SUMMARY OF SAFETY AND PROBABLE BENEFIT (SSPB)

I. GENERAL INFORMATION

Device Generic Name: Intracranial Neurovascular Stent

Device Trade Name: PulseRider® Aneurysm Neck Reconstruction Device ("PulseRider")

Device Procode: NJE

Applicant's Name and Address: Pulsar Vascular, Inc.
130 Knowles Drive, Suite E
Los Gatos, California 95032

Date(s) of Panel Recommendation: None

Humanitarian Device Exemption (HDE) Number: H160002

Humanitarian Use Device (HUD) Designation Number: HUD # 09-0223

Date of HUD Designation: March 11, 2010

Date of Notice of Approval to Applicant: June 19, 2017

II. INDICATIONS FOR USE

PulseRider® is indicated for use with neurovascular embolic coils in patients ≥ 18 years of age for the treatment of unruptured wide-necked intracranial aneurysms with neck widths ≥ 4 mm or dome to neck ratio < 2 originating on or near a vessel bifurcation of the basilar tip or carotid terminus with at least a portion of the aneurysm neck overlapping the lumen of the parent artery. The inflow vessels should have diameters from 2.7 mm to 4.5 mm.

The indication for use statement has been modified from that granted for the HUD designation. The HUD designation was for "use with embolic agents in the treatment of intracranial aneurysms originating on or near a vessel bifurcation of the basilar artery or carotid terminus artery." It was modified for the HDE approval because the revised indications for use (IFU) statement more clearly identifies the patient population that the PulseRider is designed to treat and in which the safety and probable benefit of the device is supported by the available clinical data. The modified IFU is within the patient population limit granted by the HUD designation.

III. CONTRAINDICATIONS

PulseRider is NOT indicated for:

1. Patients with vascular anatomy or dimensions at the targeted treatment site for which the available PulseRider sizes are not appropriate.
2. Patients with severe vascular tortuosity or anatomy that would preclude the safe introduction of the PulseRider device or the use of other devices involved with the

procedure.

3. Patients with preoperative coagulation disorder, or with contraindications to antiplatelet or anticoagulant therapy.
4. Patients with known hypersensitivity to nickel.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the PulseRider® Aneurysm Neck Reconstruction Device labeling.

V. DEVICE DESCRIPTION

The PulseRider Aneurysm Neck Reconstruction Device is a self-expanding nitinol implant designed to retain neurovascular embolic coils in unruptured wide-necked intracranial aneurysms with neck widths ≥ 4 mm or dome to neck ratio < 2 originating on or near a vessel bifurcation of the basilar tip or carotid terminus with at least a portion of the aneurysm neck overlapping the lumen of the parent artery. The inflow vessels should have diameters from 2.7 mm to 4.5 mm. The PulseRider Aneurysm Neck Reconstruction Device is comprised of a torque device, delivery wire, introducer, and implant (see Figure 1).

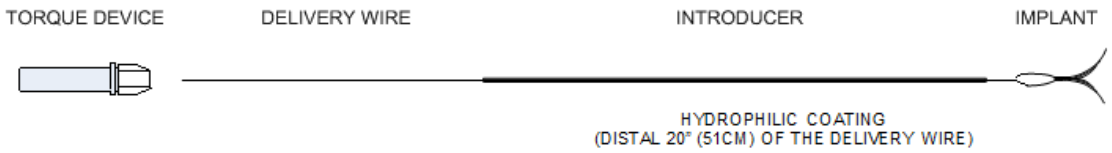

Figure 1: PulseRider® Device (not to scale)

The implant is provided attached to the delivery wire. See Table 1 for a list of the materials of construction for the implant and delivery wire. The delivery wire has a working length of 190 cm and a nominal diameter of 0.36 mm (0.014”). The introducer has a working length of 67 cm and a nominal diameter of 1.32 mm (0.052”). The PulseRider implant and delivery wire are insulated to allow electrolytic current to be delivered to the detachment junctions using commercially available detachment controllers. The torque device provided may be attached to the proximal end of the delivery wire to aid in orienting the implant prior to detachment.

Component	Implant	Delivery Wire
Base Material	Nitinol	Stainless Steel
Radiopaque Markers	Platinum/Iridium alloy	Platinum/Iridium alloy
Solder	Gold-Tin alloy	Gold-Tin alloy
Detachment Zone	Stainless Steel	Stainless Steel
Coatings, Outer Materials	Parylene	Parylene, Polyester Heatshrink, Hydrophilic Coating

Table 1: Materials of Construction of PulseRider Implant and Delivery Wire

All of the PulseRider Aneurysm Neck Reconstruction Device components are packaged in a sealed pouch, for single use only, and provided sterile by ethylene oxide gas exposure. The PulseRider Aneurysm Neck Reconstruction Device is available in two implant configurations: T and Y shapes with 8 mm and 10 mm wide arches. The anchor base is available in sizes to treat parent arteries from 2.7 mm to 4.5 mm. Depending on the size of the aneurysm neck and parent vessel, the appropriately sized PulseRider implant must be chosen to ensure adequate stability and anatomical fit (see Table 2 for PulseRider implant

sizing for the T and Y shapes and the device labeling for additional instructions for implant sizing and implantation).

	Catalog Number	Target Aneurysm Neck Width (mm)	Parent Vessel Diameter (mm)	Implant Arch Width (mm)
 T Shape Implant	**201-D**	8	2.7 - 3.5	8.6
	203-D	8	3.5 - 4.5	8.6
	211-D	10	2.7 - 3.5	10.6
	213-D	10	3.5 - 4.5	10.6
 Y Shape Implant	**301-D**	8	2.7 - 3.5	8.6
	303-D	8	3.5 - 4.5	8.6
	311-D	10	2.7 - 3.5	10.6
	313-D	10	3.5 - 4.5	10.6

Table 2: PulseRider Implant Sizing Guidelines

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Conventional procedures used in the treatment of unruptured wide-necked intracranial aneurysms originating on or near a vessel bifurcation of the basilar tip or carotid terminus include open surgical clipping and endovascular treatment using embolization coiling. Surgical clipping may be difficult or impossible in cases where there is no true aneurysm neck present and the aneurysm location is difficult to access. Coiling involves endovascular placement of neurovascular embolic coils into the aneurysm sac, but aneurysms with wide necks cannot often structurally retain embolization coils and complications such as protrusion of the coil into the parent artery may occur. Endovascular therapy of wide neck aneurysms using coiling is sometimes limited to parent artery occlusion, if there is adequate collateral flow, or by a balloon-assisted technique using a balloon catheter to aid in retaining the coils within the aneurysm sac during the procedure.

