SUMMARY OF SAFETY AND PROBABLE BENEFIT (SSPB)

I. GENERAL INFORMATION

Device Generic Name: Intracranial Stent

Device Trade Name: Neuroform Atlas™ Stent System

Device Procode: NJE

Applicant's Name and Address: Stryker Neurovascular
47900 Bayside Parkway
Fremont, California 94538

Date(s) of Panel Recommendation: None

Humanitarian Device Exemption (HDE) Number: H020002/S046

Humanitarian Use Device (HUD) Designation Number: HUD # 00-0059

Date of HUD Designation: August 14, 2000

Date of Notice of Approval to Applicant: November 2, 2017

II. INDICATIONS FOR USE

The Neuroform Atlas Stent System is indicated for use with neurovascular embolic coils in patients who are ≥ 18 years of age for the treatment of wide neck, intracranial, saccular aneurysms arising from a parent vessel with a diameter of ≥ 2 mm and ≤ 4.5 mm that are not amenable to treatment with surgical clipping. Wide neck aneurysms are defined as having a neck ≥ 4 mm or a dome-to-neck ratio of < 2.

The indication for use statement has been modified from that granted for the HUD designation. The HUD designation was for use with embolic coils for the "treatment of wide-necked, intracranial saccular aneurysms that are not amenable to treatment with surgical clipping." It was modified for the HDE approval because the device was only investigated for subjects who were ≥ 18 years of age in the clinical study for the Neuroform Atlas Stent System. Therefore, the indication for use statement for the HDE was modified to include the age limit for use of the device. This change in indication does not significantly impact the total number of patients in this population and does not affect the HUD designation.

III. CONTRAINDICATIONS

Patients in whom antiplatelet and/or anticoagulation therapy is contraindicated.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Neuroform Atlas Stent System labeling.

V. DEVICE DESCRIPTION

The Neuroform Atlas Stent System is an intracranial stent intended to be used with neurovascular embolization coils to treat wide-neck intracranial aneurysms. The Neuroform Atlas Stent System consists of:

- An implantable self-expanding stent;
- Stent delivery wire;
- Introducer sheath; and
- Accessory pouch with a torque device.

The Neuroform Atlas Stent System is delivered through a microcatheter. The device is offered in the stent configurations shown in Table 1. The delivery system is available in two tip configurations: with an 8.5 mm distal tip and without a distal tip. All of the devices are compatible with Stryker Neurovascular Excelsior XT-17 and SL-10 Microcatheters.

Table 1. Stent Configurations

Device Diameter	**Device Length**			
	15 mm	**21 mm**	**24 mm**	**30 mm**
3.0 mm	X	X	X	X
4.0 mm	X	X	X	X
4.5 mm	X	X	X	X

Description of the Stent:

The Neuroform Atlas Stent is a self-expanding, open cell, nitinol stent with flared proximal and distal ends. The stent ring is comprised of zig-zag-shaped stent struts joined by interconnects. There are six radiopaque marker bands on the stent, three on each end. The stent is pre-loaded on the stent delivery wire and is constrained by the introducer sheath until transferred into the microcatheter.

Description of the Delivery System:

The Neuroform Atlas Stent Delivery System consists of the stent delivery wire and introducer sheath. The stent delivery wire is similar in construction to a guidewire. The delivery wire is a stainless steel wire with an overall length of 185 cm. The delivery wire has a radiopaque distal tip marker and a fluoro-saver marker on the proximal end. The delivery system is available in two configurations: with a distal tip (8.5 mm) and without a distal tip on the delivery wire. The introducer sheath consists of a clear thin-walled polymer shaft and a distal tapered tip. It has an overall length of 49 cm and inner diameter of 0.0165 inches.

