SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Stent, Carotid
Device Trade Name[1]:	Roadsaver™ / CASPER™ Carotid Stent System
Device Procode:	NIM
Applicant's Name and Address:	MicroVention, Inc. 35 Enterprise Aliso Viejo, CA 92656
Date(s) of Panel Recommendation:	None
Premarket Approval Application (PMA) Number:	P210030
Date of FDA Notice of Approval:	11/20/2024

[1]The Roadsaver Carotid Stent System and the CASPER Carotid Stent System are identical in design and labeling except for the product name and branding. Terumo Interventional Systems (Terumo) markets the device under the product name Roadsaver Carotid Stent System while MicroVention, a wholly owned subsidiary of Terumo, markets the device under the product name CASPER Carotid Stent System.

II. INDICATIONS FOR USE

The Roadsaver (or CASPER) Carotid Stent System, when used in conjunction with the Nanoparasol (or EmPro) embolic protection system, is intended for the treatment of carotid artery stenosis in patients with elevated risk for adverse events following carotid endarterectomy and meet the criteria outlined below:

1. Patients who have either de novo atherosclerotic or post endarterectomy restenotic lesion(s) in the internal carotid arteries or at the carotid bifurcation with ≥50% stenosis if symptomatic or ≥80% stenosis if asymptomatic (both defined by angiography),

   AND

2. Patients having a vessel with reference diameters between 3.5 mm and 9.0 mm at the target lesion.

III. CONTRAINDICATIONS

The Roadsaver / CASPER Carotid Stent System is contraindicated for use in:

- Patients in whom anticoagulant, antiplatelet therapy or thrombolytic drugs are contraindicated
- Patients with known hypersensitivity to nickel-titanium
- Patients with severe vascular tortuosity or anatomy that would preclude the safe introduction of a guide catheter, sheath, embolic protection system or stent system
- Patients with uncorrected bleeding disorders
- Lesions in the ostium of the common carotid artery
- Carotid vessel with <25mm gap between the target location of the distal end of the stent and the proximal end of the distal protection device.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Roadsaver / CASPER Carotid Stent System Instructions for Use.

V. DEVICE DESCRIPTION

The Roadsaver / CASPER Carotid Stent System consists of a self-expanding braided nickel titanium (nitinol) stent (implant) and a rapid exchange (RX) delivery catheter/pusher for use in patients who require carotid revascularization and are at high risk for adverse events from carotid endarterectomy (CEA). The Roadsaver / CASPER System is available in multiple stent sizes and the catalog numbers and sizes are provided below in **Table 1.**

Table 1: Roadsaver and CASPER Carotid Stent System Models and Dimensions

Catalog Number		Stent Implant Unconstrained Dimensions		Reference Vessel Diameters	Foreshortening (%)*
Roadsaver (Terumo)	CASPER (MicroVention)	Outer Diameter (mm)	Overall / Dual Layer Length (mm)		
RDS-0520-143RX	CPR-0520-143RX	5	25 / 20	3.5-4	6.33-10.15
RDS-0530-143RX	CPR-0530-143RX	5	37 / 30	3.5-4	9.88-14.08
RDS-0540-143RX	CPR-0540-143RX	5	47 / 40	3.5-4	9.50-13.38
RDS-0616-143RX	CPR-0616-143RX	6	22 / 16	4-5	9.94-15.59
RDS-0625-143RX	CPR-0625-143RX	6	33 / 25	4-5	10.31-17.66
RDS-0630-143RX	CPR-0630-143RX	6	40 / 30	4-5	8.27-15.95
RDS-0718-143RX	CPR-0718-143RX	7	25 / 18	5-6	12.57-18.69
RDS-0725-143RX	CPR-0725-143RX	7	35 / 25	5-6	13.31-21.03
RDS-0730-143RX	CPR-0730-143RX	7	40 / 30	5-6	13.85-22.11
RDS-0820-143RX	CPR-0820-143RX	8	25 / 20	6-7	16.21-22.49
RDS-0825-143RX	CPR-0825-143RX	8	35 / 25	6-7	17.23-25.05

RDS-0830-143RX	CPR-0830-143RX	8	40 / 30	6-7	17.05-25.44
RDS-0840-143RX	CPR-0840-143RX	8	47 / 40	6-7	18.44-27.29
RDS-0920-143RX	CPR-0920-143RX	9	33 / 20	7-8	16.47-23.64
RDS-0930-143RX	CPR-0930-143RX	9	40 /30	7-8	17.58-26.70
RDS-1020-143RX	CPR-1020-143RX	10	35 / 20	8-9	20.26-26.07
RDS-1030-143RX	CPR-1030-143RX	10	43 / 30	8-9	21.21-27.89

* Percent %) foreshortening for each size was calculated using the following equation where L_C is the crimped length and L is the stent length at each target diameter (minimal and maximum reference vessel diameters: $[(L_C - L)/ L_C]x100$

The self-expanding implant is designed to expand to a pre-determined diameter when deployed by the delivery catheter. The implant is produced with various outer diameters ranging from 5-10 mm and with lengths of 16-40 mm. The nitinol stent is constructed from 2 layers of tubular nitinol mesh. The outer layer consists of a woven closed cell structure with flared ends. The inner layer consists of a braided closed cell structure with micro sized pores. Upon exiting the delivery catheter at the target lesion, the implant expands to the vessel lumen diameter.

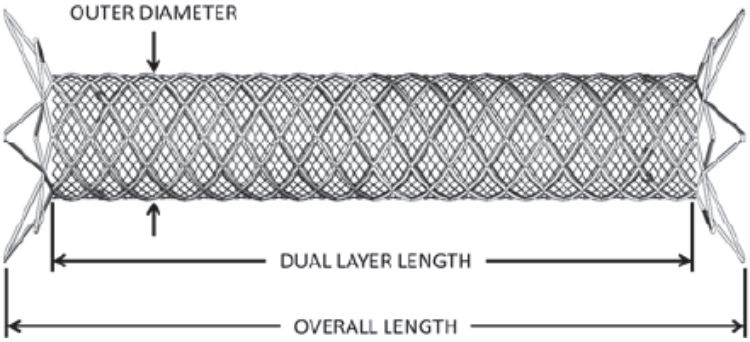


Figure 1: Roadsaver / CASPER Implant – Unconstrained

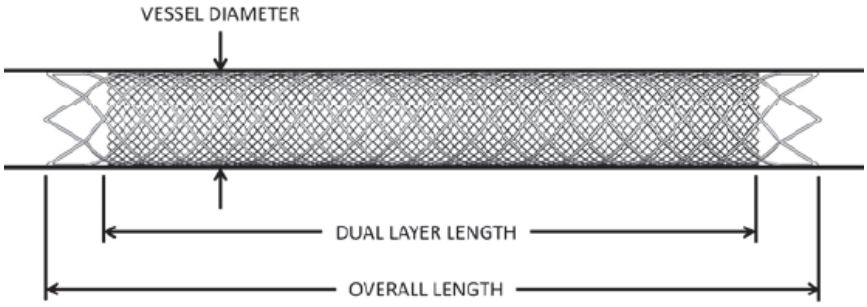


Figure 2: Roadsaver / CASPER Implant – Constrained

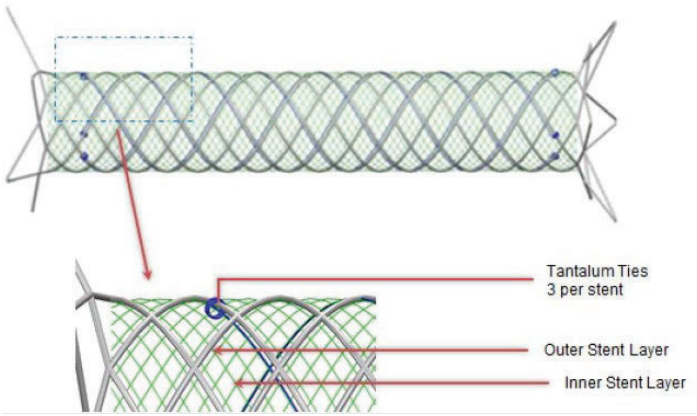


Figure 3: Roadsaver / CASPER Implant Detail

The delivery system is composed of a rapid exchange (RX) delivery catheter, pusher assembly, and rotating hemostasis valve (RHV). The RX delivery catheter consists of multiple fused composite polymer tubes. The pusher assembly consists of a polymer conical distal tip, a composite tube fused to a stainless-steel push wire, and a plastic knob. The RHV is bonded to the RX delivery catheter and functions for the purpose of hydraulic sealing and securement of the pusher assembly. The delivery pusher retains control of the stent via a retention feature designed to secure the stent while inside the delivery catheter.