An additional alternative treatment of wide-neck intracranial aneurysms originating on or near a vessel bifurcation is using neurovascular stents approved through the Humanitarian Device Exemption (HDE) regulatory pathway (i.e., Stryker Neuroform Stent System (H020002), Codman & Shurtleff Enterprise Vascular Reconstruction Device and Delivery System (H060001), MicroVention Low-Profile Visualized Intraluminal Support Device (LVIS) (H130005)) to aid in retaining neurovascular embolization coils in the aneurysm sac. The scientific literature demonstrates that stenting wide-neck bifurcation aneurysms using HDE approved neurovascular stents can result in a 4.4% mortality rate, 8.9% complication rate, and 92% Raymond I and II combined aneurysm occlusion rate according to the publication by K.M. Fargen et al. (*Neurosurgery*, 2013).

VII. MARKETING HISTORY

The PulseRider® was Conformité Européene (CE) marked in October 2013 and was first placed on the market in Europe in April 2014 for use with embolic coils for the treatment of unruptured wide-necked intracranial aneurysms originating on or near a vessel bifurcation. The European countries in which the PulseRider is marketed are: United Kingdom, France, Germany, Italy, Spain, Portugal, Netherlands, Denmark, Norway, Sweden, Finland, Hungary, Switzerland, Latvia, Belgium, and Austria.

The PulseRider Aneurysm Neck Reconstruction Device has not been withdrawn from marketing for any reason relating to the safety and effectiveness of the device.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (i.e., complications) associated with the use of the device.

1) Adverse tissue reaction
2) Allergic reaction and anaphylaxis from contrast media
3) Allergy to nickel
4) Aneurysm perforation or rupture
5) Incomplete aneurysm occlusion and/or recanalization
6) Arteriovenous fistula
7) Coagulopathy
8) Device misplacement or migration
9) Coil migration, herniation or prolapsed into normal vessels through or around device
10) Emboli (air, tissue, thrombotic, device-related)
11) Access site complications such as hemorrhage, hematoma, pain, or infection
12) Intracranial or intracerebral hemorrhage
13) Neurological sequelae including, but not limited to, ischemia, hemorrhage, embolic stroke, cranial nerve deficit, and death
14) Visual disorders (diplopia, blurred vision)
15) Deep vein thrombosis (DVT)
16) Hypoesthesia
17) Fever
18) Hypothermia
19) Vessel occlusion
20) Cranial nerve palsy/disorder
21) Stenosis or occlusion of treated vessel segment or device occlusion
22) Pseudoaneurysm formation
23) Vascular sequelae including vasospasm, thrombosis, dissection, perforation, or other trauma
24) Hydrocephalus
25) Increase in intracranial pressure (ICP)
26) Cognitive impairment
27) Coma
28) Infarction
29) Phlebitis
30) Infection including urinary tract infection (UTI)

31) Myocardial infarction
32) Cardiac arrhythmia
33) Temporary cortical blindness
34) Nausea and/or vomiting
35) Headache
36) Pneumonia
37) Ecchymosis
38) Dizziness
39) Death

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

IX. SUMMARY OF PRECLINICAL STUDIES

A. Laboratory Studies

Objectives. The objectives of the laboratory studies were to test the design verification and validation of the PulseRider Aneurysm Neck Reconstruction Device and its materials of construction, the biocompatibility of the materials, shelf-life stability, and sterilization validation.

Design Verification and Validation Testing

The devices used for testing were assembled and packaged in a controlled environment. The PulseRider implant and delivery wire were subjected to two sterilization cycles with ethylene oxide using a sterilization cycle equivalent to the cycle used for the devices in the clinical study. Tables 3 and 4 below summarizes the design verification and validation testing conducted for the PulseRider implant only and the entire PulseRider Aneurysm Neck Reconstruction Device components (implant and delivery system).

Table 3: Design Verification and Validation Testing for PulseRider Implant

Test	Purpose	Results/Conclusions
Material Composition	To evaluate the surface composition and the depth of the nickel depleted layer of the implant.	PASS
Shape Memory & Superelasticity (Material Transition Temperature)	To confirm that the nitinol raw material of the implant will reach its intended size and shape at the average basal human core temperature.	PASS
Corrosion Resistance	To evaluate pitting and crevice corrosion resistance per ASTM F2129-08 and galvanic corrosion resistance per ASTM G71.	PASS
Dimensional Verification	To verify the device meets defined dimensional specifications.	PASS
Percent Surface Area	To determine the percentage of the vessel wall along the length encompassed by the implant that is not covered with the implant	PASS

	material.	
Foreshortening	To determine the deviation of the implant's diameter when expanded to its maximum indicated vessel diameter and to determine the change in implant length as it expands from its crimped to maximum indicated vessel diameter.	PASS
Stent Integrity	To demonstrate that the implant integrity is maintained throughout its life cycle from manufacturer through the end of its service life.	PASS
Radial Outward Force	To measure the reactive radial pressure of the implant in response to compression. It is meant to ensure that the implant retains adequate radial force after sterilization and multiple deployment cycles.	PASS
Apposition	This testing is conducted in a mock vessel to ensure that the implant achieves adequate apposition to the vessel wall throughout the labeled size range.	PASS
Mechanical Properties	To evaluate the mechanical properties of the nitinol in the raw material and the finished device.	PASS
Stress/Strain Analysis	To determine the stress/strain levels experienced by the device during crimping conditions.	PASS
Fatigue Analysis	To determine the stress/strain levels experienced by the device during long term fatigue conditions.	PASS
Accelerated Durability	To provide evidence that the device can withstand pulsatile fatigue loading throughout its service life.	PASS
Radiopacity	To show that the radiopaque markers are visible under fluoroscopy and can facilitate positioning, advancement, deployment, and detachment.	PASS

Table 4: Design Verification and Validation Testing – PulseRider Implant and Delivery System