Description of the Accessory Pouch:

An accessory pouch containing an optional torque device is also included. The physician may attach the torque device to the proximal end of the stent delivery wire to facilitate

handling and stabilization.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Conventional procedures used in the treatment of wide neck, intracranial, saccular aneurysms arising from a parent vessel with a diameter of ≥ 2 mm and ≤ 4.5 mm that are not amenable to treatment with surgical clipping include endovascular treatment with balloon-assisted neurovascular embolization coiling, which is a balloon-assisted technique using a balloon catheter to aid in retaining the coils within the aneurysm sac during the procedure. However, intracranial aneurysms with wide necks often cannot structurally retain the embolization coils and protrusion of the coils into the parent artery may occur.

Additional alternative treatment of wide-neck intracranial aneurysms include use with other neurovascular stents approved through the Humanitarian Device Exemption (HDE) regulatory pathway (i.e., Stryker Neuroform EZ and 3 Stent Systems (H020002), Codman & Shurtleff Enterprise Vascular Reconstruction Device and Delivery System (H060001), MicroVention Low-Profile Visualized Intraluminal Support Device (LVIS) (H130005), Pulsar Vascular PulseRider Aneurysm Neck Reconstruction Device (H160002)) that are deployed across the neck of the aneurysm to aid in retaining neurovascular embolization coils in the aneurysm sac.

There is also the availability of neurovascular flow diverters to treat large and giant wide-neck intracranial aneurysms in the internal carotid artery from the petrous to the superior hypophyseal segments using an endovascular technique (i.e., Medtronic Pipeline Embolization Device (P100018)).

VII. MARKETING HISTORY

The Neuroform Atlas Stent System is available in the following countries: Argentina, Australia, Austria, Bahrain, Belgium, Bulgaria, Canary Islands, Chile, Colombia, Costa Rica, Croatia, Cyprus, Czech Republic, Denmark, Dominican Republic, Egypt, Ecuador, Estonia, Finland, France, Germany, Georgia, Great Britain (UK), Greece, Honduras, Hong Kong, Hungary, Iceland, India, Iran, Ireland, Israel, Italy, Jamaica, Japan, Jordan, Kuwait, Latvia, Lithuania, Malta, Malaysia, Mexico, Netherlands, New Zealand, Norway, Oman, Peru, Philippines, Poland, Portugal, Qatar, Romania, Russia, Saudi Arabia, Serbia, Singapore, Slovakia, Slovenia, South Africa, Spain, Sweden, Switzerland, Taiwan, Thailand, Tunisia, Turkey, and United Arab Emirates.

The Neuroform Atlas Stent System 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. Allergic reaction to nitinol metal, medications, and contrast media
2. Aneurysm perforation or rupture
3. Coil herniation through stent into parent vessel

4. Death
5. Embolus
6. Intracranial or intracerebral hemorrhage
7. In-stent stenosis
8. Infection
9. Ischemia
10. Neurological deficit/intracranial sequelae
11. Pseudoaneurysm
12. Stent fracture
13. Headache
14. Stent migration/embolization
15. Stent misplacement
16. Stent thrombosis
17. Stroke
18. Transient ischemic attack (TIA)
19. Vasospasm
20. Vessel occlusion or closure
21. Vessel perforation/rupture, dissection, trauma, or damage
22. Vessel thrombosis
23. Visual impairment
24. Hypotension and hypertension
25. Hydrocephalus
26. Increase in intracranial pressure (ICP)
27. Coagulopathy
28. Access site complications such as hemorrhage, hematoma, pain, or infection
29. Deep vein thrombosis (DVT)
30. Hypoesthesia
31. Fever
32. Phlebitis
33. Nausea and/or vomiting
34. Dizziness
35. Ecchymosis

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 Neuroform Atlas Stent System and its materials of construction, the biocompatibility of the materials, shelf-life stability, and sterilization validation.