The RX delivery catheter has 2 marker bands, one at the distal tip of the catheter and one at the proximal end where the stent resides. The distal and proximal markers provide visual confirmation of the relative locations of the stent to the delivery catheter. The central marker (outer sheath marker) is used in conjunction with the proximal marker to define a deployment zone that will still allow for re-sheathing of the stent.

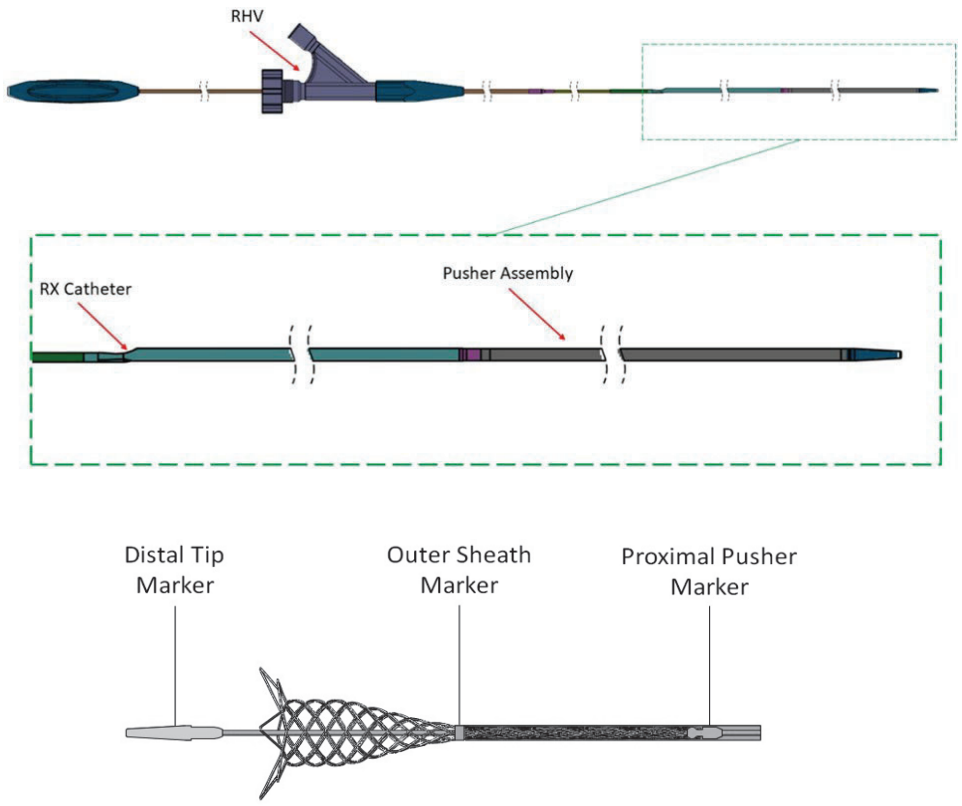


Figure 4: Roadsaver / CASPER Delivery System Detail

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the correction of carotid artery disease. Current treatment options include lifestyle changes, medical therapy, open surgery and endovascular management with other devices. Available treatment options, and their resulting impact, are dependent on the severity and degree of atherosclerotic stenosis of the carotid artery and other risk factors. 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 Roadsaver / CASPER Carotid Stent System received CE mark in December 2013 and is commercially available for patients in the European Union. In addition, the carotid stent system (under the branding of Roadsaver and/or CASPER) is approved or legally marketed in approximately 75 countries (See **Table 2** and **Table 3** below).

Table 2: CASPER System – Countries Approved or Legally Marketed

Asia-Pacific	Europe, Middle East, Africa		Latin America	North America
Australia	Austria	Libya	Argentina	--
Bangladesh	Albania	Liechtenstein	Bolivia	
Hong Kong	Armenia	Lithuania	Brazil	
India	Azerbaijan	Luxembourg	Chile	
Indonesia	Belarus	Malta	Colombia	
Mongolia	Belgium	Martinique	Costa Rica	
New Zealand	Bulgaria	Morocco	Ecuador	
New Caledonia	Croatia	Netherlands	Guadeloupe	
Pakistan	Cyprus	Norway	Guatemala	
Singapore	Czech Rep.	Poland	Honduras	
Tajikistan	Denmark	Portugal	Panama	
Japan	Estonia	Romania	Paraguay	
	Finland	Russia	Peru	
	France	Saudi Arabia	Uruguay	
	Georgia	Slovakia		
	Germany	Slovenia		
	Greece	South Africa		
	Hungary	Spain		
	Iceland	Sweden		
	Iran	Switzerland		
	Ireland	Syria		
	Italy	Tunisia		
	Kazakhstan	Turkey		
	Latvia	Turkmenistan		
	Lebanon	Ukraine		
		United Arab Emirates		
		United Kingdom		
		Uzbekistan		

Table 3: Roadsaver System – Countries Approved or Legally Marketed				
Asia-Pacific	**Europe, Middle East, Africa**		**Latin America**	**North America**
Armenia	Algeria	Lebanon	Bolivia	--
Azerbaijan	Austria	Liechtenstein	Chile	
Bangladesh	Belarus	Lithuania	Colombia	
Hong Kong	Belgium	Luxembourg	Dominican Republic	
Mongolia	Bulgaria	Malta	Guadeloupe	
New Caledonia	Croatia	Martinique	Honduras	
New Zealand	Cyprus	Netherlands	Panama	
Turkmenistan	Czech Rep.	Norway		
Uzbekistan	Estonia	Poland		
	Finland	Portugal		
	France	Romania		
	Georgia	Slovakia		
	Germany	Slovenia		
	Greece	South Africa		
	Hungary	Spain		
	Iceland	Sweden		
	Ireland	Switzerland		
	Italy	Turkey		
	Kuwait	United Arab Emirates		
	Latvia	United Kingdom		

The Roadsaver / CASPER Carotid Stent System has not been withdrawn from the market from any country for any reason.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the carotid stents.

- Arrhythmia
- Aneurysm and pseudoaneurysm formation
- Abrupt vessel closure
- Allergic reactions (including to antiplatelet agents, contrast
- medium or stent materials)
- Arteriovenous fistula
- Bleeding from anticoagulation/antiplatelet medication
- Bradycardia and hypotension
- Carotid artery spasm
- Angina/Coronary ischemia
- Cerebral Edema
- Cerebral Hemorrhage
- Congestive Heart failure
- Death
- Disseminated intravascular coagulation
- Emboli (air, tissue, plaque, thrombus, device or other)
- Emergency artery bypass graft surgery

- Hematoma
- Hemorrhagic or embolic stroke/transient ischemic attach (TIA)
- Hyperperfusion Syndrome
- Infection and/or pain at insertion site/Sepsis
- Intimal tear/dissection
- Myocardial Infarction (MI)
- New or worse encephalopathy
- Pain
- Renal failure/insufficiency
- Respiratory arrest
- Restenosis of stented segment
- Stent misplacement
- Seizure
- Severe Unilateral Headache
- Tissue necrosis
- Total occlusion of carotid artery
- Vessel injury/dissection/perforation/rupture/trauma
- Vessel occlusion or thrombosis
- Vessel spasm or recoil

For the specific adverse events that occurred in the clinical study, please see Section X.D.3 below.

IX. SUMMARY OF NON-CLINICAL STUDIES

The Roadsaver / CASPER Carotid Stent System underwent non-clinical mechanical, functional, and animal testing, sterilization validation, packaging and shelf-life validation, and biocompatibility testing to support the commercial use of the device.

A. In-Vitro Testing

In vitro studies were performed per FDA's guidance documents, "*Non-Clinical Engineering Test and Recommended Labeling for Intravascular Stents and Associated Delivery Systems*", issued on April 18, 2019, and "*Select Updates for Non-Clinical Engineering tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems*," issued on August 18, 2015, and applicable ISO standards. **Table 4** below provides a summary of the testing performed.