Test	Purpose	Results/Conclusions
Dimensional Verification	To verify the device meets defined dimensional specifications.	PASS
Trackability	This testing evaluates the ability of the delivery system to facilitate delivery and deployment of the implant through a simulated tortuous path.	PASS
Retraction Force	To evaluate the force required to retract the implant into a microcatheter during repositioning	PASS

	and/or retrieval of the device.	
Detachment Time	To evaluate the device's ability to reliably detach at the detachment junctions within a specified time.	PASS
Tensile Strength	To ensure that the device is capable of safely withstanding the forces of introduction, deployment, and retraction by determining the maximum tensile load of the implant and delivery system.	PASS
Implant Marker Separation Shear Force	To demonstrate that the radiopaque markers remain attached after experiencing various forces it may see during advancement, deployment and retraction.	PASS
Flexibility and Kink Test	To evaluate that the device delivery system will not kink at a bend radius that is appropriate for the intended anatomy.	PASS
Torque Strength	To ensure that the device is capable of safely withstanding the forces of positioning and/or repositioning by determining how many turns the implant and delivery system can withstand without breaking	PASS
Coating Integrity	To ensure that the device's polymer coating remains intact after multiple deployments.	PASS
Particulate Evaluation	This test evaluates particulate release during simulated use in a tortuous path model per the requirements of USP <788> and AAMI Technical Information Report (TIR) 42:2010.	PASS
Lubricity	To evaluate the performance of the hydrophilic coating in a simulated use model.	PASS

Biocompatibility

The PulseRider implant is a permanently implantable nitinol device and the PulseRider delivery system is an externally communicating device in contact with tissue and circulating blood, with a temporary duration of contact of < 24 hrs. All patient contacting components of the PulseRider Aneurysm Neck Reconstruction Device were tested to characterize the materials for biocompatibility and toxicity in accordance with EN/ISO 10993 and the FDA Blue Book Memorandum #G95-1. Tables 5 and 6 summarize the biocompatibility tests conducted for the PulseRider implant and delivery system, respectively.

Table 5: Biocompatibility Testing for PulseRider Implant Only

Test	Method	Results/Conclusions
Cytotoxicity (EN/ISO 10993-5)	ISO Minimum Essential Medium (MEM) Elution Assay with L-929 Mouse Fibroblast	Non-cytotoxic
Sensitization (EN/ISO 10993-10)	ISO Guinea Pig Maximization Test	Non-sensitizing
Irritation or Intracutaneous Reactivity (EN/ISO 10993-10)	ISO Intracutaneous Reactivity Test	Non-irritating
Systemic Toxicity (EN/ISO 10993-11)	ISO Acute Systemic Injection Test	Non-toxic acutely
Pyrogenicity (EN/ISO 10993-11)	ISO Materials Mediated Rabbit Pyrogen Test	Non-pyrogenic
Chronic Toxicity (EN/ISO 10993-11)	Pulsar Vascular, Inc. In-Vivo Test (at 30, 90, and 180 days)	Non-toxic chronic
Genotoxicity (EN/ISO 10993-3)	Bacterial Mutagenicity Test - Ames Assay	Non-mutagenic
	In Vitro Mouse Lymphoma Assay	Non-mutagenic
	In Vitro Mouse Lymphoma Assay – Extended Treatment	Non-mutagenic
	In Vivo Mouse Micronucleus Assay	Non-mutagenic
Implantation (EN/ISO 10993-6)	Intramuscular Implantation in Rabbits for 2 weeks	Non-irritant
Hemocompatibility (EN/ISO 10993-4)	ASTM Hemolysis Assay - Direct Contact and Extract Method	Non-hemolytic
	Complement Activation C3a and SC5b-9	Comparable to approved device; PASS
	Partial Thromboplastin Time (PTT)	Non-activator of intrinsic coagulation pathway
	Platelet and Leukocyte Counts	No adverse effects observed

Table 6: Biocompatibility Testing for PulseRider Delivery System

Test	Method	Results/Conclusions
Cytotoxicity (EN/ISO 10993-5)	ISO MEM Elution Using L-929 Mouse Fibroblast Cells	Non-cytotoxic
Sensitization (EN/ISO 10993-10)	ISO Guinea Pig Maximization Test	Non-sensitizing
Irritation/Intracutaneous Reactivity (EN/ISO 10993-10)	ISO Intracutaneous Irritation Test	Non-irritating
Systemic Toxicity (Acute Toxicity) (EN/ISO 10993-11)	ISO Acute Systemic Injection	Non-toxic acutely
	Materials Mediated Rabbit Pyrogen Test	Non-pyrogenic
Subchronic Toxicity (EN/ISO 10993-11)	13 Week Animal (Rabbit) Implantation	Non-toxic subchronic
Hemocompatibility (EN/ISO 10993-4)	ASTM Hemolysis Assay – Direct Contact Method	Non-hemolytic
	ASTM Hemolysis Assay – Extract Method	Non-hemolytic
	Complement Activation C3a and	Comparable to approved

	SC5b-9	device; PASS
	Four Hour Thrombo-Resistance in Two Dogs	Comparable to approved device; PASS
Genotoxicity (EN/ISO 10993-3)	Bacterial Mutagenicity Test - Ames Assay	Non-mutagenic
	In Vitro Mouse Lymphoma Assay	Non-mutagenic
	In Vivo Mouse Micronucleus Assay	Non-mutagenic

Shelf-Life Testing

PulseRider test samples were subjected to real time aging for a time period equal to 3 years in addition to dual sterilization and distribution conditioning. The devices were then tested for compliance to the device specifications including package integrity, sterility, simulated use, particulate evaluation, lubricity, and physical strength performance testing. All test samples met the acceptance criteria supporting a 3-year shelf-life for the PulseRider.

Sterilization Validation

The PulseRider is sterilized using ethylene oxide (EO). The EO cycle was validated to a sterility assurance level (SAL) of 10^{-6} per EN ISO 11135:2014. The device was tested and met specifications after two sterilization cycles.

B. Animal Studies

Objectives. The objectives of the animal studies were to evaluate the ability of the PulseRider to perform as intended to support neurovascular embolization coils within the aneurysm sac, device stability, intra-procedural safety and performance, and vessel injury and healing characteristics in an acute and chronic animal study.

Acute Animal Study

Acute in vivo testing of the PulseRider was performed using the canine carotid bifurcation model in two studies with 5 canines in each study. The acute testing evaluated the stability of the PulseRider for retaining neurovascular embolization coils within the aneurysm sac and remaining in position. In addition, the intra-procedural safety and performance aspects of the PulseRider implant and delivery system were evaluated. In the second animal study, a core lab reviewed the pre- and post-procedure fluoroscopic images and provided independent evaluation of the occlusion status after coiling. No failures of the implant or delivery systems or device-related safety events occurred in these studies. The implants and delivery systems performed as intended in all cases and were able to retain a high density of coils in the aneurysms.