Design Verification and Validation Testing:

The finished and sterile Neuroform Atlas Stent System was evaluated for design verification and validation in accordance to the FDA guidances titled "Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems" and

"Select Updates for Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems." In addition, the design verification and validation testing plan utilized the standards EN ISO 25539-2:2012 "Cardiovascular Implants – Endovascular Devices – Part 2: Vascular Stents, ISO 11070:2014 "Sterile, Single-Use Intravascular Catheter Introducers," and EN ISO 10555-1:2013 "Intravascular Catheters – Sterile and Single-Use Catheters – Part 1: General Requirements" for guidance. Table 2 summarizes the design verification and validation testing performed on the Neuroform Atlas Stent System. The results demonstrate that all pre-specified acceptance criteria were met.

Table 2. Design Verification and Validation Testing of the Neuroform Atlas Stent System

Tests	Test Description	Results
Stent Dimensional and Functional Attributes		
Corrosion Resistance	The implant shall not exhibit excessive pitting and crevice corrosion after simulated in vivo conditions (10 years).	Pass
Dimensional Verification	The implant shall be suitable for implantation in cerebrovascular vessels of 2.0 mm to 4.5 mm diameter and provide a working length from 15 mm to 30 mm.	Pass
Percent Surface Area	For each stent model, the free surface area in the smallest recommended vessel diameter must be > 75%.	Pass
Foreshortening	The change in stent length from when it is loaded in the recommended 0.0165" to 0.017" microcatheter prior to deployment to post deployment in the largest recommended vessel size for that stent must be less than 20%.	Pass
Stent Integrity	The implant should be free from visual defects, such as broken struts, pits, dents, and bumps, after deployment in the unconstrained state.	Pass
Radial Outward Force	The implant radial force shall be sufficient to provide stent fixation without causing vessel injury	Pass
Stress/Strain Analysis	Worst-case laid conditions show to be less than yield strength of stent materials.	Pass
Fatigue Analysis	Fatigue stress amplitude shown to be less than endurance limit of stent	Pass

Tests	Test Description	Results
	materials.	
Accelerated Durability Testing	The device shall be suitable for implantation in cerebrovascular arteries without mechanical compromise as a result of being subjected to simulated 10 years of expected pulsatile flow and physiological stress loading.	Pass
Particulate Evaluation	Particulates shall be acceptable following simulated delivery and device deployment.	Pass
Magnetic Resonance Imaging (MRI) Safety and Compatibility	Stent shall be MRI conditional for 1.5T and 3T MRI equipment immediately after implantation.	Pass
Radiopacity	Stent shall provide sufficient radiopacity with equally spaced radiopaque markers on each end of the stent for proper stent placement and secondary treatment.	Pass
Kink Resistance	Implant shall conform to the indicated vessel size with a bend radius of 6.5 mm (centerline) without kinking.	Pass
Delivery System Dimensional and Functional Testing		
Dimensional Verification	The stent delivery system, when used with the recommended 0.0165" to 0.017" microcatheter shall reach the intended cerebrovascular anatomical location. It will deliver and deploy implants into vessel diameters of 2.0 mm to 4.5 mm with a working length between 15 mm to 30 mm.	Pass
Delivery, Deployment, and Retraction	The delivery system must be able to safely: • deliver the implant to the intended location, • deploy the stent accurately • withdrawn from the anatomy post deployment	Pass
Catheter Bond Strength	The stent delivery system must be able to deliver and deploy the implant to the intended location without damage and be able to be withdrawn safely without damage.	Pass
Tip Pull Test		Pass
Flexibility and Kink Test		Pass

Tests	Test Description	Results
Corrosion Resistance	The delivery wire shall show no visible signs of corrosion after testing.	Pass

Biocompatibility:

Biocompatibility testing was conducted on the Neuroform Atlas Stent System and on the previous generation Neuroform Stents in accordance with the provisions in EN ISO 10993-1 and Good Laboratory Practices (GLP) regulations specified in 21 CFR 58. Tables 3 and 4 summarize all of the biocompatibility testing performed on the Neuroform Atlas Stent System. The results demonstrate that the Neuroform Atlas Stent System is biocompatible.