Table 4: Design Verification and Validation Testing

Test	Purpose	Acceptance Criteria	Results
Material Characterization			
Material Composition	To determine if materials are suitable for implant	Materials must meet biocompatibility requirements per ISO 10993 for the following classifications: • Stent implant -permanent contact duration (>30days). • Delivery catheter, limited patient contact (<24hrs).	Pass
Austenite Finish Transition Temperature (Af)	To determine if stent will achieve its pre- determined size and shape when exposed to normal body temperature	The device must have an Af at or below 37ºC (body temperature).	Pass

Mechanical Properties	To specify the mechanical properties of the stent materials	The mechanical properties of the raw materials must meet drawing specifications.	Pass
Corrosion (Pitting)	To determine the corrosion susceptibility of the stent	The average Breakdown Potential (Eb) of the test samples should be at or greater than 500 mV (Eb ≥ 500 mV).	Pass
Galvanic Corrosion	To assess the galvanic corrosion susceptibility of two dissimilar metals (nitinol and tantalum)	The stent must exhibit a maximum coupled current (Ic) of 12 nA.	Pass
Stent (Implant) In Vitro Testing			
Dimensional Verification	To confirm the stent is within dimensional specifications.	Unconstrained Dimensions: Stent OD: 5mm - 10mm; Overall lengths: 20-60mm; Dual layer lengths: 15mm-55mm Constrained Dimensions: Stent OD: 3.0mm – 9.0mm; Overall lengths: 25-80mm; Dual layer lengths: 15mm-70mm	Pass
Stent Integrity	To report any defects on deployed stent.	The device shall be free from visual defects after deployment and free from kinks, bends, and must meet diameter requirements.	Pass
Stent Crush Resistance	To demonstrate the ability of the stent to recover to desired size and shape after application and removal of external loads or deformation.	After being crushed to 50% of its unconstrained OD, the stent OD must recover to the range of indicated for use vessel diameter	Pass
Foreshortening	To determine if the stent length shortens once deployed	Resulting percentage of foreshortening is dependent on braiding pattern and diameter	For characterization only
Percent Surface Area	To determine the metal surface area of stent in contact with vessel wall	Resulting percent surface area is dependent on pore size and diameter configuration	For characterization only
Stent Radial Forces	To ensure stent meets radial force requirements at indicated vessel diameters	For all stents at indicated reference vessel diameters: Chronic Outward Force: ≥ 5gf and ≤ 300gf Crush Resistance Force: ≥ 5gf and ≤ 660gf	Pass
Kink & Ovalization	To assess capability of stent to conform to 4 mm diameter curvature without kinking and/or ovalization	The stent must be capable of conforming to a 4 mm diameter curvature without kinking	Pass
Stent Bond Strength	To evaluate tensile bond strength of subassemblies and laser weld area (outer stent)	Stent laserweld strength must be ≥ 3N. The attachment strength between the inner stent and the outer stent must be ≥ 3N.	Pass
Finite Element Analysis (FEA)	To demonstrate the static and fatigue durability of stent through range of vessel sizes.	The device's stress analysis at 10-years equivalence of the static and fatigue loading cases (crimp, deployment, and pulsatile fatigue) must have factors of	Pass

		safety above 1.0.	
Accelerated Durability Testing	To assess long-term fatigue resistance of stent in physiologically simulated environment for 380 million cycles (equivalent to 10-years)	The device shall have no loss of mechanical integrity after being subjected to 380 million cycles of cyclic load/ unload, or an equivalence of 10-yr of fatigue loading.	Pass
Magnetic Resonance Imaging (MRI) Safety	To assess MRI safety and compatibility of the stent	Stent system must be, at minimum MRI Conditional, and conforms to applicable ASTM standards and requirements of: 1. Magnetic field interactions at 3 Tesla. 2. MR-related heating at 1.5 Tesla and 3 Tesla 3. Artifacts at 3 Tesla.	The test results demonstrated the stent did not pose additional unacceptable risk to the patient. The stent was determined to be MR Conditional per ASTM 2503. The MRI Conditional scanning parameters are specified in the labeling
Radiopacity	To determine if the device is visible under fluoroscopy	The device shall be visible under fluoroscopy.	Pass
Delivery System and/or Full System In Vitro Testing			
Dimensional Verification	To confirm the delivery system is within dimensional specifications.	The delivery system must have a working length of 143 +1/-3 cm and a maximum crossing profile of .070" for 5Fr. system and .079" for 6Fr. System	Pass
Torque Test	To evaluate torque strength of delivery system	The delivery system must be capable of withstanding at minimum 4 complete rotations	Pass
Delivery System Bond Strength	To evaluate tensile bond strength of the delivery system	Smallest outside diameter (mm) joint strength minimum force at break to be: >.550 and <.750 = 3 N >.750 and <1.150 = 5 N >1.150 and 1.850 = 10 N	Pass
Simulated Use Testing	To evaluate the performance characteristics of the device including: flexibility and kink resistance, stent deployment accuracy, delivery and retraction of the delivery system, guidewire compatibility, sheath compatibility, and compatibility with the Nanoparasol embolic protection system.	Performance characteristics were scored on a scale of 1-5 with a required minimum passing score of 3.	Pass
Particulate Evaluation	To evaluate particulate generation of the Carotid Stent System	The device shall meet the acceptance criteria: Less than 25 particles ≥10µ and less than 3 particles ≥25µ per 1ml of volume	Pass

B. Biocompatibility

The Roadsaver / CASPER Carotid Stent 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.

Since the Roadsaver / CASPER stent is constructed of identical or similar materials using the same processes (with the exception of sterilization method) as the LVIS stent (approved under P170013), biocompatibility testing was leveraged, and subsequent confirmatory testing was performed to ensure continued biocompatible results. All testing that was performed for the stent and delivery system met the requirements as specified within the applicable standard and are summarized below in **Table 5**.

Table 5: Biocompatibility

Test	Purpose	Results
Biocompatibility (Confirmatory) - Stent		
Cytotoxicity - L929 MEM Elution Test	To determine potential biological reactivity of a mammalian cell culture in response to test article.	Test Article assessed to be Grade 0, "Non-Cytotoxic"
Cytotoxicity - Agar Diffusion Test	To determine potential biological reactivity of a mammalian monolayer cell culture in response to test article.	Test Article assessed to be Grade 0, "Non-Cytotoxic"
Irritation or Intracutaneous Reactivity – Injection Test in Rabbits	To determine the potential irritation effects of test article extract as a result of an intracutaneous injection in rabbits.	Test Article assessed to be "Non-irritant."
Acute Systemic Toxicity – Systemic Injection Teste Study in Mice	To determine the potential toxic effects of test article extract as a result of single-dose systemic injection in mice.	Test Article assessed to be "Non-toxic."
Acute Systemic Toxicity – Rabbit Pyrogen Test (Material Mediated)	To determine the potential presence of chemical pyrogens in extracts of test article.	Test Article assessed to be, "Non-Pyrogenic."
Implantation – 1 Week Muscle Implantation	To test for local tissue response/effects of implant material on living muscle tissue of rabbits.	The Bioreactivity rating for the 1 week was 0.8, indicating no reaction as compared to the control implant sites.
Hemocompatibility – ASTM Hemolysis (Direct and Indirect)	To determine the potential hemolytic activity on rabbit blood in response to the test article and/or extract.	Test Article assessed to be, "Non-hemolytic."
Sub-chronic & Chronic systemic toxicity	The sub-chronic & chronic systemic toxicity and carcinogenicity endpoints were evaluated by toxicological risk assessment on the leachables from the device which concluded a negligible risk.	
Carcinogenicity		

Biocompatibility – Delivery System		
Cytotoxicity - L929 MEM Elution Test	To determine potential biological reactivity of a mammalian cell culture in response to test article.	Test Article assessed to be Grade 0, "Non-Cytotoxic"
Sensitization – Kligman Maximization Test	To determine potential allergenic or sensitizing capacity of test article.	Test Article assessed to be Grade I, "Weak Allergenic Potential."
Irritation or Intracutaneous Reactivity – Injection Test in Rabbits	To determine the potential irritation effects of test article extract as a result of an intracutaneous injection in rabbits.	Test Article assessed to be "Non-irritant."
Acute Systemic Toxicity – Systemic Injection Teste Study in Mice	To determine the potential toxic effects of test article extract as a result of single-dose systemic injection in mice.	Test Article assessed to be "Non-toxic."
Acute Systemic Toxicity – Rabbit Pyrogen Test (Material Mediated)	To determine the potential presence of chemical pyrogens in extracts of test article.	Test Article assessed to be, "Non-Pyrogenic."
Hemocompatibility – ASTM Hemolysis (Indirect Contact)	To determine the potential hemolytic activity on rabbit blood in response to the test article and/or extract.	Test Article assessed to be, "Non-hemolytic."
Hemocompatibility – Unactivated Partial Thromboplastin (UPTT) Test (Direct Contact)	To determine the potential effect on the coagulation of human plasma via measurement of the UPTT in response to the test article and/or extract.	Test article assessed to have "No effect on coagulation."
Hemocompatibility – Complement Activation Assay (C3a, SC5b-9) (Direct Contact)	To determine the potential activation of the complement system in the human plasma in response to the test article and/or its extract.	Test Article did not induce complement activation of C3 or C5 proteins in human plasma.
Hemocompatibility – (*In Vivo* Thrombogenicity evaluation during chronic animal study)	To determine the potential of thrombogenicity in an animal model.	No thrombogenic related events were observed on any of the catheter devices or manifested in the implanted animals during the implant durations (30, 90, 180 and 365 day durations).