Chronic Animal Study

Chronic in vivo testing of the proximal anchoring portion of the device was performed in rabbit aortas. Devices were implanted for 30, 90 and 180 day time periods, then explanted by a board certified pathologist and histologically evaluated. The results showed that the vascular response and healing was stable over all time points with no

significant histological differences noted between 30, 90 and 180 days implant duration. Additionally, no evidence of systemic toxicity or systemic tissue reaction was associated with the device.

A chronic vessel injury study was also performed on the PulseRider implant in swine arteries. The PulseRider was introduced into five different swines in four to six locations per animal. The PulseRider was expanded and resheathed a total of three times per location to simulate the maximum number of allowed deployments per location (consistent with the device Instructions for Use). The device was then resheathed and removed. No devices were implanted. Each animal was recovered and the arteries were allowed to heal for six to seven days before sacrifice, necropsy was performed, and the treated arteries were harvested for histological analysis. The gross and histopathological findings reported in this study were consistent with a device that produces only a minimal, or rarely mild, degree of vascular reaction or mechanical trauma when deployed in artery segments of different sizes in the healthy swine model. In addition, there were no biologically significant pathologic findings associated with the test procedure. The PulseRider demonstrated in this study that it is atraumatic to arterial walls during multiple deployment cycles, causing no significant injury or damage intra-procedurally.

C. Additional Studies

Magnetic Resonance Imaging (MRI) Compatibility

Pulsar Vascular, Inc. commissioned an independent laboratory to evaluate the MRI safety of the PulseRider Aneurysm Neck Reconstruction Device, specifically the permanent nitinol implant. The independent laboratory tested the PulseRider implant for MRI compatibility per ASTM F2503 including magnetically induced displacement force (ASTM F2052), magnetically induced torque (ASTM F2213), heating by radiofrequency fields (ASTM F2182), and image artifact (ASTM F2119). The results of the MRI compatibility and safety testing is presented in the "MRI Safety Information" section of the Instructions for Use (device labeling) to inform the end user on the proper parameters and conditions in which a patient with the PulseRider implant can be safely scanned in the event a MRI is needed.

X. SUMMARY OF CLINICAL INFORMATION

Study Design

An overview of the clinical study design to support the safety and probable benefit of the PulseRider Aneurysm Neck Reconstruction Device is summarized in Table 7 below.

Table 7: Summary of ANSWER Clinical Study Design

Title:	**Adjunctive Neurovascular Support for Wide-Neck Aneurysm Embolization and Reconstruction (ANSWER) Clinical Study**
Study Design:	A prospective, multi-center, single-arm, non-randomized study.
Objective:	The objective of this study is to assess the safety and probable benefit of the PulseRider in the minimally invasive endovascular treatment of wide-neck basilar or carotid terminus bifurcation intracranial aneurysms.
Study Duration:	• Anticipated patient enrollment in 12 months • Anticipated completion of follow-up 12 months after last patient enrolled
Patient	Patients will undergo a follow-up assessment immediately post-procedure, prior to

Follow-Up:	hospital discharge and at 30-days, 180-days and 365-days post procedure.
Patient Population:	Patients who meet the protocol inclusion/exclusion criteria with at least one bifurcation intracranial aneurysm that is acceptable for minimally invasive treatment.
Sample Size:	The objective is to enroll up to 35 patients to yield at least 30 evaluable patients.
Number of Sites:	Up to 15 sites worldwide may participate in this multi-center study.
Study Endpoints:	Primary Endpoints: • Safety: Neurological death and major ipsilateral or downstream stroke to 180-days post-procedure. Major stroke is defined as a stroke, which is present after seven days and increases the National Institute of Health Stroke Scale (NIHSS) of the patient by ≥ 4. • Technical Success: Device placement success and ability to retain coils within the aneurysm (as judged by the treating physician at the time of the procedure). Core lab will review images at a later time. • Probable Benefit: Rate of aneurysm occlusion at day zero (0) based on Raymond I • Probable Benefit: Rate of aneurysm occlusion at 180-days follow-up as defined using Raymond I and II. Additional Evaluations to 180-Days and 365-Days Follow-Up: • Rate of aneurysm occlusion at 365 days • Device movement or migration defined as any relative change in the position of the device with respect to the parent and/or daughter vessels that is greater than 2 mm by conventional catheter angiography (180 days) and by conventional catheter angiography or magnetic resonance angiography (MRA) or computed tomography angiography (CTA) (365 days) • Stenosis defined as > 50% at implant site by conventional catheter angiography at 180 days and MR angiography or conventional catheter angiography or CTA at 365 days • Rate of incidence of new neurological deficits • Complication rate (neurological and non-neurological)

Clinical Study Enrollment Criteria

The following is a list of the inclusion/exclusion criteria for enrollment in the ANSWER clinical study. Patients were required to meet all inclusion criteria and none of the exclusion criteria to be considered eligible for study participation in the ANSWER trial.

Inclusion Criteria

Candidates for this study must meet ALL of the following criteria:

a) Patient who presents with an angiographically confirmed, wide neck (≥ 4 mm or dome to neck ratio < 2) intracranial aneurysms located at a bifurcation of the basilar artery or carotid terminus artery.
b) The target aneurysm is in a vessel with a diameter of 2.7 mm to 4.5 mm.
c) The patient is 18 years or older at the time of consent.
d) The patient has signed the Institutional Review Board (IRB)/Ethics Committee (EC) approved informed consent form.
e) In the opinion of the physician, placement of the PulseRider is technically feasible and clinically indicated.
f) Subject has mental capacity and is willing and able to comply with protocol requirements and follow-up.

Exclusion Criteria

Candidates will be excluded if ANY of the following conditions apply:

a) Unstable neurological deficit (condition worsening within the last 90 days)
b) Subarachnoid hemorrhage (SAH) within the last 60 days
c) Irreversible bleeding disorder
d) Modified Rankin Scale (mRS) score ≥ 3
e) Patient has another aneurysm which, in the Investigator's opinion, will require treatment within the follow up period (365 days).
f) Platelet count < 100 x 103 cells/mm^3
g) Inability to tolerate, adverse reaction, or contraindication to taking aspirin or clopidogrel.
h) A history of contrast allergy that cannot be medically controlled
i) Known allergy to nickel
j) Relative contraindication to angiography (e.g., serum creatinine > 2.5 mg/dL)
k) Woman with child-bearing potential who cannot provide a negative pregnancy test
l) Evidence of active infection (fever with temperature > 38 °C and/or white blood cell (WBC) > 15,000).
m) Other conditions of the heart, blood, brain or intracranial vessels that carry a high risk of neurologic events.
n) Evidence of disease or condition expected to compromise survival or ability to complete follow-up assessments during the 365-day follow-up period.
o) Extracranial stenosis greater than 50% in the parent artery requiring access to the lesion.
p) Intracranial stenosis greater than 50% in the treated vessel.
q) Extreme vessel tortuosity that prohibits appropriate control of the micro-guide wire and/or the PulseRider delivery wire.