Table 3. Biocompatibility Testing of Neuroform Atlas™ Stent

Test Performed	Test Description	Results
Cytotoxicity	Minimum Essential Medium (MEM) Elution Test	Pass. No cytotoxicity or cell lysis, Score: 0
Sensitization	Guinea Pig Maximization	Pass. No evidence of sensitization
Irritation	Intracutaneous Study in Rabbits	Pass. Difference between Test – Control is 0.0 for 0.9% sodium chloride (SC) and 0.0 for sesame oil (SO)
Systemic Toxicity	Systemic Toxicity Study in Mice	Pass. No mortality or evidence of systemic toxicity
	Rabbit Pyrogen Study – Material Mediated	Pass. Nonpyrogenic, max rise: 0.2°C
Systemic Toxicity & Intramuscular Implantation	Implant/Chronic Toxicity 13 Week Systemic Toxicity	Pass. No evidence of systemic toxicity. Test article was classified as a nonirritant. Local macroscopic tissue reaction was not significant as compared to the control article.
Implantation	Muscle Implantation Study in Rabbits (2 & 6 weeks)	Pass. Microscopic reaction was not significant as compared to the negative control article. Test article was classified as a nonirritant as compared to the negative control article.
Genotoxicity	Mouse Peripheral Blood Micronucleus Study	Pass. Test article did not induce micronuclei in mice and is considered non-mutagenic.
	Ames Assay	Pass. Non genotoxic.
	Mouse Lymphoma	Pass. Non genotoxic.

Test Performed	Test Description	Results
Hemocompatibility	Hemolysis Direct Contact & Extract Method	Pass. Test article is considered non-hemolytic.
	Complement Activation Assay	Pass. The test article did not induce complement activation.
	In Vitro Hemocompatibility Assay	Pass. Results comparable to Negative Control White Blood Cell (WBC): 124%, Red Blood Cell (RBC): 100%, Hemoglobin: 100%, Hematocrit: 99%, Platelets 125%
	Partial Thromboplastin Time (PTT)	Pass. Test article average clotting time: 243.0 sec, 81% of negative control, minimal activator.
	Complement Activation	Pass. The test article did not induce complement activation.
	Preclinical Study Report (GLP Canine Study)	Pass. Results were consistent with a positive safety profile. In addition, there was no evidence of thrombus formation at 30 days or at 180 days.

Table 4. Biocompatibility Testing of Neuroform Atlas™ Stent Delivery System

Test Performed	Test Description	Result
Cytotoxicity	MEM Elution	Pass. No toxicity or cell lysis. Grade 0
Sensitization	Guinea Pig Maximization	Pass. Sensitization rate: 0
Irritation	Intracutaneous Study in Rabbits	Pass. Difference between Test – Control is 0.0 for SC and 0.2 for SO
Systemic Toxicity	Systemic Toxicity Study in Mice	Pass. No mortality or evidence of systemic toxicity.
	Rabbit Pyrogen Study - Materials Mediated	Pass. Nonpyrogenic, max rise: 0.1°C.
Hemocompatibility	Hemolysis – Rabbit Blood	Pass. Hemolytic index: 1.2% (direct contact) and 0.1% (extract)
	SC5b-9 and C3a Complement Activation	Pass. The test article did not induce complement activation.

Shelf-Life Testing:

The Neuroform Atlas Stent System was accelerated aged equivalent to 5 years, and then tested for package integrity, sterility, and physical device specification and performance

testing. The results support a 5 year expiration date for the Neuroform Atlas Stent System.

