of > 80% as determined by the angiographic core lab within 12 months of the index procedure;
- In-Stent Restenosis (ISR), defined as > 70% narrowing observed within the Neuroguard stent per core lab ultrasound analysis through 12 months, 24 months and 36 months post index procedure;

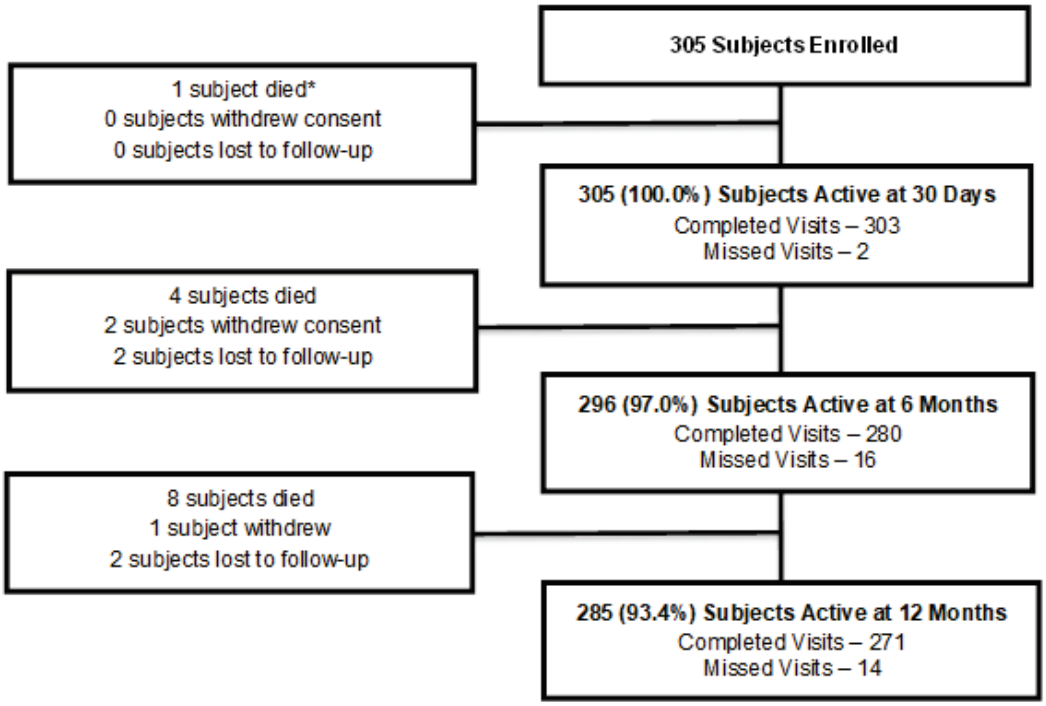
- Major stroke, defined as a new focal ischemic neurological deficit of abrupt onset which is present after 7 days and results in ≥ 4-point increase in NIHSS compared to baseline through 30 days post index procedure;
- Minor stroke through 30 days, defined as a new focal ischemic neurological deficit of abrupt onset lasting > 24 hours and increasing NIHSS by ≤ 3 points at 7 days;
- Neurological death, defined as death after a stroke that is either a direct consequence of the stroke or a complication of the stroke, through 12 months post index procedure.

All clinical events were adjudicated by an independent Clinical Events Committee (CEC).

B. Accountability of PMA Cohort

At the time of database lock, of 305 subjects enrolled in the PMA study, 93.4% (n = 285) subjects were active at 12 months for primary endpoint analysis. The Intent-to-treat (ITT) cohort consisted of all 305 patients enrolled in the study, regardless of treatment received. Subject disposition is presented in **Figure 5** below.

Figure 5. Subject Disposition per ITT Analysis



* One subject completed the scheduled 30-day follow-up visit on Day 25 post-procedure and died on Day 30 post-procedure (non-neurological death). As the 30-day visit was within the follow-up window, the subject visit is included in the analysis.

C. Study Population Demographics and Baseline Parameters

A total of 305 subjects with 305 lesions were treated at 23 U.S. and 9 OUS investigational sites. All subjects were considered at high-risk for complications if treated with CEA; 19.67% of subjects were categorized as symptomatic as described in **Table 7** below.