Demographic Data

Thirty-four (N=34) patients were enrolled and treated in the ANSWER clinical study. The mean age was 60.9 years with a preponderance of women (n/N = 29/34 or 85.3%) as is common in studies of intracranial aneurysms. Therefore, the selection ratio of men versus women in the ANSWER clinical study is reflective of the underlying distribution of the disease. Nine (9) patients had undergone previous treatment for the target aneurysm with coil embolization. Five (5) patients (n/N = 5/34 or 14.7%) had a previous subarachnoid hemorrhage that occurred more than 60 days prior to the PulseRider procedure. Two (2) patients had a previous stroke (n/N = 2/34 or 5.9%) and 24 patients (n/N = 24/34 or 70.6%) had concurrent hypertension. More detailed baseline characteristics of the treated patient population are shown in the following Tables 8-11.

Table 8: Demographics

Demographics	
Age (years): Mean ± Std (Min – Max)	60.9 ± 13.4 (26 – 86) Median: 65.0; 95% Confidence Interval (CI) (56.3, 65.6)
Male (% (n/N))	14.7% (5/34)
Female (% (n/N))	85.3% (29/34)

Table 9: Patient History

Characteristic	% (n/N)
Medical History	
Subarachnoid Hemorrhage	14.7% (5/34)
Stroke	5.9% (2/34)
Coronary Artery Disease	5.9% (2/34)
History of Myocardial Infarction	2.9% (1/34)
Hypertension	70.6% (24/34)
Diabetes	11.8% (4/34)
Smoking	
Never Smoked	26.5% (9/34)
Previous Smoker	32.3% (11/34)
Current Smoker	41.2% (14/34)
Prior Treatment of Target Aneurysm	
Coil Embolization • Basilar • Carotid Terminus • Total Prior Treatment of Target Aneurysm	 23.5% (8/34) 2.9% (1/34) 26.5% (9/34)
Surgery – no patients had prior open surgery for the target aneurysm	0% (0/34)

Table 10: Aneurysm Location

Location	# of Patients (n)	% (n/N)
Basilar	27	79% (27/34)
Carotid Terminus	7	21% (7/34)

Table 11: Aneurysm Size

Measurement	N	Mean	SD	Min	Max
Dome width (mm)	34	7.0	3.2	2.8	16.3
Neck length (mm)	34	5.2	2.2	2.3	11.6
Dome to neck ratio	34	1.4	0.3	0.5	1.9
Parent vessel pre-aneurysm (mm)	34	3.1	0.3	2.7	4.2

Clinical Data Analysis and Results:

The clinical study was sized to provide a characterization of the safety and probable benefit profile associated with the device and to summarize its performance using traditional statistical techniques (descriptive statistics). The sample size for this trial was not derived via traditional power methods as no formal statistical hypothesis testing was planned. All of the observed adverse events recorded in the ANSWER clinical study for the N=34 treated patients through the 180 ± 45 days follow-up visit are shown in Table 12.

Table 12: Observed Adverse Events through 180 ± 45 Days Follow-Up

	Time of Occurrence				
Adverse Event	**Procedure**	**≤ 30 Days**	**> 30 Days**	**Total (n)**	**Frequency % (n/N*100%)**
Allergy to Protonix	0	1	0	1	2.9%
Anemia, drop in hemoglobin	0	1	2	3	8.8%
Cauda equina syndrome	0	0	1	1	2.9%
Cerebral hematoma	0	0	1	1	2.9%
Coil perforation of aneurysm	1	0	0	1	2.9%
Confusion	0	1	0	1	2.9%

Constipation	0	1	1	2	5.9%
Death	0	0	1	1	2.9%
Deep vein thrombosis	0	1	0	1	2.9%
Depression – mild	0	1	1	2	5.9%
Dizziness	0	1	0	1	2.9%
Dysarthria	0	0	1	1	2.9%
Dysphagia	0	0	1	1	2.9%
Ecchymosis	0	2	0	2	5.9%
Emboli/Thrombus	1	0	0	1	2.9%
Fatigue, lower leg	0	1	0	1	2.9%
Femoral occlusion	0	1	0	1	2.9%
Fractured leg	0	0	1	1	2.9%
Gastroenteritis - viral	0	0	1	1	2.9%
Gastrointestinal bleed	0	0	1	1	2.9%
Gingivobuccal sulcus with mucosal injury	0	0	1	1	2.9%
Headache	0	9	1	10	29.4%
Hematoma, hemorrhage at access site	1	1	0	2	5.9%
Hematuria	0	1	0	1	2.9%
Hyperglycemia	0	0	1	1	2.9%
Hypotension	1	1	1	3	8.8%
Itching	0	1	0	1	2.9%
Leukocytosis	0	0	1	1	2.9%
Lumbago	0	0	1	1	2.9%
Migraine headaches	0	0	1	1	2.9%
Nausea and/or vomiting	0	3	1	4	11.8%
Night sweats	0	0	1	1	2.9%
Numbness left leg	0	1	0	1	2.9%
Nose bleed	0	1	0	1	2.9%
Otitis	0	0	1	1	2.9%
Oozing at site	0	1	0	1	2.9%
Pain	0	0	1	1	2.9%
Pain – leg	0	0	1	1	2.9%
Periodontitis	0	1	0	1	2.9%
Pleurisy	0	1	0	1	2.9%
Pneumonia	0	1	1	2	5.9%
Possible seizure	0	0	1	1	2.9%
Respiratory problems	0	1	6	7	20.6%
Renal mass	0	0	1	1	2.9%
Retinal hemorrhage	0	1	0	1	2.9%
Retroperitoneal hematoma (left side)	0	1	0	1	2.9%
Shingles	0	0	1	1	2.9%
Shortness of breath	0	1	2	3	8.8%
Stroke* (adverse events included cerebellar hemorrhage, contrast induced encephalopathy transient, delayed minor occipital, diplopia and mass effect)	0	3	2	5	14.7%
Transient ischemic attack (TIA)	0	1	0	1	2.9%
Unsteady gait	0	0	1	1	2.9%
Urinary tract infection	0	1	1	2	5.9%
Uterine bleeding	0	1	0	1	2.9%
Vessel dissection	1	0	0	1	2.9%
Weakness, left side	0	0	1	1	2.9%
Weakness, right side	0	0	1	1	2.9%
*Stroke is defined as radiologically confirmed stroke or increase in NIHSS that persists for $\geq$ 24 hours.					