Sterilization Validation:

The Neuroform Atlas Stent System is sterilized using ethylene oxide (EO). The EO cycle was validated to a sterility assurance level of 10^{-6} per EN ISO 11135-1 *Sterilization of Health Care Products – Ethylene Oxide – Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices*. The Neuroform Atlas Stent System was tested and met specifications after 1x and 2x sterilization exposures. In addition, the entire Neuroform Atlas Stent System was tested for bacterial endotoxins per AAMI/ANSI ST72:2011(R)2016 *Bacterial Endotoxins – Test Methods, Routine Monitoring, and Alternatives to Batch Testing* and the FDA Guidance for Industry "Pyrogen and Endotoxins Testing: Questions and Answers" (issued June 2012), and met the specified endotoxin specification of < 0.06 endotoxin units (EU)/mL or < 2.15 EU/device for devices with potential contact with cerebrospinal fluid (CSF).

B. Animal Studies

Objectives. The objectives of the GLP animal study were to assess the safety and vascular compatibility of the Neuroform Atlas Stent System when used as intended at approximately 30, 90, and 180 days post-implantation in elastase-induced aneurysms in laprine carotid arteries of New Zealand white rabbits.

The Neuroform Atlas Stent System (test) and the Neuroform EZ Stent System (control) were implanted in 41 New Zealand white rabbits. Animals were sacrificed for analysis at 30 days (10 test and 3 control animals), 90 days (10 test and 5 control animals), and 180 days (10 test and 3 control animals) post-implantation. Excised vessel and organ samples were submitted for gross, histopathology, and morphometric analyses. The findings showed at implant and during in-life there were no deaths related to the Neuroform Atlas Stent System. Vessel stenosis remained below 50% via morphometric analysis for both test and control device treated vessels. Acceptable healing response via histopathology evaluation was observed for Neuroform Atlas Stent System treated vessels. The Neuroform Atlas Stent System also showed no or minimal inflammatory response, which demonstrates local biocompatibility of the implant. At 30, 90, and 180 days, there was absence of clinically relevant stenosis and thrombosis (full patency); near complete or complete endothelialization; and optimal formation of a generally mature and stable neointima with no residual fibrin. Histologically, there were no adverse changes in the test device treated vessels at any time point evaluated. Acute safety during and immediately following implantation of the Neuroform Atlas Stent System showed no vessel spasm, no vessel perforations, and no thrombosis. In conclusion, safety and vascular compatibility of the Neuroform Atlas Stent System was demonstrated at all time points up to 180 days post-implantation.

C. Additional Studies

Magnetic Resonance Imaging (MRI) Compatibility:

The Neuroform Atlas Stent System was evaluated when used as intended 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 Neuroform Atlas Stent can be safely scanned under the following conditions:

- Static magnetic field of 1.5 and 3.0 Tesla (T)
- Maximum spatial gradient field up to 2500 Gauss/cm (25 T/m)
- Maximum MR system reported whole body averaged specific absorption rate of 2 W/kg (Normal Operating Mode) and head averaged specific absorption rate of 3.2 W/kg.

Under the scan conditions defined above, the Neuroform Atlas Stent is expected to produce a maximum temperature rise of 4 °C after 15 minutes of continuous scanning. The Neuroform Atlas Stent should not migrate in this MRI environment. In non-clinical testing, the image artifact caused by the device extends approximately 2 mm from the Neuroform Atlas Stent when imaged with a spin echo pulse sequence and 3 T MRI. The artifact may obscure the device lumen. It may be necessary to optimize MRI parameters for the presence of the device.

X. SUMMARY OF CLINICAL INFORMATION

Study Design:

The clinical data used to demonstrate the safety and probable benefit of the Neuroform Atlas Stent System was obtained for the first 30 subjects enrolled in the pivotal, prospective, multi-center, single-arm, non-randomized "Safety and Effectiveness of the Treatment of Wide Neck, Saccular Intracranial Aneurysms with the Neuroform Atlas Stent System (ATLAS)" clinical trial conducted under Investigational Device Exemption (IDE) G150006. These 30 subjects were enrolled and treated at 8 sites in the United States (U.S.). The subjects in the ATLAS study were evaluated at screening, treatment, hospital discharge, and followed at 2, 6, and 12 months post-procedure.