Table 7. PERFORMANCE II Study Subject Comorbidity Status

Subject Characteristics	Symptomatic (N=60)	Asymptomatic (N=245)	Total (N=305)
High-Risk for CEA Conditions			
Anatomic only	21.67% (13/60)	24.90% (61/245)	24.26% (74/305)
Comorbid only	51.67% (31/60)	46.12% (113/245)	47.21% (144/305)
Both conditions	26.67% (16/60)	28.98% (71/245)	28.52% (87/305)
None of the conditions above	0.00% (0/60)	0.00% (0/245)	0.00% (0/305)

Per ITT analysis, the mean age of the study population was 69.59 ± 7.47 SD years and 201/305 (65.90%) were male. The prevalence of traditional cardiovascular risk factors in enrolled subjects included 132/305 (43.28%) diabetes mellitus, 219/305 (71.80%) current/former smoker, and coronary artery disease 184/305 (60.33%). **Table 8** below presents subject baseline demographics and medical history.

Table 8. PERFORMANCE II Study Subject Demographics and Medical History

Subject Characteristics	Neuroguard IEP System (N=305)
Age (years)	
Mean±SD (N)	69.59±7.47 (305)
Median	71.08
Range (Min,Max)	(43.38,80.96)
Male gender at birth, %(n/N)	65.90% (201/305)
Ethnicity, %(n/N)	
American Indian or Alaska Native	0.00% (0/305)
Asian	0.98% (3/305)
Native Hawaiian or Other Pacific Islander	0.00% (0/305)
Black or African American	5.25% (16/305)
White	92.79% (283/305)
Other	0.98% (3/305)
Current or Former Smoker, %(n/N)	71.80% (219/305)
Alcohol intake in the past or at present, %(n/N)	30.82% (94/305)
Coronary artery disease, %(n/N)	60.33% (184/305)
Previous Q wave or non-Q wave MI, %(n/N)	17.70% (54/305)
Known Left Ventricular dysfunction, %(n/N)	6.89% (21/305)
Hyperlipidemia requiring medication, %(n/N)	92.79% (283/305)
History of hypertension, %(n/N)	92.79% (283/305)
History of Clinical COPD, %(n/N)	22.62% (69/305)
History of NYHA Class III or IV congestive heart failure, %(n/N)	2.95% (9/305)
History of chronic renal impairment with serum creatinine > 2.5 ml/dL or estimated GFR < 30 cc/min, %(n/N)	0.66% (2/305)

Subject Characteristics	Neuroguard IEP System (N=305)
Diabetes mellitus, %(n/N)	43.28% (132/305)
History of cancer, %(n/N)	20.66% (63/305)
Previous carotid endarterectomy, %(n/N)	10.49% (32/305)
Current contralateral disease, %(n/N)	37.38% (114/305)
History of peripheral vascular disease, %(n/N)	32.79% (100/305)
Previous coronary stenting or angioplasty, %(n/N)	35.88% (108/301)
Previous or planned CABG, %(n/N)	19.02% (58/305)
History of TIA, %(n/N)	19.02% (58/305)
History of stroke, %(n/N)	21.31% (65/305)
History of amaurosis fugax ipsilateral to the carotid lesion, %(n/N)	11.15% (34/305)
History of non-lateralizing symptoms (dizziness, etc.), %(n/N)	16.39% (50/305)
Other neurological events, %(n/N)	7.21% (22/305)

Table 9 below presents lesion and vessel characteristics while **Table 10** presents procedural characteristics. Target lesions were categorized as *de novo* (92.76%, 282/304) and restenotic CEA (7.24%, 22/304). All lesion and vessel characteristics were interpreted by an independent angiographic core laboratory.

Table 9. PERFORMANCE II Study Lesion and Vessel Characteristics

Subject Characteristics	Neuroguard IEP System (N=305)
Core peripheral artery segment	
Right common carotid artery	0.66% (2/304)
Right internal carotid artery	50.66% (154/304)
Left common carotid artery	2.63% (8/304)
Left internal carotid artery	46.05% (140/304)
Lesion Length, mm	
Mean ± SD (N)	19.08±6.66 (304)
Median	19.08
Range (Min,Max)	(4.61,38.58)
Eccentric, % (n/N)	22.04% (67/304)
ICA Calcification, % (n/N)	
None / Mild	33.88% (103/304)
Moderate	31.58% (96/304)
Severe	34.54% (105/304)
ICA Tortuosity, % (n/N)	7.24% (22/304)
Lesion Bend, degrees	
Mean±SD (N)	39.40±22.82 (41)
Median	32.00
Range (Min,Max)	(0.00,90.00)
Bifurcation, % (n/N)	
No Bifurcation	11.18% (34/304)