Table 13 below provides all of the serious adverse events (SAEs) observed in the ANSWER clinical study with the number of SAEs adjudicated as procedure or device related:

Table 13: Observed Serious Adverse Events through 180 ± 45 Days Follow-Up

Serious Adverse Events	Time of Occurrence			Total (n)	Related	
	Procedure	≤ 30 Days	> 30 Days		Procedure	Device
Stroke* (adverse events included cerebellar hemorrhage, contrast induced encephalopathy transient, delayed minor occipital, diplopia and mass effect)	0	3	2	5	3	1
Respiratory problems	0	1	3	4	0	0
Pneumonia	0	1	1	2	0	0
Anemia, drop in hemoglobin	0	1	0	1	0	0
Hypotension	1	0	0	1	1	0
Cauda equina syndrome	0	0	1	1	0	0
Cerebral hematoma	0	0	1	1	0	0
Coil perforation of aneurysm	1	0	0	1	1	0
Death	0	0	1	1	0	0
Deep vein thrombosis	0	1	0	1	1	0
Dysphagia	0	0	1	1	0	0
Femoral occlusion	0	1	0	1	1	0
Fractured leg	0	0	1	1	0	0
Gastrointestinal bleed	0	0	1	1	0	0
Possible seizure	0	0	1	1	0	0
TIA	0	1	0	1	1	1
Uterine bleeding	0	1	0	1	0	0
Weakness, left side	0	0	1	1	0	0
*Stroke is defined as radiologically confirmed stroke or increase in NIHSS that persists for ≥ 24 hours.						

Primary Safety Endpoint: There were no reported neurological deaths or major ipsilateral/downstream strokes within 180 days of the PulseRider procedure (see Table 14). A major stroke was defined in the ANSWER clinical protocol as a stroke, which is present after 7 days and increases the National Institutes of Health Stroke Scale (NIHSS) score of the patient by ≥ 4. The one-sided upper limit of the 95% confidence interval for neurological death or major ipsilateral/downstream stroke to 180-days post-procedure is 8.4% based on the observed rate of 0% (n/N = 0/34) using the Clopper-Pearson method.

Table 14: Neurological Death and Major Ipsilateral or Downstream Stroke through 180 ± 45 Days

	% (n/N)	Upper 95% Confidence Limit
Neurological Death	0% (0/34)	--
Major Stroke – Ipsilateral or Downstream	0% (0/34)	--
Composite	0% (0/34)	8.4%

Although not analyzed to be a major ipsilateral/downstream stroke based on the major stroke definition pre-specified in the ANSWER clinical protocol for the primary safety endpoint, there were a total of five (5) strokes presented in Tables 12 and 13 above that occurred in 5 patients. These 5 strokes are defined either through an imaging finding

and/or a change in the NIHSS score with symptoms that persists for ≥ 24 hours based on the clinical guidelines definition for stroke (R.L. Sacco et al. *Stroke* 2013). Three of the five strokes were adjudicated by the Clinical Events Committee (CEC) to be categorized as a stroke event. The other two stroke patients were categorized using a worst-case assessment. One patient exhibited neurological deficits caused by mass effect that was pre-existing; however, this patient also developed diplopia and worsening vision 3 days post-procedure which worsened over time and caused on-going neurologic deterioration. The possibility of a stroke in this patient cannot be ruled out based on the clinical evidence and the neurological deterioration cannot be solely attributed to mass effect. The second patient that was counted as a worst-case assessment for having a stroke event suffered visual disorder 4 days post-procedure and the symptom was ongoing at the 180 day follow up visit. The MRI was negative for any parenchymal or vascular changes in this patient; however, considering the onset of the visual disorder post-procedure and its duration, a stroke event cannot be ruled out. Of the 5 strokes reported in Tables 12 and 13, four (4) strokes were peri-procedural and one (1) delayed. Two of the patients with peri-procedural strokes recovered completely, and the other two patients with peri-procedural strokes and the patient with the delayed stroke recovered with sequelae such as ongoing blurred vision. In addition, one patient from the 34 total patients treated had a transient ischemic attack (TIA) peri-procedure.

The available modified Rankin Scale (mRS) scores were also analyzed to determine the severity of a stroke in support of understanding the safety profile of the PulseRider for those 5 patients categorized as having a stroke in Tables 12 and 13. Table 15 below presents the pre-procedure, post-procedure, 30-day and 180-day mRS scores for the 5 patients who exhibited a stroke during the course of the clinical study.

Table 15: Modified Rankin Scale (mRS) Scores for 5 Patients with Stroke Event Before and after the Procedure, 30 Days, and 180 Days Follow-Up

Patient ID	Pre-Operative Visit	Post-Procedure	30-Day Follow-up	180-Day Follow-up
005-006	1	1	1	1
008-001	1	1	1	4
008-003	0	0	0	0
015-006	0	0	0	0
016-002	0	4 decreased to 2 within 2 days	0	1

A 90-day mRS was not conducted as part of the clinical study; therefore, the 180-day mRS was compared to the patient's pre-operative mRS to understand the severity of the stroke symptoms. The safety outcome based on both neurological death and stroke resulting in a mRS ≥ 3 at 180 days post-procedure is presented in Table 16.

Table 16: Safety Outcome Assessed Based on Neurological Death and Stroke Resulting in mRS ≥ 3 at 180 ± 45 Days Follow-Up*

	% (n/N)
Neurological Death	0% (0/34)
Stroke resulting in mRS ≥ 3	2.9% (1/34)

*The 90-day mRS was not conducted and only 180-day long-term follow-up was available. The 180-day mRS was assessed by office visit by a non-blinded assessor to the treatment.

The mRS at 180 days post-procedure was also analyzed for all 34 treated patients and a good clinical outcome (mRS 0-2) for neurological deficit and disability was achieved in

94.1% of patients (n/N = 32/34) and only 2 patients had an unfavorable clinical outcome (mRS ≥ 3). There are some limitations to this mRS assessment since the 90 day mRS was not assessed/available and the 180 day mRS was conducted by an unblinded assessor, which may introduce some bias into the final mRS scores favoring a good clinical outcome.