The primary safety of the Neuroform Atlas Stent System was based on the occurrence of major ipsilateral stroke or neurological death within 12 months post-procedure. A major ipsilateral stroke is defined as an ipsilateral stroke that is associated with an increase of ≥ 4 points on the NIHSS at 24 hours after symptom onset. An ipsilateral stroke is defined as an acute episode of focal or global neurological dysfunction due to brain or retinal infarction, or due to an intracranial hemorrhage inclusive of subarachnoid, intraventricular or intraparenchymal hemorrhage, occurring in the same hemisphere as the target aneurysm.

The primary probable benefit of the device was based on complete aneurysm occlusion (Raymond I) in the absence of re-treatment and significant parent artery stenosis (> 50%) at the target location at 12 months post-procedure assessed using digital subtraction angiography (DSA). Additional secondary endpoints to support the safety and probable benefit of the Neuroform Atlas Stent System include assessing the National Institutes of Health Stroke Scale (NIHSS), modified Rankin Scale (mRS), device-related serious adverse events (SAEs), rates of subarachnoid hemorrhage and aneurysm rupture, and procedural technical success and rates of coil prolapse into the parent artery.

Clinical Study Enrollment Criteria:

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

Inclusion Criteria:

1. Subject is between 18 and 80 years of age.
2. Documented wide neck (neck ≥ 4 mm or a dome-to-neck ratio of < 2) intracranial, saccular aneurysm arising from a parent vessel with a diameter of ≥ 2 mm and ≤ 4.5 mm, which will be treated with bare metal coils.
3. Subject or legal representative is willing and able to provide informed consent.
4. Subject is willing and able to comply with protocol follow-up requirements.

Exclusion Criteria:

1. Known multiple untreated cerebral aneurysms, other than non-target blister aneurysm, infundibulum, or aneurysm measuring < 3 mm for each of three dimensions assessed (height, width, and depth) that will not require treatment during the study period.
2. Target lesion is a blister aneurysm, infundibulum, or aneurysm measuring < 3 mm for each of three dimensions assessed (height, width, and depth).
3. Target aneurysm that will require an Investigator to intentionally leave a neck remnant in order to preserve blood flow in a bifurcation or branch.
4. Coiling or stenting of a non-target intracranial aneurysm within 30 days prior to study treatment.
5. Target aneurysm is in the anterior circulation proximal to the superior hypophyseal internal carotid artery (ICA).
6. Acute target aneurysm rupture less than 14 days prior to study treatment.
7. Hunt and Hess score ≥ 3 or a pre-morbid mRS score ≥ 4.
8. An admission platelet count of < 50,000, any known coagulopathy, or an International Normalized Ratio (INR) > 3.0 without oral anticoagulation therapy.
9. A known absolute contraindication to angiography.
10. Evidence of active cancer, terminal illness or any condition which, in the opinion of the treating physician, would/could prevent subject from completing the study (e.g., a high risk of embolic stroke, atrial fibrillation, co-morbidities, psychiatric disorders, substance abuse, major surgery ≤ 30 days pre-procedure, etc.).
11. Known absolute contraindication to the use of required study medications or agents (e.g., heparin, aspirin, clopidogrel, and radiographic contrast agents, etc.).
12. Female subject who is pregnant or intends to become pregnant during the study.
13. Moya-Moya disease, arteriovenous malformation(s), arteriovenous fistula(e), intracranial tumor(s), or intracranial hematoma(s) (unrelated to target aneurysm).
14. Significant atherosclerotic stenosis, significant vessel tortuosity, vasospasm refractory to medication, unfavorable aneurysm morphology or vessel anatomy, or some other condition(s) that, in the opinion of the treating physician, would/could prevent or interfere with access to the target aneurysm and/or successful deployment of the Neuroform Atlas Stent.
15. Previous treatment (e.g., surgery, stenting) in the parent artery that, in the opinion of the treating physician, would/could prevent or interfere with successful use of the

Neuroform Atlas Stent System and/or successful adjunctive deployment of embolic coils.