Subject Characteristics	Neuroguard IEP System (N=305)
A	0.99% (3/304)
B	76.64% (233/304)
C	3.62% (11/304)
D	2.30% (7/304)
E	1.32% (4/304)
F	0.00% (0/304)
G	3.95% (12/304)
Bifurcation Angulation, degrees	
Mean±SD (N)	46.96±15.16 (303)
Median	45.00
Range (Min,Max)	(16.90,89.10)
ECA, %	
Mean±SD (N)	54.27±27.03 (67)
Median	45.00
Range (Min,Max)	(0.00,100.00)
TIMI Flow, % (n/N)	
Normal	100.00% (304/304)
ECA TIMI Flow, % (n/N)	
Normal	97.04% (295/304)
Decreased	1.32% (4/304)
No flow	1.64% (5/304)
Calcification, % (n/N)	
None/Mild	99.32% (290/292)
Moderate	0.00% (0/292)
Severe	0.68% (2/292)

Table 10. PERFORMANCE II Study Procedural Characteristics

Procedure Characteristics	Neuroguard IEP System (N=305)
Duration of procedure, minutes (sheath insertion to removal)	
Mean±SD (N)	50.50±19.97 (305)
Median	47.00
Range (Min,Max)	(16.00,165.00)
Primary EPD deployment to retrieval	
Mean±SD (N)	16.03±8.08 (303)
Median	14.00
Range (Min,Max)	(3.00,70.00)
Neuroguard filter deployment to retrieval	
Mean±SD (N)	4.63±3.41 (294)
Median	4.00
Range (Min,Max)	(0.00,32.00)
Pre-dilation performed prior to EPD	0.66% (2/305)
Pre-dilation performed prior to Neuroguard	63.93% (195/305)

Procedure Characteristics	Neuroguard IEP System (N=305)
Total Contrast Injection, mL	
Mean±SD (N)	121.16±51.50 (303)
Median	115.00
Range (Min,Max)	(30.00,375.00)
Primary Embolic Protection, % (n/N)	100.00% (305/305)
Procedure Medications	
Anticoagulant therapy	
Heparin	67.54% (206/305)
Angiomax (bivalirudin)	32.13% (98/305)
Other	0.33% (1/305)
Pre-dilation Balloon Parameters	
Maximal diameter, mm	
Mean±SD (N)	3.85±0.58 (224)
Median	4.00
Range (Min,Max)	(2.00,6.00)
Maximal length, mm	
Mean±SD (N)	25.12±6.68 (221)
Median	30.00
Range (Min,Max)	(12.00,60.00)

The Neuroguard IEP System is indicated to be used in conjunction with an available primary distal embolic protection device as described in the IFU. **Table 11** below presents the distribution of primary distal embolic protection devices used in the PERFORMANCE II study by successfully implanted stent size. Twelve (12) of 305 subjects did not receive a successful Neuroguard stent implantation. The safety and effectiveness of the Neuroguard IEP System has not been evaluated with primary distal embolic protection devices other than those listed in **Table 11**.

Table 11. PERFORMANCE II Primary Distal Embolic Filters Used

Neuroguard IEP System Model Number	Stent Diameter (mm)			Stent Length (mm)	Stents implanted (N)	Primary Distal Filter Used (n)		
	Proximal Tapered Diameter	Nominal Diameter	Distal Tapered Diameter			Emboshield NAV6	FilterWire EZ	SpiderFX
NG-0730-140-2	9	7	8	30	138	121	8	9
NG-0740-140-2	9	7	8	40	92	71	14	7
NG-0630-140-2	8	6	7	30	15	8	4	3
NG-0640-140-2	8	6	7	40	48	38	6	4
				TOTAL	293	238	32	23

D. Safety and Effectiveness Results

1. Primary Safety and Effectiveness Endpoint

The analysis of the primary endpoint of 30-day rate of Major Adverse Event (MAE), defined as death, all stroke, and myocardial infarction (MI) within 30 days of the index carotid stenting procedure, plus ipsilateral stroke through 12 months post-procedure was carried out on all ITT subjects who experienced the primary endpoint or had at least 330 days of follow-up (i.e., complete cases). All clinical events were adjudicated by an independent CEC.