Technical Success for Device Placement: The PulseRider was placed successfully in 34/34 (100%) study patients. There have been no cases of an attempted PulseRider placement without success. In 34/34 (100%) cases, the treating physicians viewed the procedure as a technical success if they were able to access the target aneurysm, deploy the device accurately, and detach the device successfully (see Table 17).

Table 17: Primary Endpoint - Technical Success

	% (n/N)	95% CI
Technical Success	100% (34/34)	91.6%, 100%

Rate of Aneurysm Occlusion at Day Zero (0) and 180-Days Post-Procedure: The success rate with respect to the primary probable benefit endpoint of aneurysm occlusion (Raymond I) at day zero is 52.9% (n/N = 18/34). The success rate with respect to the primary probable benefit endpoint of aneurysm occlusion (Raymond I/II) at 180-days post-procedure is 87.9% (n/N = 29/33 subjects) as adjudicated by a blinded core laboratory (see Tables 18 and 19). One treated patient was excluded from the 180 day aneurysm occlusion analysis because this patient received a magnetic resonance angiography (MRA) instead of a digital subtraction angiogram (DSA) at the 180 day assessment. This patient was excluded from the 180 day aneurysm occlusion analysis in order to ensure the occlusion data presented was obtained using consistent imaging measurements for accuracy. The lower limit of the one-sided 80% confidence interval is 80.5%, which is based on the observed rate of 87.9% (n/N = 29/33) using the Clopper-Pearson method. Of the 29 subjects who had an aneurysm occlusion of Raymond I/II at 180-days, no subjects had clinically significant stenosis > 50%.

Please note that the 365 day follow-up data was only available for 8 patients at the time of HDE submission; therefore, Table 18 does not include aneurysm occlusion data for all 34 treated patients at 365 days follow-up.

Table 18: Aneurysm Occlusion

Report of Raymond Score			
Score	**Day Zero** n/N (%)	**180 Days**[1] n/N (%)	**365 Days** n/N (%)
Raymond I	18/34 (52.9%)	20/33 (60.6%)	6/8 (75%)
Raymond II	9/34 (26.5%)	9/33(27.3%)	2/8 (25%)
Raymond III	7/34 (20.6%)	4/33 (12.1%)	0/8 (0%)

[1]One enrolled subject had MRA performed instead of an angiogram and is excluded from this analysis.

Table 19: Blinded Core Lab Adjudicated Raymond I and II at 180-Days Follow-Up

Raymond Score	**180 Days % (n/N)**	**Lower 80% Confidence Limit**
I/II	87.9% (29/33[1])	80.5%

[1]One enrolled subject had MRA performed instead of an angiogram and is excluded from this analysis.

Pediatric Extrapolation

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

XI. 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 32 investigators of which none were full-time or part-time employees of the sponsor and 7 investigators 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 investigators
- Significant payment of other sorts: 7 investigators
- Proprietary interest in the product tested held by the investigator: 0 investigators
- Significant equity interest held by investigator in sponsor of covered study: 6 investigators

Statistical analyses were conducted by FDA to determine whether the financial interests/arrangements had any impact on the clinical study outcome. FDA determined the information provided did raise questions about the reliability of the data. The following additional actions were taken and deemed necessary to ensure the reliability of the data (21 CFR 54.5(c)). FDA requested Pulsar Vascular, Inc. to submit further analyses of the clinical data stratified by investigators who had financial interests compared to those who did not, and to evaluate the effect of the investigator's data on the overall study outcome. In addition, audits of the data derived from selected clinical investigators in question with financial conflicts and Pulsar Vascular, Inc. was conducted by the FDA Bioresearch Monitoring Program (BIMO) to ensure the validity and reliability of the study data. No significant findings were observed based on the additional FDA actions.

XII. RISK PROBABLE BENEFIT ANALYSIS

A. Probable Benefit Conclusions

Immediately following the procedure with the PulseRider, aneurysm occlusion assessed as Raymond I or II were obtained in the majority of cases (79.4% or n/N = 27/34). This result demonstrates that the majority of treated patients achieved 100% occlusion or near complete occlusion of their unruptured wide-neck intracranial aneurysm originating near or at a vessel bifurcation of the basilar tip or carotid terminus immediately post-procedure. This combined aneurysm occlusion rate of Raymond I or II assessed at 180-days post-procedure increased to 87.9% (n/N = 29/33 patients), which was adjudicated by a blinded core laboratory. In addition, in

34/34 (100%) cases, the treating physicians viewed the procedure as a technical success if they were able to access the target aneurysm, deploy the device accurately, and detach the device successfully. Therefore, the PulseRider Aneurysm Neck Reconstruction Device demonstrated in the ANSWER clinical study that there is probable benefit in successfully stabilizing the intracranial aneurysm using endovascular embolization coiling assisted by the PulseRider to retain the neurovascular embolization coils within the aneurysm sac to achieve 100% or near complete aneurysm occlusion from cerebral blood flow.

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory and animal studies as well as data collected in the ANSWER clinical study conducted to support HDE approval as described above. In Table 12, which reports all of the observed adverse events in the ANSWER clinical study, the most common adverse event was headache (29.4% (n/N = 10/34)) followed by respiratory problems (20.6% (n/N = 7/34)), stroke (14.7% (5/34)), nausea and/or vomiting (11.8% (n/N = 4/34)), hypotension (8.8% (n/N = 3/34)), shortness of breath (8.8% (n/N = 3/34)), and anemia or drop in hemoglobin (8.8% (n/N = 3/34)). The majority of these adverse events can be clinically managed shortly after symptom onset and will not result in long-term clinical sequelae. All of the 5 stroke patients recovered to a favorable clinical outcome of mRS 0-2 at 180 days post-procedure with minimal disabilities except for one patient who was wheelchair bound; that patient had a confounding mass effect. There were no adverse events of neurological death caused by the device and/or procedure and no major debilitating strokes. For all 34 treated patients, there is a low rate of peri-procedural complications (8.8% ongoing neurological events) and a satisfactory outcome (mRS 0 – 2) was achieved in 94.1% of patients (n/N = 32/34) at the 180-day follow-up visit.