C. Animal Studies

A chronic animal study was performed to evaluate the *in-vivo* performance, histology, histopathology, and morphometric analysis of the Roadsaver / CASPER stent and delivery system in the porcine model at 30, 90, 180, and 365 days. A total of 12 animals were implanted with 48 stents in various locations of the carotid and subclavian arteries by a cardiology specialist. Performance ratings: preparation, tracking, deployment, repositioning and removal of delivery catheter, based on a score rating scale were recorded for the delivery system and the implant performance: radiopacity, stability, flow anomalies, patency of bifurcations, thrombus and vessel irregularities (during implantation and during follow-up angiography). Histological, histopathological, and morphometric analyses were evaluated at all of the time points.

The adverse events seen in a minority of systems during the chronic study were the following, inadequate radiopacity, migration and incomplete wall apposition. These adverse events were primarily contributed to an early version of the delivery catheter. The delivery catheter design has

been revised to mitigate this issue. Additionally, varying degrees of narrowing of vessels were observed in a small portion of implants during all study time points.

Delivery system performance during implantation was rated excellent or acceptable for all criteria for all systems. Implant performance during implantation and follow-up angiographies were rated mostly excellent or acceptable. Widely patent lumens with complete neointimal incorporation were observed for most systems for all study time points.

The results of the chronic animal study demonstrated that the stent and delivery system performed as expected and demonstrated the safety of the device for use in humans in the pivotal clinical study.

An acute animal study was performed to evaluate the *in-vivo* performance of the Roadsaver / CASPER stent and delivery system in the canine model. A total of 10 stents were implanted in one canine animal in various target vessels and locations. During each stent deployment, various performance attributes were evaluated. Commercially available accessories such as vascular sheaths, embolic protection devices (EPD), dilatation balloons, guidewires, and guiding catheters were used in accordance with the manufacturer's instructions for use. The results of the acute animal study demonstrated that all devices performed successfully.

D. Sterilization Validation

The Roadsaver / CASPER stent and delivery system are sterilized via a validated 100% ethylene oxide sterilization process in accordance with ISO 11135:2014, "*Sterilization of health care products -- Ethylene oxide -- Requirements for the development, validation and routine control of a sterilization process for medical devices*". Results from the sterilization validation studies demonstrate that the Roadsaver Carotid Stent System satisfies a minimum Sterility Assurance Level (SAL) of 10^{-6}. In addition, bioburden evaluation, pyrogen and ethylene oxide residuals assessments were performed and results demonstrate that all test samples met the predetermined acceptance criteria.

E. Shelf Life and Packaging Validation

The Roadsaver / CASPER stent and delivery system are packaged together and provided sterile for single use only. Performance testing of the sterile barrier and shipping containers were validated per ISO 11607-1:2019, "*Packaging for terminally sterilized medical devices - Part 1: Requirements for materials, sterile barrier Systems and packaging Systems*" and ISO 11607-2:2019, "*Packaging for terminally sterilized medical devices - Part 2: Validation requirements for forming, sealing and assembly processes*". Packaging testing included evaluation of visual inspection, pouch seal integrity, seal strength, dye penetration and simulated use. Test results demonstrated that all design specification requirements were met.

The Roadsaver / CASPER Carotid Stent System was qualified for a shelf-life of 3 years.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of the Roadsaver / CASPER Carotid Stent System used in conjunction with the Nanoparasol / EmPro Embolic Protection System for the treatment of carotid artery stenosis in patients at increased risk for adverse events from carotid endarterectomy in the US under IDE # G140249. 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 April 21, 2016, and February 19, 2020. The database for this PMA reflected data collected through February 24, 2021 and included the first 256 enrolled patients through the 12-month milestone. There were 30 investigational sites.

The study, titled "*CONFIDENCE Trial - Carotid Stent Trial to Evaluate the Safety and Efficacy of the Roadsaver™ Stent Used in Conjunction with the Nanoparasol Embolic Protection System for Patients at Increased Risk for Adverse Events from Carotid Endarterectomy*," was an open-label, multicenter, prospective, single-arm study with follow-up at hospital discharge, 30 days, 180 days and 12 months post-procedure. Two hundred and fifty-six (256) patients were enrolled in 30 investigational sites in the US.

The safety and effectiveness of the Roadsaver Stent used in conjunction with the Nanoparasol Embolic Protection System in the CONFIDENCE study was evaluated with the primary endpoint of Clinical Events Committee (CEC)-adjudicated Major Adverse Event (MAE) rate, which consisted of death, stroke, or myocardial infarction (MI) events within 30 days of the index procedure plus ipsilateral stroke 31–365 days post-procedure. The performance goal (PG) rate is set at 13.9%, derived from a comparable subset of patients from other recent randomized trials. That is, if the upper limit of the 95% CI for the event (failure) was <13.9%, the null hypothesis was rejected, and the study endpoint was considered to be met.

This study included an independent CEC, Data Safety and Monitoring Board (DSMB), angiographic imaging core laboratory ("core lab"), and study monitors who confirmed neurological assessments, adverse events, imaging data, and study data with source documentation.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the CONFIDENCE study was limited to patients who met the following inclusion criteria.

General Inclusion Criteria

Patients were eligible for inclusion in the study if they met **all** the following inclusion criteria:

1. Patient was between ≥21 and ≤80 years of age.
2. Patient was willing and capable of complying with all study protocol requirements, including specified follow-up period and could be contacted by telephone.
3. Patient or LAR provided written informed consent before enrollment in study.
4. Patient was diagnosed with carotid artery stenosis and considered a high perioperative risk for carotid endarterectomy (CEA).
5. Patient was either:
   a. Symptomatic with carotid stenosis ≥50% as determined by angiography using NASCET methodology. Symptomatic was 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
   b. Asymptomatic with carotid stenosis ≥80% as determined by angiography using NASCET methodology.
6. Patient had a target lesion located at the carotid bifurcation and/or proximal internal carotid artery (ICA).
7. Patient had a single, de novo or restenotic (post CEA) target lesion or severe tandem lesions close enough to be covered by a single Roadsaver stent.

8. Patient had a vessel with reference diameters 3.5–9.0 mm at the target lesion and met the criteria for device use per Instructions for Use.

High-risk Inclusion Criteria

For inclusion in the study, a patient had to qualify in ≥1 anatomic and/or ≥1 comorbid high-risk condition per below:

Anatomic high-risk conditions

1. Patient had a target lesion at or above the second vertebral body (level of jaw) or below the clavicle.
2. Patient had an inability to extend the head due to cervical arthritis or other cervical disorders.
3. Patient was status/post radiation therapy to the neck.
4. Patient had a previous head and neck surgery in the region of the carotid artery.
5. Patient had spinal immobility of the neck.
6. Patient had the presence of a tracheostomy stoma.
7. Patient had laryngeal palsy or laryngectomy.
8. Patient had a hostile neck or surgically inaccessible lesion.
9. Patient had severe tandem lesions.