The 12-month MAE rate was 2.84% (8/282). **Table 12** presents the primary endpoint and individual components below.

Table 12. PERFORMANCE II Study Primary Endpoint Analysis

Study Endpoints	Neuroguard IEP System (N=305)
Major Adverse Event, %(n/N)	2.84% (8/282)
Death to 30 days post-procedure, %(n/N)	0.35% (1/282)
All Stroke to 30 days post-procedure, %(n/N)	1.42% (4/282)
Minor, %(n/N)	1.42% (4/282)
Major, %(n/N)	0.00% (0/282)
Myocardial Infarction to 30 days post-procedure, %(n/N)	0.71% (2/282)
Ipsilateral stroke to 360 days post-procedure, %(n/N)	1.79% (5/280)
Minor, %(n/N)	1.79% (5/280)
Major, %(n/N)	0.00% (0/279)

The corresponding Z-score was 5.316, greater than the Z-score of 1.645 pre-defined in the study protocol and statistical analysis plan. Thus, the null hypothesis is rejected and the study goal was met ($p<0.05$, 1-sided test).

Examination of individual components of the MAE primary endpoint reveal event rates of 0.35% (1/282) for all death, 1.42% (4/282) for all stroke and 0.71% (2/282) for any MI through 30 days post-procedure. The one subject death was due to cardiac arrest and adjudicated by the independent CEC as unlikely related to the study procedure or device. All strokes occurring through 30 days were minor (ipsilateral) strokes; no major strokes were reported.

From 30-days post-procedure through 12-month follow-up, only 1 subject experienced ipsilateral (minor) stroke 276 days post-procedure, yielding a 30-day all-stroke plus ipsilateral stroke through 12 months rate of 1.79% (5/280). Importantly, no major strokes occurred post-procedure through 12-month follow-up.

2. Secondary Endpoint Results

Secondary clinical and angiographic endpoint results for the ITT population were descriptive in nature; no formal statistical hypotheses were tested. Through 30 days post-procedure, minor stroke (all ipsilateral) occurred in 1.31% (4/305) of subjects and no subjects experienced major stroke.

No subjects experienced neurological death through 12 months post-procedure. Also at 12 months post-procedure, no subjects experienced CD-TLR, defined as any revascularization procedure of the original treatment site associated with narrowing of > 80% as determined by the angiographic core laboratory. All TLR through 12 months post-procedure was 1.08% (3/279).

In-stent restenosis, defined as > 70% narrowing observed within the Neuroguard stent per angiographic core laboratory ultrasound analysis, was 3.65% (10/274) through 12 months post-procedure.

Overall, in-hospital and 30-day MAE rates were 0.98% (3/305) and 2.30% (7/305), respectively. **Table 13** below describes secondary endpoints per ITT analysis.

Table 13. PERFORMANCE II Study Secondary Endpoint Analysis

Study Endpoints	Neuroguard IEP System (N=305)	95% Confidence Interval
Acute Success Rates		
Procedure Success	96.69% (292/302)	[93.99%,98.40%]
Successful Neuroguard carotid stent implantation	96.07% (293/305)*	[93.23%,97.95%]
≤ 50% residual angiographic stenosis of the target lesion as determined by the angiographic core lab	99.67% (301/302)	[98.17%,99.99%]
Technical Success	95.68% (288/301)	[92.73%,97.68%]
Successful deployment of the Neuroguard carotid stent in the targeted treatment location with a residual diameter stenosis ≤ 50% immediately after post-dilation as determined by the angiographic core lab	96.69% (292/302)	[93.99%,98.40%]
Successful delivery and deployment of the Neuroguard filter beyond the target lesion and retrieval after completion of the stent placement	96.07% (293/305)	[93.23%,97.95%]
Successful post-dilation of the Neuroguard carotid stent with the integrated angioplasty balloon	95.72% (291/304)	[92.80%,97.70%]
Successful removal of the delivery system	100.00% (305/305)	[98.80%,100.00%]
Clinical Events		
Clinically-driven target lesion revascularization to 360 days post-procedure	0.00% (0/279)	[0.00%,1.31%]
Any target lesion revascularization to 360 days post-procedure	1.08% (3/279)	[0.22%,3.11%]
In-stent restenosis to 360 days post-procedure	3.65% (10/274)	[1.76%,6.61%]
Major stroke through 30 days	0.00% (0/305)	[0.00%,1.20%]
Minor stroke through 30 days	1.31% (4/305)	[0.36%,3.32%]
Neurological death through 12 months	0.00% (0/279)	[0.00%,1.31%]

* Twelve (12) of 305 subjects did not receive successful Neuroguard stent implantation due to inability to cross the target lesion (n=4) or inability to deploy the integrated filter (n=8).