C. Probable Benefit-Risk Conclusions

The probable benefits of the device are also based on data collected in a clinical study conducted to support HDE approval as described above. The clinical data of the combined aneurysm occlusion rate of Raymond I or II assessed at 180-days post-procedure was 87.9% (n/N = 29/33 patients), which was adjudicated by a blinded core laboratory. This result demonstrates that the PulseRider is able to successfully assist in retaining neurovascular embolization coils within the aneurysm sac for unruptured, wide-necked, intracranial aneurysms originating on or near a vessel bifurcation of the basilar tip or carotid terminus arteries to achieve 100% or near complete occlusion of the intracranial aneurysm to prevent cerebral blood flow from entering the aneurysm sac for a majority of patients in the clinical study. In addition, the observed adverse events and associated rates of adverse events were similar compared to endovascular treatment of wide-neck intracranial aneurysms using HDE approved neurovascular stents, considering that the subject patient population with bifurcation wide-necked intracranial aneurysms is much more difficult to treat with respect to access to the aneurysm location using endovascular or open surgical techniques, limited treatment options, and etiology of the disease. After treatment with the PulseRider, the majority of patients had a favorable clinical outcome assessed using the mRS of 0-2 (i.e., 94.1% (n/N = 32/34 patients)) at the 180 day follow-up visit, which measures functional independence and disability.

Additional factors to be considered in determining probable risks and benefits for the PulseRider Aneurysm Neck Reconstruction Device included the quality of the clinical study design in that it was a single arm study which limits the ability to draw comparisons to alternative treatments, financial conflicts of interest as some of the investigators in the study had a significant payment from Pulsar Vascular, Inc., the study was not statistically powered for hypothesis testing of the safety and probable benefit endpoints, and the mRS was not conducted by an unblinded assessor at the 180 day follow-up visit that can introduce bias into this measurement. However, the uncertainty introduced by these limitations is considered to be acceptable given the severity of the underlying condition and the ability of this device to address an unmet need. In addition, there were more basilar tip bifurcation aneurysms (n=27) treated in the ANSWER clinical study than carotid terminus bifurcation aneurysms (n=7). Although the two aneurysm locations have different safety and probable benefit profiles, the data was analyzed separately for the two different aneurysm locations and no significant difference in the results were observed. Furthermore, the basilar tip aneurysms can be considered a worst-case treatment with respect to accessing the aneurysm for treatment since it is located in the posterior circulation. The quantity of aneurysms treated in the ANSWER clinical study in the basilar tip and carotid terminus locations are also similar to the prevalence of aneurysms in these regions from an epidemiology perspective (K.M. Fargen et al., *Neurosurgery* 2013).

Considering all of these limitations to the clinical study design and after a thorough review of all of the clinical data including the Case Report Forms (CRFs), the results generally support that the risks of the PulseRider are similar to marketed HDE neurovascular stents and the majority of patients in the study were able to achieve occlusion of their unruptured, wide-necked, intracranial aneurysm originating on or near a vessel bifurcation of the basilar tip and carotid terminus arteries as assessed by Raymond I and II scores. In addition, the PulseRider is specifically designed to be implanted at a vessel bifurcation.

1. Patient Perspectives

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

In conclusion, given the available information above, the data support that for patients ≥ 18 years of age, the PulseRider Aneurysm Reconstruction Device used with neurovascular embolic coils for the treatment of unruptured wide-necked intracranial aneurysms with neck widths ≥ 4 mm or dome to neck ratio < 2 originating on or near a vessel bifurcation of the basilar tip or carotid terminus with at least a portion of the aneurysm neck overlapping the lumen of the parent artery and the inflow vessels should have diameters from 2.7 mm to 4.5 mm, the probable benefits outweigh the probable risks.

D. Overall Conclusions

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

clinical data of the combined aneurysm occlusion rate of Raymond I or II assessed at 180-days post-procedure was 87.9% (n/N = 29/33 patients), which was adjudicated by a blinded core laboratory. This result demonstrates that the PulseRider is able to successfully assist in retaining neurovascular embolization coils within the aneurysm sac for unruptured, wide-necked, intracranial aneurysms originating on or near a vessel bifurcation of the basilar tip or carotid terminus arteries to achieve 100% or near complete occlusion of the intracranial aneurysm to prevent cerebral blood flow from entering the aneurysm sac for a majority of patients in the clinical study. In addition, the observed adverse events and associated rates of adverse events were similar compared to marketed HDE neurovascular stents. After treatment with the PulseRider, the majority of patients had a favorable clinical outcome assessed using the mRS of 0-2 (i.e., 94.1% (n/N = 32/34 patients)) at the 180 day follow-up visit, which measures functional independence and disability.

Therefore, it is reasonable to conclude that the probable benefit to health from using the device for the target population outweighs the risk of illness or injury, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment when used as indicated in accordance with the directions for use.

XIII. PANEL RECOMMENDATION

This HDE was not taken to a meeting of the Neurological Devices Panel of the Medical Devices Advisory Committee because this HDE does not raise unanticipated safety issues compared to marketed HDE approved neurovascular stents. Therefore, it was determined that this application does not require feedback from an advisory panel.

XIV. CDRH DECISION

CDRH has determined that, based on the data submitted in the HDE, the PulseRider Aneurysm Neck Reconstruction Device will not expose patients to an unreasonable or significant risk of illness or injury and the probable benefit to health from using the device outweighs the risks of illness or injury. CDRH issued an approval order on June 19, 2017. The final conditions of approval cited in the approval order are described below.

In addition to the Annual Report requirements, Pulsar Vascular, Inc. must provide the following data in post-approval study (PAS) reports for each PAS listed below every six (6) months until study completion:

ODE Lead HDE Post-Approval Study Report - Adjunctive Neurovascular Support for Wide-Neck Aneurysm Embolization and Reconstruction (ANSWER): The Office of Device Evaluation (ODE) will have the lead for this clinical study, which was initiated prior to device approval. The ANSWER study is a prospective, multi-center, single-arm, non-randomized clinical study conducted under Investigational Device Exemption (IDE) G130268. The ANSWER clinical study is a one (1) year follow-up clinical study evaluating both safety and probable benefit of the PulseRider Aneurysm Reconstruction Device in 34 treated patients with unruptured wide-neck intracranial aneurysms on or near a vessel bifurcation of the basilar tip or carotid terminus. The study endpoints evaluated at 1 year follow-up are neurological death or stroke, technical success, rate of aneurysm occlusion, device movement or migration, stenosis, rate of incidence of new

neurological deficits, and complication rate (neurological and non-neurological).

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 the device labeling.

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

Post-Approval Requirements and Restrictions: See approval order.

XVI. REFERENCES

K.M. Fargen et al. "A Multicenter Study of Stent-Assisted Coiling of Cerebral Aneurysms with a Y configuration." Neurosurgery. 2013; 73: 466-472.

R.L. Sacco et al. "An Updated Definition of Stroke for the 21st Century." Stroke. 2013; 44: 2064-2089.