Comorbid high-risk conditions

1. Patient was ≥70 years of age (maximum 80 years) at the time of enrollment.
2. Patient had New York Heart Association (NYHA) Class III or IV congestive heart failure (CHF) with left ventricular ejection fraction (LVEF) ≤35%.
3. Patient had chronic obstructive pulmonary disease (COPD) with forced expiratory volume (FEV) ≤30%.
4. Patient had unstable angina.
5. Patient had a recent MI ≥30 days before stenting procedure).
6. Patient had coronary artery disease with ≥2 vessels with ≥70% stenosis.
7. Patient had planned coronary artery bypass grafting (CABG) or valve replacement surgery 31–60 days after the carotid artery stenting (CAS) procedure.
8. Patient required peripheral vascular surgery or abdominal aortic aneurysm repair between 31–60 days after the CAS procedure.
9. Patient had contralateral laryngeal nerve paralysis.
10. Patient had restenosis after a previous CEA.
11. Patient had contralateral occlusion in the ICA as the only comorbid high-risk condition.

Patients were not permitted to enroll in the CONFIDENCE study if they met any of the following exclusion criteria:

General Exclusion Criteria

Patients were excluded from the study for any of the following reasons:

1. Patient had life expectancy of <1 year.
2. Patient was experiencing (or had experienced) an evolving, acute, or recent disabling stroke in the last 30 days.
3. Patient had anticipated or potential sources of emboli (eg, known previously symptomatic patent foramen ovale (PFO), mechanical heart valve, or deep vein thrombosis (DVT) treated within 6 months) that were not adequately treated with antithrombotics for ≥2 weeks with documented coagulation parameters in the target therapeutic range.

4. Patient had atrial fibrillation.
5. Patient had an acute MI within 60 days prior to the index procedure.
6. Patient had or planned to have any major surgical procedure (ie, intra-abdominal or intrathoracic surgery or any surgery/interventional procedure involving cardiac or vascular system) within 30 days of the index procedure.
7. Patient had a history of major ipsilateral stroke.
8. Patient had >60% carotid stenosis contralateral to the target lesion requiring treatment before completion of the study-required 12-month follow-up.
9. Patient had a mRS score >2 or had another neurological deficit not due to stroke that may confound the neurological patient assessments.
10. Patient had chronic renal insufficiency (serum creatinine ≥2.5 mg/dL) or had a history of severe hepatic impairment, malignant hypertension, and/or was morbidly obese.
11. Patient had platelet count <100,000/μL.
12. Patient had known sensitivity to heparin or previous incidence of heparin-induced Thrombocytopenia (HIT) type II.
13. Patient had contraindication to standard-of-care study medications, including antiplatelet therapy.
14. Patient had known sensitivity to contrast media that could not be controlled adequately with pre-medication.
15. Patient had known bleeding diathesis or hypercoagulable state or refuses blood transfusions.
16. Patient had intracranial pathology that, in the opinion of the Investigator, made the patient inappropriate for study participation (eg, brain tumor, arteriovenous malformation [AVM], cerebral aneurysm, cerebral vascular disease [microangiopathy or large vessel], etc.) or would confound neurological evaluation.
17. Patient had intracranial hemorrhage within the last 90 days.
18. Patient was enrolled in another investigational study protocol and had not completed its primary endpoint or that may have confounded the current study endpoints. Patients who were involved in the long-term surveillance of a clinical study were eligible.
19. Patient suffered from confusion or dementia or was unable or unwilling to cooperate with the study requirements and/or follow-up procedures.
20. Patient had a known, unresolved history of drug use or alcohol dependency.
21. Patient had an active infection.
22. Patient had renal failure and/or was on dialysis.
23. Patient had documented uncontrolled diabetes.
24. Patient was pregnant.

Angiographic Exclusion Criteria

A patient was not eligible for enrollment if s/he met any of the following angiographic exclusion criteria:

1. Patient had a total occlusion of the target carotid arteries (ie, common carotid artery (CCA), internal carotid artery (ICA)).
2. Patient had a previously placed stent in the ipsilateral carotid artery.
3. Patient had severe lesion calcification or vascular tortuosity that precluded the safe introduction of the sheath, guiding catheter, embolic protection system, or stent.
4. Patient had a mobile filling defect or thrombus in target vessel.
5. Patient had occlusion or presence of "string sign" of the target vessel.
6. Patient had carotid (intracranial) stenosis located distal to target stenosis that was more severe than the target stenosis.
7. Patient had known mobile plaque or thrombus in the aortic arch.

8. Patient had a type III aortic arch.
9. Patient in whom femoral access was not possible.
10. Patient had intracranial AVMs in the territory of the target carotid artery.
11. Patient had an aneurysm in the territory of the target carotid artery that required treatment within 12 months.
12. Patient's ipsilateral carotid artery had ≥2 90-degree bends in the target landing zone.

2. Follow-up Schedule

All patients were scheduled to return for follow-up examinations post-procedure/prior to discharge and at 30 days (±7 days), 6 months ±28 days), 12 months (±56 days), 24 months (±56 days) and 36 months (±56 days).

Assessments were performed and data was collected from patients at the preoperative, surgical, and postoperative visits. The key timepoints are also shown below in **Table 6.**

Table 6: Study Timeline

Visit (Window)	Pre-Procedure Visits			Post- Procedure Visits (with visit window periods)						
	Screening <45 days	Pre-Procedure Within 24hrs	At Enrollment	Before Hospital Discharge	30 days (±7 days)	6 months (±28 days)	12 months (±56 days)	24 & 36 months (±56 days)	Early Withdrawal	Unscheduled Visit
Informed consent	X									
Demographic Evaluation	X									
mRS	X*									
NIHSS		X☑		X☑	X‡	X‡	X‡	X‡	X‡	X‡
CT or MRI	X**☑									
Head/Neck/ChestCTA or MRA	X****									
Carotid Duplex Ultrasound	X***☑				X☑	X☑	X☑	X☑	X	X‡
Carotid/Cerebral Angiography			X☑			X‡‡	X‡‡	X‡‡	X‡‡	X‡‡
Index Procedure			X☑							
12-lead ECG	X*☑			X☑	X☑					X‡
P2Y12 Reaction Units (PRU) Assessment		X ϕ		X ϕ						
Cardiac Enzymes (CK-MB)		X‡		X‡	X‡					X‡
Antiplatelet Therapy		X☑		X☑	X☑	X☑	X☑	X☑	X	X
Concomitant Medications	X☑	X☑		X☑	X☑	X☑	X☑	X☑	X	X
Adverse Events				X☑	X☑	X☑	X☑	X☑	X	X

NOTES:	
*	May be obtained at either screening or pre-procedure visit
**	Required for symptomatic patients only within 180 days before screening visit
***	Obtained within the 180 days preceding the screening visit
****	Standard of Care for symptomatic cases
‡	If clinically indicated; NIHSS score will be collected 7 days post-stroke or before discharge.
‡‡	Performed if carotid follow-up intervention is required. Pre- and post-procedure scans will be submitted to the Core Lab.
☑	Standard of Care
ϕ	Required if only done per site's standard of care.
NIH Stroke Scale	Neurological assessments should be done by a physician or research personnel certified in the administration of NIHSS
Standard of Care	For the purposes of this study protocol, 12-lead ECG at 30 days, carotid duplex ultrasound, and an Intra-procedure CK-MB are considered standard of care

3. Clinical Endpoints

The primary endpoint to establish a reasonable assurance of the safety and effectiveness of the device is a Major Adverse Event (MAE) composite endpoint consisting of death, stroke, or myocardial infarction (MI) within 30 days of the index procedure plus ipsilateral stroke within 12 months. MI was defined as a creatine kinase-MB level that was 2× the upper limit of normal (ULN) according to the center's laboratory, in addition to either chest pain or symptoms consistent with ischemia or electrocardiographic evidence of ischemia, including new ST segment depression or elevation of >1 mm in ≥2 contiguous leads.