3. Adverse effects that occurred in the PMA clinical study

Adverse events (AEs) were defined as any untoward medical occurrence, unintended disease or injury, or untoward clinical sign (including abnormal laboratory findings) in subjects whether or not related to the investigational medical device. Serious Adverse Events (SAEs) were defined as adverse events that led to the following:

- Death,
- Serious deterioration in the health of the subject, that either resulted in
  1) a life-threatening illness or injury, or
  2) a permanent impairment of a body structure or a body function, or
  3) in-patient or prolonged hospitalization, or
  4) medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function,
- Fetal distress, fetal death or a congenital abnormality or birth defect.

Planned hospitalization for a pre-existing condition, or a procedure required by the clinical investigational plan (protocol), without serious deterioration in health, was not considered a serious adverse event.

Of the 305 subjects, 114 (37.4%) subjects experienced an adverse event through 30-day follow-up, and 186 (61.0%) subjects experienced an adverse event through 12-month follow-up as described below in **Table 14**. Fifty-nine (59) subjects (19.3% experienced a serious adverse event through the 30-day follow-up, and 107 (35.1%) subjects experienced a serious adverse event through the 12-month follow up. No subject experienced an unanticipated adverse event.

Table 14. Adverse Events to 360 Days Post-procedure – ITT Population

System Organ Class/Preferred Term	Number of Events	Number of Subjects (N= 305)
Any Adverse Event	565	186 (61.0%)
Blood And Lymphatic System Disorders	**18**	**13 (4.3%)**
Anemia	12	
Other Blood and Lymphatic Disorders	6	
Cardiac Disorders	**77**	**52 (17.0%)**
Acute Coronary Syndrome	3	
Angina	14	
Arrhythmia	6	
Atrial Fibrillation	3	
Atrial Flutter	3	
Bradycardia	9	
Cardiogenic Shock	3	
Congestive Heart Failure	11	
Coronary Artery Disease Progression	3	
Non ST Segment Elevation Myocardial Infarction	6	
Unstable Angina	4	
Other Cardiac Disorders	12	
Ear And Labyrinth Disorders	**2**	**2 (0.7%)**

System Organ Class/Preferred Term	Number of Events	Number of Subjects (N= 305)
Vertigo	2	
Endocrine Disorders	**1**	**1 (0.3%)**
Diabetic Ketoacidosis	1	
Eye Disorders	**8**	**7 (2.3%)**
Amaurosis Fugax	4	
Glaucoma	2	
Other Eye Disorders	2	
Gastrointestinal Disorders	**32**	**24 (7.9%)**
Abdominal Pain	5	
Constipation	4	
Gastrointestinal Bleed	3	
Nausea and Vomiting	3	
Other Gastrointestinal Disorders	17	
General Disorders And Administration Site Conditions	**24**	**19 (6.2%)**
Non-Cardiac Chest Pain	7	
Non-specific Chest Pain	3	
Peripheral Edema	6	
Other General Disorders and Administration Site Conditions	8	
Hepatobiliary Disorders	**4**	**4 (1.3%)**
Cholecystitis	1	
Choledocholithiasis	1	
Cholelithiasis	1	
Hepatopathy	1	
Immune System Disorders	**2**	**2 (0.7%)**
Allergic Drug Rash	2	
Infections And Infestations	**79**	**54 (17.7%)**
Cellulitis of Foot	3	
Coronavirus (COVID-19) Infection	13	
Pneumonia	14	
Sepsis	3	
Urinary Tract Infection	14	
Viral Infection	3	
Other Infections and Infestations	29	
Injury, Poisoning And Procedural Complications	**19**	**18 (5.9%)**
Vascular Access Site Hematoma	3	
Vascular Access Site Pain	3	
Vascular Access Site Pseudoaneurysm	3	
Other Injury, Poisoning and Procedural Complications	10	
Investigations	**12**	**11 (3.6%)**
Doppler Ultrasound Abnormal	8	
Other Investigations	4	
Metabolism And Nutrition Disorders	**17**	**13 (4.3%)**
Diabetes Mellitus	3	
Hypokalemia	3	
Other Metabolism and Nutrition Disorders	11	
Musculoskeletal And Connective Tissue Disorders	**22**	**19 (6.2%)**
Pain, Musculoskeletal	9	
Other Musculoskeletal and Connective Tissue Disorders	13	
Neoplasms Benign, Malignant And Unspecified (Incl Cysts And Polyps)	**10**	**9 (3.0%)**
Basal Cell Carcinoma	2	