Secondary Endpoints:

1. Procedure Success: Successful Roadsaver implantation, <50% residual angiographic stenosis as determined by the angiography Core Laboratory by visual North American Symptomatic Carotid Endarterectomy Trial (NASCET) assessment immediately post procedure at the target lesion, and no in-hospital (pre-discharge) MAE (stroke, MI, or death).
2. Stent Technical Success: Successful Roadsaver deployment in the planned targeted treatment location with a residual diameter stenosis <50% immediately after post-dilatation as determined by the angiography Core Laboratory and successful removal of the delivery system.
3. EPD Technical Success: EPD successfully delivered and deployed beyond the target lesion and successfully retrieved after completion of the stent placement.
4. Target Lesion Revascularization (TLR): any clinically driven revascularization procedure of the original treatment site associated with narrowing of >80% within 12 months post-procedure, including angioplasty, stenting, endarterectomy, or thrombolysis, performed to open or increase the luminal diameter inside or ≤5 mm of the previously treated lesion.
5. In-stent Restenosis ISR): Patients with >70% residual stenosis were determined by ultrasound (peak systolic velocity (PSV) >300 cm/s and/or ICA/CCA PSV ratio >4.0) in stented lesion at the 30-day and 12-month follow-ups.
6. Major stroke within 30 days
7. Minor stroke within 30 days
8. TIA within 30 days
9. Neurologic death (days 31–365)

Study Success Criteria:

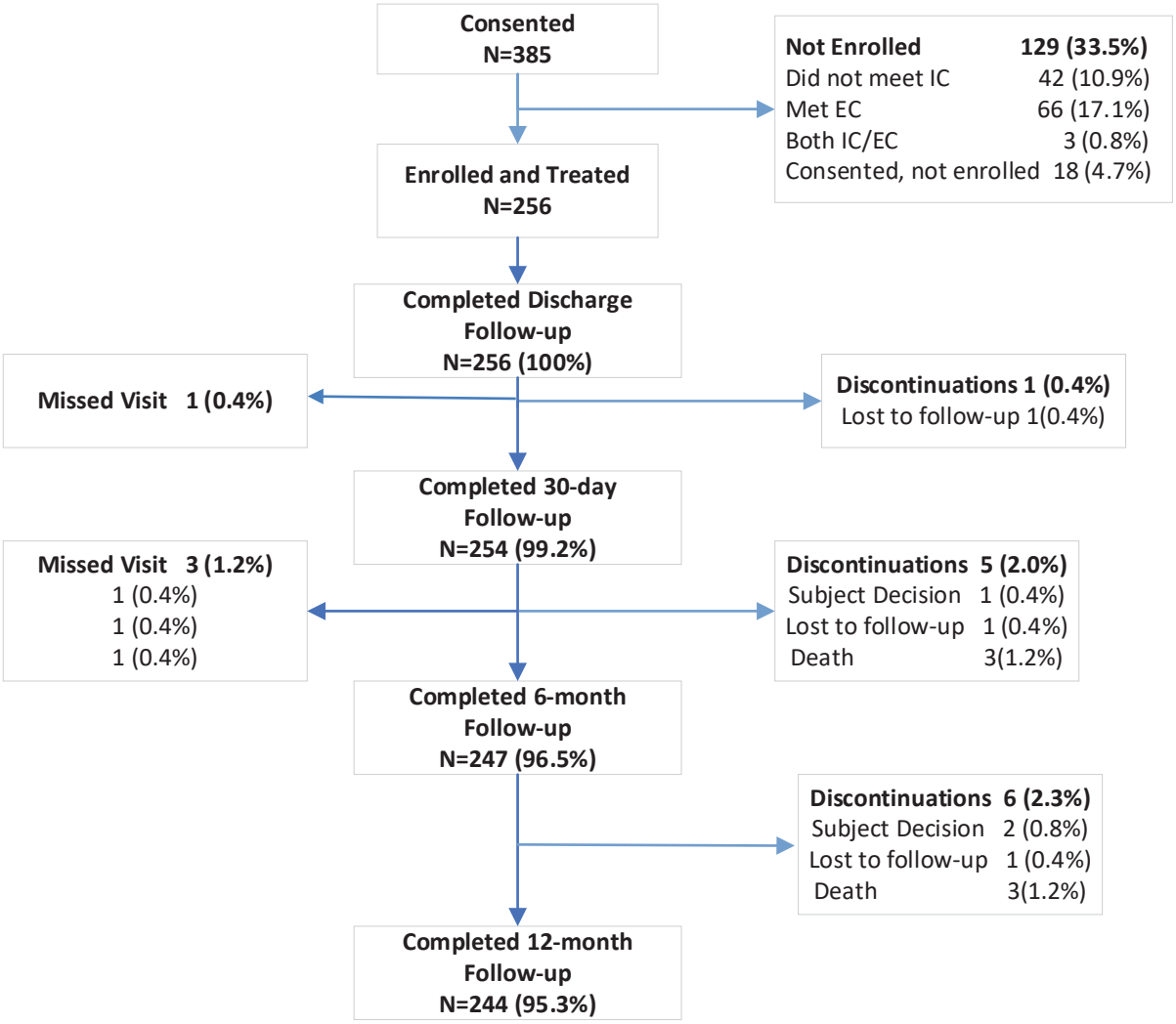
The null hypothesis was that the true primary endpoint rate in patients treated with the Roadsaver stent used in conjunction with the Nanoparasol EPD was greater than or equal to the performance goal (PG) that represented acceptable performance for patients treated with CAS who were at high risk for complications if treated with CEA. Symbolically, the null and alternative hypotheses are:

$$\text{Ho: } \pi \geq \text{PG (failure}$$
$$\text{H1: } \pi < \text{PG (success),}$$

where π is the primary endpoint failure proportion, determined from the nominal month-12 visit. Primary Analysis for the Primary Endpoint: The two-sided 95% upper limit on the observed primary endpoint rate was computed using an exact binomial test. If the two-sided 95% upper confidence interval limit for the event failure rate is less than 13.9%, the null hypothesis will be rejected, and the study goal will be considered to be met.

B. Accountability of PMA Cohort

At the time of database lock, of 256 patients enrolled in the PMA study, 95.3% (244 patients) were available for analysis at the 12-month follow-up assessment. A summary of subject disposition is presented in **Figure 5** below.



Note: the number of patients who discontinued or missed a visit will not add up to the total number of patients that completed each visit because patients who missed a visit were not excluded from further analysis. They may have completed subsequent visits.

Figure 5: Summary of subject disposition

C. Study Population Demographics and Baseline Parameters

The baseline demographic characteristics for the intent to treat (ITT) population in the pivotal clinical study are summarized in **Table 7**. In the ITT population, the mean (SD) age was 69.6 (6.8 years, and the majority of the subjects were men 65.2% [n=167]). 91% [n 233] of subjects were white, 4.7% of subjects identified themselves as Hispanic or Latino; 4.3% (n=11) identified themselves as Black or African American. In the ITT population, mean (SD) height was 67.0 (4.0) inches, mean (SD) weight was 185.5 (43.1) pounds, and mean (SD) body mass index (BMI) was 28.8 (5.5) kg/m2. Overall, these demographic characteristics are consistent with a typical cohort of subjects with carotid artery stenosis at high operative risk for CEA.

Table 7: Demographics and Baseline Characteristics (ITT Population)

Characteristic	ITT (N=256)
Age (years)	
Mean (SD)	69.6 6.8)
Median (min, max)	71.0 (46.0, 80.0)
Gender, n %)	
Male	167 65.2%
Female	89 (34.8%)
Ethnicity, n %)	
Not Hispanic or Latino	244 95.3%
Hispanic or Latino	12 4.7%)
Race, n %)	
White	233 91.0%
Black or African American	11 4.3%)
Other	6 2.3%)
Asian	5 2.0%)
American Indian or Alaska Native	1 0.4%)
Height (inches)	
Mean (SD)	67.0 (4.0)
Weight (pounds)	
Mean (SD)	185.5 (43.1)
Body Mass Index (kg/m^2)	
Mean (SD)	28.8 (5.5)

As presented in **Table 8** among all enrolled subjects, 23.8% 61/256) were symptomatic i.e., amaurosis fugax ipsilateral to the carotid lesion, TIA or non-disabling stroke within 180 days of the procedure within the cerebral hemisphere supplied by the target vessel), and 76.2% (195/256) were asymptomatic. Among all enrolled subjects, 40.2% of subjects 103/256) had ≥1 anatomic high-risk conditions; 84.4% of subjects (216/256) had ≥1 comorbid high-risk conditions.

Table 8: Summary of Symptomatic/Asymptomatic Subjects and Subjects with High-risk Conditions (ITT Population)

Characteristic	N=256 n (%)
Symptomatic Asymptomatic	61 23.8%) 195 76.2%
Subjects with ≥1 anatomic high-risk conditions Subjects with ≥1 clinical comorbid high-risk conditions	103 40.2% 216 84.4%

The target lesion characteristics and extent of stenosis are presented in **Table 9**. There was a total of 132 (51.6%) lesions in the right carotid artery. The mean SD) percent stenosis was 82.4% (7.76).

Table 9: Target Lesion Characteristics & Extent of Stenosis – Site-reported Angiography (ITT Population)

Parameters and Statistics	ITT (N=256) n (%)
Location of target lesion	
Right carotid artery	132 51.6%
Left carotid artery	124 48.4%
Minimum lumen diameter	
Mean (SD)	1.0 (0.55)
Median (min, max)	0.9 (0, 3)
95% CI)	(0.9, 1.1)
Percent Stenosis	
Mean (SD)	82.4 (7.76)
Median (min, max)	81.0 (50, 99)
95% CI)	(81.5, 83.4)

The results for the pre-procedure target lesion morphology performed by the Core Angiography Laboratory are summarized in **Table 10**. Overall, the target lesion location was contiguous for the majority of subjects (85.3% [215/252]). The mean (SD) distance of the lesion from the ostium was 7.2 8.0) mm; the median length (range) was 21.3 (5.0–40.0) mm. ICA calcification was severe in 23.4% of subjects (59/252).

Table 10: Target Lesion Morphology – Core Laboratory Angiography (ITT Population)

Parameters and Statistics	ITT (N=252) n (%)
Lesion Location	
Both	1 0.4%)
Contiguous	215 85.3%
Remote	36 14.3%)
Distance (mm) from ostium	
Mean (SD)	7.2 8.0)
Median (min, max)	5.0 (0.0, 32.0)
95% CI)	(6.2, 8.2)
Length (mm)	
Mean (SD)	20.9 8.2)
Median (min, max)	21.3 (5.0, 40.0)
95% CI)	19.8, 21.9)
Eccentricity, concentric / eccentric	
Concentric	220 87.3%
Eccentric	32 12.7%)
ICA calcification	
Moderate	39 15.5%)
None/Mild	154 61.1%
Severe	59 23.4%)

D. Safety and Effectiveness Results

The primary analysis was conducted on the Intent-To-Treat (ITT) population, which includes 256 subjects that were enrolled and treated with the device. The Complete Case (CC) population includes all ITT subjects completing the 12-month follow-up evaluation. 15 ITT subjects were considered to have missing data for the following reasons: death after 30 days (6); missed visit (3); lost to follow-up (3); subjects' decision to discontinue (3). FDA considers the CC population to be most relevant, since the method of multiple imputations used for outcomes of 15 subjects with missing data in the ITT population differed from the method that was prespecified.

1. Primary Endpoint Results

The primary endpoint was MAE, a composite measure of death, stroke, or MI within 30 days of the index procedure plus ipsilateral stroke 31–365 days after the procedure. In the study, 15 patients (5.9% [95% exact binomial CI: 3.32, 9.48]; p=0.0002 experienced a MAE. The upper limit of the 95% exact binomial CI was 9.48%, which was below the PG of 13.9%. Because the upper limit of the CI was less than the PG, the null hypothesis (H_0) is rejected, and the alternative hypothesis is accepted (H_1). Thus, the primary endpoint of the study was met.

Table 11: CEC-adjudicated MAE Rate Endpoint

	ITT Population[§] **N=256**	**CC Population N=244**
Subjects who had an MAE*, n %	15 5.9%)[‡]	15 (6.1%)[‡]
95% exact binomial CI	(3.32, 9.48)	(3.48, 9.94)
p-value[†]	0.0002	0.0005
Subjects who died within 30 days of the index procedure	1 0.4%)	1 (0.4%)
Subjects who had a stroke within 30 days of the index procedure	7 2.7%)	7 (2.9%)
Subjects who had an MI within 30 days of the index procedure	1 0.4%)	1 (0.4%)
Subjects who had an ipsilateral stroke 31-365 days post-index procedure	7 2.7%)	7 (2.9%)

*MAE is defined as death, stroke, or MI within 30 days of the procedure plus ipsilateral stroke 31-365 days post-index procedure.
[§] Presented in this table for the ITT population is data based on recorded data, without imputation, and assuming no events for patients who discontinued.
[‡] Two MAE events occurred in one subject
[†] Probability value derived from the 2-sided binomial test vs. an a priori Performance Goal of 13.9%.

2. Secondary Endpoints Results

Secondary endpoints include technical success, procedure success, embolic protection device technical success, target lesion revascularization within 12 months of follow-up, and in-stent restenosis at 30-day and 12-month follow-up.

As shown in **Table 12**, Technical Success was achieved in 96.9% 248/256) of subjects; 8 subjects did not achieve residual stenosis diameter <50%. In all ITT subjects, the Roadsaver device was successfully deployed, and the delivery system was successfully retrieved. Procedure Success was achieved in 94.9% (243/256) of subjects; 8 subjects did not achieve residual stenosis diameter <50%. Four subjects (1.6%) had a stroke pre-discharge, and 1 subject 0.4%) had a MI pre-discharge. There were no pre-discharge deaths. Embolic Protection Device Technical Success was

achieved in 98.8% (253/256) of subjects. Nine subjects 3.5% required 10 TLRs within 12 months of the index procedure. ISR was reported in 5 subjects (2.0%) at the 30-day follow-up and 14 subjects (5.5%) at the 12-month follow-up.

Table 12: Performance Analysis

Endpoint	ITT Population N=256 n (%)	CC Population N=244 n (%)
Technical Success[a]	248 (96.9%	236 (96.7%
Successful deployment	256 100.0%	244 (100%
Residual diameter stenosis <50%[b]	248 (96.9%	236 (94.7%
Successful removal of delivery system	256 100.0%	244 (100%
Procedure Success[c]	243 94.9%	231 (94.7%
Successful Roadsaver implantation	256 100.0%	244 (100%
Residual angiographic stenosis <50%[d]	248 (96.9%	236 (96.7%
No in-hospital (pre-discharge) MAE (stroke, MI, or death)	251 98.0%	239 (98.0)
Stroke	4 1.6%)	4 (1.6%)
MI	1 0.4%)	1 (0.4%)
Death	0	0
Embolic Protection Technical Success[e]	253 98.8%	241 (98.8%
Target Lesion Revascularization[f]	9 3.5%)	9 (3.7%)
In-stent Restenosis at 30-day follow-up[g]	5 2.0%)	5 (2.0%)
In-stent Restenosis at 12-month follow-up[g]	14 5.5%)	14 (5.7%)

[a]Successful deployment of Roadsaver in targeted treatment location with a residual diameter stenosis <50% immediately after post-dilatation as determined by the angiography Core Laboratory and with successful removal of delivery system.

[b]Determined by the Core Angiography Laboratory immediately after post-dilatation.

[c]Successful Roadsaver implantation, <50% residual angiographic stenosis as determined by the angiography Core Laboratory by visual NASCET assessment immediately post procedure at the target lesion and no in- hospital (pre-discharge) MAE (stroke, MI or death)

[d]Determined by Angiography Core Laboratory by visual NASCET assessment immediately after the procedure. [e]Successful delivery and deployment beyond the target lesion and successful retrieval after completion of the stent placement.

[f]TLR was defined as any clinically driven revascularization procedure of the original treatment site associated with narrowing >80% within 12 months post-procedure, including angioplasty, stenting, endarterectomy, or thrombolysis, performed to open or increase the luminal diameter ≤5 mm of the previously treated lesion. Based on recorded events without imputation and assuming no events for patients with missing data.

[g]In-stent Restenosis included subjects with >70% residual stenosis determined by ultrasound (PSV >300 cm/s and/or ICA/CCA PSV ratio >4.0) within the stented lesion. Based on recorded events without imputation and assuming no events for patients with missing data.

3. Adverse Events

Adverse Events (AEs) were defined as any unfavorable and unintended sign (including laboratory findings), symptom or disease that occurred to a patient and resulted in a change in normal baseline health while enrolled in this clinical investigation. Serious Adverse Events (SAE) were defined as an AE that led to a patient death or serious deterioration in the health of the patient that resulted in:

- a life-threatening illness or injury; or
- a permanent impairment of a body structure or a body function; or
- in-patient or prolonged hospitalization; or
- medical or surgical intervention to prevent permanent impairment to a body structure or a body function; or
- fetal distress, fetal death, or a congenital abnormality or birth defect

Table 13 presents possibly, probably, or definitely device- or procedure-related adverse events occurring at a rate of >1% that were observed through 12 months in the Roadsaver pivotal clinical study for the ITT population. **Table 14** presents possibly, probably, or definitely device- or procedure-related serious adverse events occurring at a rate of >1%. No unanticipated adverse device effects (UADE) occurred during this trial.