System Organ Class/Preferred Term	Number of Events	Number of Subjects (N= 305)
Lung Cancer	2	
Squamous Cell Carcinoma	2	
Other Neoplasms Benign, Malignant and Unspecified	4	
Nervous System Disorders	**51**	**45 (14.8%)**
Dizziness	7	
Headache	11	
Minor Ischemic Stroke	4	
Transient Ischemic Attack	12	
Other Nervous System Disorders	17	
Psychiatric Disorders	**4**	**4 (1.3%)**
Depression	2	
Other Psychiatric Disorders	2	
Renal And Urinary Disorders	**13**	**11 (3.6%)**
Acute Kidney Injury	3	
Other Renal and Urinary Disorders	10	
Reproductive System And Breast Disorders	**5**	**3 (1.0%)**
Balanitis	1	
Benign Prostatic Hyperplasia	1	
Hydrocele	1	
Testicular Pain	1	
Varicocele	1	
Respiratory, Thoracic And Mediastinal Disorders	**34**	**22 (7.2%)**
Chronic Obstructive Pulmonary Disease	3	
Dyspnea	6	
Pleural Effusion	4	
Respiratory Failure	6	
Other Respiratory, Thoracic and Mediastinal Disorders	15	
Skin And Subcutaneous Tissue Disorders	**11**	**7 (2.3%)**
Foot Ulcer	3	
Other Skin and Subcutaneous Tissue Disorders	8	
Surgical And Medical Procedures	**19**	**17 (5.6%)**
Non-Target Vessel Revascularization	6	
Target Lesion Revascularization	4	
Other Surgical and Medical Procedures	9	
Vascular Disorders	**101**	**75 (24.6%)**
Atherosclerosis of Arteries of the Extremities with Intermittent Claudication	19	
Carotid Artery Stenosis, Non-Target Vessel	4	
Edema of Lower Extremity	4	
Hypertension	6	
Hypotension	15	
Orthostatic Dizziness	3	
Orthostatic Hypotension	7	
Procedural Hypotension	20	
Other Vascular Disorders	23	

4. Subgroup Analyses

To assess the consistency of the treatment effect, primary endpoint outcomes were analyzed in subgroups defined according to pre-specified factors: race, gender, age (< 75 years), symptomatic status, high-risk status for CEA and site region (US vs. EU). High-risk status was based on the anatomic and co-morbid conditions specified in the eligibility criteria of the study protocol. Consistency was assessed using Fisher's Exact

test for 2 subgroups (i.e., for sex, age, symptom status, and site location) and Chi Square test for more than 2 subgroups (i.e., for ethnicity and high-risk CEA conditions) at a 0.05 level of significance. Within the ITT population, primary endpoint outcomes were consistent across all subgroups as described in **Table 15** below.

Table 15. MAE Subgroup Analyses to 360 Days Post-procedure – ITT Population

Subject Characteristics	Major Adverse Event, % (n/N)	P-Value*
Ethnicity		
American Indian or Alaska Native	--,--	
Asian	0.00% (0/3)	
Black or African American	0.00% (0/13)	0.897
Native Hawaiian or Other Pacific Islander	--,--	
White	3.04% (8/263)	
Other	0.00% (0/3)	
Sex		
Male	2.67% (5/187)	1.000
Female	3.16% (3/95)	
Age		
<75 years	1.90% (4/210)	0.118
>=75 years	5.56% (4/72)	
Symptomatic Status		
Asymptomatic	2.64% (6/227)	0.656
Symptomatic	3.64% (2/55)	
High-Risk For CEA Conditions		
Anatomic	1.39% (1/72)	
Comorbid	1.52% (2/132)	0.082
Both	6.41% (5/78)	
Site Location		
US	2.70% (6/222)	0.679
Europe	3.33% (2/60)	

* Note that the study was not powered to detect differences between subgroups.