Table 13: Site Reported Device and Procedure-related Adverse Events (Within 1 Year, ITT Population)

Preferred Term Relationship	**N=256 n (%)**
Possibly, probably, or definitely Roadsaver related AEs	
Carotid Artery Restenosis	8 3.1%)
Carotid Artery Stenosis	4 1.6%)
Cerebral Vasoconstriction	5 2.0%)
Cerebrovascular Accident	4 1.6%)
Possibly, probably, or definitely Nanoparasol related AEs	
Cerebral Vasoconstriction	8 3.1%)
Vascular Disorders	4 1.6%)
Vasospasm	3 1.2%)
Possibly, probably, or definitely procedure related AEs	
Bradycardia	8 3.1%)
Urinary Tract Infection	3 1.2%)
Incision Site Hemorrhage	3 1.2%)
Procedural Headache	5 2.0%)
Cerebral Vasoconstriction	9 3.5%)
Transient Ischemic Attack	3 1.2%)
Hypotension	26 10.2%)

Table 14: Site Reported Device and Procedure-related Serious Adverse Events (Within 1 Year, ITT Population)

System Organ Class Preferred Term and Relationship	**N=256 n (%)**
Possibly, probably, or definitely Roadsaver related SAEs	
Nervous System Disorders	11 4.3%)
Carotid Artery Occlusion	1 0.4%)
Carotid Artery Restenosis	5 2.0%)
Carotid Artery Stenosis	3 1.2%)
Cerebrovascular Accident	4 1.6%)
Possibly, probably, or definitely procedure related SAEs	
Hypotension	9 3.5%)

4. Subgroup Analyses

At the Agency's request, MicroVention conducted subgroup analyses by gender, race, ethnicity, age, symptomatic status and anatomic risk factors using the proportion of patients who experience the primary endpoint with 2-sided 95% exact binomial confidence intervals. Although the study was not specifically powered to detect such differences, the results suggest that the proportion of patients who experienced the primary endpoint is similar between subgroups defined for gender, ethnicity, age, symptomatic status and anatomic risk factors. Please note that the subgroup analysis for race suggested a slightly higher likelihood of an event among the Black/African American population. However, there is a limited sample size for this race subgroup (n=11); therefore, it is difficult to draw any conclusions from this data. The subgroup analyses results are listed in Table 15 below.

Table 15. Proportion of Patients Who Experienced the Primary Endpoint (Major Adverse Event) Stratified by Sub-Group

Sub-Group Parameter	Sub-Group Category	Number of Patients	Patients Who Experienced the Event of Interest, Number (%	Lower Bound of the 2-Sided 95% Exact Binomial Confidence Interval*	Upper Bound of the 2-Sided 95% Exact Binomial Confidence Interval*
Gender	Female	89	4 (4.5%)	1.24	11.11
	Male	167	11 (6.6%)	3.33	11.48
Race	American Indian or Alaska Native	1	0	0.00	97.5
	Asian	5	0	0.00	52.18
	Black / African American	11	4 (36.4%)	10.93	69.21
	Other (3 Hispanic, 1 Unspecified, 2 Multiracial	6	0	0.00	45.93
	White	233	11 (4.7%)	2.38	8.29
Ethnicity	Hispanic / Latino	12	1 (8.3%)	0.21	38.48
	Not Hispanic / Latino	244	14 (5.7%)	3.17	9.44
Age	<60 Years of Age	27	1 (3.7%)	0.09	18.97
	60 to <70 Years of Age	79	2 (2.5%)	0.31	8.85
	70 to <=80 Years of Age	150	12 (8.0%)	4.20	13.56
Symptomatic Classification	Asymptomatic	195	9 (4.6%)	2.13	8.58
	Symptomatic	61	6 (9.8%)	3.70	20.19
Anatomic Risk Factors	No	153	8 (5.2%)	2.28	10.04
	Yes	103	7 (6.8%)	2.78	13.50

Note: Population: Restricted to the Clinical Sites With a Minimum of 8 Patients
* Based on the Percentage of Patients Who Experienced the Event of Interest

A poolability assessment of the primary endpoint was performed across 8 sites enrolling ≥ 8 patients. Data was determined poolable (p = 0.7969, Fisher's exact test) after excluding a single site (site 36) which reported 5 MAEs among 16 patients enrolled in comparison to 5 MAEs among 164 total patients enrolled across the other 7 high-enrolling sites. Because site 36 reported a cluster

of MAEs while all other high-enrolling sites-maintained MAE rates below the expected performance goal, enrollment was suspended at this site upon recommendation of the study DSMB and it was excluded from the poolability assessment as an outlier.

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. The pivotal clinical study included 137 investigators of which none were full-time or part-time employees of the sponsor and 6 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: 6
- 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. 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. 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 Systems 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 Conclusion

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 Roadsaver / CASPER Carotid Stent 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 Roadsaver / CASPER 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 3 years.

The CONFIDENCE study was designed to assess the safety and effectiveness of the Roadsaver Carotid Stent System used in conjunction with the Nanoparasol EPD for the treatment of carotid artery stenosis in patients at increased risk for adverse events from carotid endarterectomy. The primary study endpoint is MAE, a composite measure of death, stroke, or MI within 30 days of the index procedure plus ipsilateral stroke 31–365 days after the procedure. The proportion of subjects with 1-year MAE was 5.9 % and the upper limit of the 95% exact binomial CI was 9.48%, which was below the prespecified performance goal of 13.9%. Therefore, the study met its primary study endpoint for the treatment of carotid artery disease.

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 CONFIDENCE study has established the safety and effectiveness of the device, and the results are in alignment with other approved carotid stents.

The probable risks of the device are also based on data collected in a clinical study conducted to support PMA approval as described above. The results of the CONFIDENCE Pivotal Trial show that the Roadsaver Carotid Stent System met its primary endpoint, which is a composite of Major Adverse Events (MAEs) consisting of death, stroke, or myocardial infarction (MI) within 30 days of the index procedure plus ipsilateral stroke within 12 months, with a performance goal of 13.9%. Secondary endpoints showed that Procedure Success was 94.9%, Stent Technical Success was 96.9%, Embolic Protection Device Technical Success was 98.8%, the 12-Month TLR rate was 3.5%, ISR at 30-days was 2.0%, ISR at 12-months was 5.5%, major stroke within 30-days was 1.2%, minor stroke within 30-days was 1.6%, TIAs within 30-days was 2.0%, and neurological death between days 31 to 365 was 0.8%. The results of the primary and secondary endpoints appear to be within the expected range for approved carotid artery stents.

Additional factors to be considered in determining probable risks and benefits for the Roadsaver Carotid Stent System device included: Other bare metal stents are currently being used for this treatment. The Roadsaver Carotid Stent System offers similar benefits that stenting with a bare metal stent offers over alternative treatments to stenting. The CONFIDENCE trial has established the safety and effectiveness of the Roadsaver Carotid Stent System, and the results are in alignment with other approved carotid stents.

1. Patient Perspectives

   This submission either did not include specific information on patient perspectives or the information did not serve as part of the basis of the decision to approve or deny the PMA for this device.

In conclusion, given the available information above, the data support that for the treatment of patients at high risk for adverse events from carotid endarterectomy who require carotid revascularization, the probable benefits of the Roadsaver Carotid Stent System used in conjunction with the Nanoparasol Embolic Protection System outweigh the probable risks.

C. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use.

The findings from the CONFIDENCE study demonstrated that the treatment of carotid artery

stenosis with the Roadsaver Carotid Stent System used in conjunction with the Nanoparasol Embolic Protection System met the prespecified performance goal. Both periprocedural and one-year outcomes have established the safety and effectiveness of the Roadsaver Carotid Stent System used in conjunction with the Nanoparasol Embolic Protection System. The benefits of treatment with these devices outweighs the risks associated with their use.

XIII. CDRH DECISION

CDRH issued an approval order on 11/20/2024. The final clinical conditions of approval cited in the approval order are described below.

1. A PMA Supplement that modifies the labeling to include the CONFIDENCE study results to 3 years follow-up within 30 days of notification that FDA has completed the review of the IDE Final Report for the CONFIDENCE study.

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.