5. Pediatric Extrapolation

In this premarket application, existing clinical data was 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. No investigators were full-time or part-time employees of the sponsor. The pivotal clinical study included four (4) 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: 1
- Proprietary interest in the product tested held by the investigator: 0
- Significant equity interest held by investigator in sponsor of covered study: 3

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. Statistical analyses were conducted by FDA to determine whether the financial interests/arrangements had any impact on the clinical study outcome. The information provided does not raise any questions about the reliability of the data.

XI. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

The PERFORMANCE I Study (Protection against Emboli using a 3-in-1 delivery system comprising an integRated Filter, nORMal Angioplasty balloon and Novel Carotid stEnt) was a prospective, multi-national, multicenter single-arm, open label study to evaluate the safety and feasibility of the Neuroguard IEP System for the treatment of carotid artery stenosis. Sixty (60) patients undergoing carotid artery stenting were enrolled at nine (9) centers in Europe (Germany, Italy, Bulgaria, Macedonia, and Slovenia) between February and December 2018. The primary endpoint was the 30-day composite rate of stroke, death, and myocardial infarction versus a prespecified performance goal of 8.1%. Secondary endpoints included procedural success, device success, and target lesion revascularization.

The 1-month rate of the primary endpoint of MAE in the 60 Neuroguard patients was 1.7% (upper 95% CI 7.7%), lower than the performance goal of 8.1%. Therefore, the performance goal was met. There were no deaths or stroke. There was one non-ST elevation myocardial infarction requiring hospitalization and percutaneous coronary intervention at Day 17. The subject was discharged home without complications.

The procedural success rate with the Neuroguard IEP System was 100% (60/60), and the technical success rate with the Neuroguard IEP System was 100% (60/60). Through 12-month follow-up, there were no strokes, neurological deaths, target lesion revascularizations, or instances of in-stent restenosis.

The study population was predominantly male (73.3%) with a mean age of age 69.1 ± 9.01 years and eleven (11) subjects (18.3%) presented with a symptomatic carotid artery stenosis.

XII. 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.

XIII. 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 Neuroguard IEP system confirmed the product design characteristics, specifications, and intended use. The non-clinical engineering testing conducted on the stent, delivery system, and embolic protection device 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 Neuroguard IEP 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 2 years.

A prospective, multi-center single arm open label study, described above, was conducted to support approval of this device. Safety and effectiveness outcomes in the study were compared to a performance goal derived from four studies for the clinical evaluation of safety and effectiveness of carotid artery stents used in the treatment of atherosclerotic carotid artery disease in patients at high risk for adverse events following carotid endarterectomy. Effectiveness of the device was analyzed by evaluating the composite primary endpoint of major adverse events (MAE) consisting of death, stroke and myocardial infarction through 30 days and one-year ipsilateral stroke. Given the weighted performance goal of 13.8% and expected primary endpoint event rate of 8.1%, the observed MAE rate of 2.84 % in the intention-to-treat population met the performance goal ($p<0.05$, 1-sided test). The observed MAE rate and descriptive statistical analysis of secondary endpoints also support the safety of the device as compared to the four reference studies of clinical outcomes with similar devices. 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. The Neuroguard IEP System with its integrated balloon and filter for stent post-dilation used with a primary distal embolic protection device offers similar benefits that stenting with a traditional stent and embolic

protection device offers over alternative treatments to stenting. The clinical trial has established the safety and effectiveness of the Neuroguard IEP System, 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 Neuroguard IEP System 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).

XIV. CDRH DECISION

CDRH issued an approval order on October 11, 2024. The final conditions of approval cited in the approval order are described below.

Post-Approval Study – Continued Follow-up Study. This study should be conducted per protocol CSP-1400 Version Number 3.3 US (dated September 8, 2023). This study is a prospective, multicenter follow-up of the pivotal study (G200007) that treated 305 subjects from 32 investigational sites. It will evaluate the long-term safety and effectiveness of the Neuroguard IEP System. All 285 remaining subjects active at the end of the 12-month evaluation will continue to be followed annually through 36 months. Follow-up at the 24- and 36-month timepoints will include the following: NIH Stroke Scale, modified Rankin Score, an assessment of serious adverse events, an assessment of concomitant medications (antiplatelet, anticoagulant, or other therapy), and carotid duplex ultrasound.

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

XV. 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