16. Previous stent-assisted coiling of the target aneurysm.

Demographic Data:

Tables 5-8 provide the demographic and patient population information for the first 30 subjects treated in the ATLAS clinical study to support the safety and probable benefit of the Neuroform Atlas Stent System for the subject HDE.

Table 5. Baseline Demographics

Subject Characteristic	**Result**
Age (Years)	
Mean ± Standard Deviation (SD) (N)	59.4 ± 11.8 (30)
Median (Q1 - Q3)	58.5 (53.0 - 68.0)
Min - Max	31.0 - 79.0
Height (Centimeters)	
Mean ± SD (N)	164.5 ± 9.7 (30)
Median (Q1 - Q3)	161.1 (157.5 - 167.6)
Min - Max	152.4 - 195.6
Weight (Kilograms)	
Mean ± SD (N)	77.6 ± 19.6 (30)
Median (Q1 - Q3)	73.5 (65.4 - 90.9)
Min - Max	45.6 - 142.0
Body Mass Index (BMI)	
Mean ± SD (N)	28.5 ± 5.4 (30)
Median (Q1 - Q3)	26.7 (25.3 - 31.7)
Min - Max	19.6 - 38.4
Gender	% (n/N)
Female	80.0% (24/30)

Subject Characteristic	Result
Male	20.0% (6/30)
Race	% (n/N)
White	83.3% (25/30)
Black or African American	10.0% (3/30)
Asian	3.3% (1/30)
Native Hawaiian or other Pacific Islander	0.0% (0/30)
American Indian or Alaskan Native	0.0% (0/30)
Other	3.3% (1/30)
Ethnicity	% (n/N)
Not Hispanic or Latino	96.7% (29/30)
Hispanic or Latino	3.3% (1/30)

Table 6. Medical History

Condition	Result [% (n/N)]
Congestive Heart Failure (CHF)	3.3% (1/30)
Coronary Artery Disease (CAD)	16.7% (5/30)
Chronic Obstructive Pulmonary Disorder (COPD)	23.3% (7/30)
Hyperlipidemia/Hypercholesterolemia	56.7% (17/30)
Hypertension	73.3% (22/30)
Atrial Fibrillation (A-Fib)	3.3% (1/30)
Patent Foramen Ovale	0.0% (0/30)
Peripheral Vascular Disease (PVD)	3.3% (1/30)
Diabetes Mellitus	30.0% (9/30)
Current Smoker	30.0% (9/30)

Past Smoker	43.3% (13/30)
Current Use of Illicit Drugs	0.0% (0/30)
Past Use of Illicit Drugs	0.0% (0/30)
Previous Transient Ischemic Attack (TIA)	13.3% (4/30)
Previous Ischemic Stroke	13.3% (4/30)
Previous Hemorrhagic Stroke	10.0% (3/30)
Previously Ruptured Target Aneurysm	6.7% (2/30)
History of Multiple Aneurysms	16.7% (5/30)
Other Significant Medical History*	80.0% (24/30)

**Other significant medical history included 114 reports of other findings in 24 subjects. The most frequently reported findings were headaches/migraines (n=14), dizziness (n=7), neck/back pain (n=5), seizures (n=4), and gastroesophageal reflux disease (n=4). All other significant medical history findings were reported to occur in 3 or fewer subjects.*

Table 72. Target Aneurysm Location

Location	Target Aneurysms in Anterior Circulation (N=24) [% (n/N)]	Target Aneurysms in Posterior Circulation (N=6) [% (n/N)]
Anterior Cerebral Artery	0.0% (0/24)	N/A
Anterior Communicating Artery	54.2% (13/24)	N/A
Middle Cerebral Artery Bifurcation	12.5% (3/24)	N/A
Middle Cerebral Artery-M1	0.0% (0/24)	N/A
Middle Cerebral Artery-M2	0.0% (0/24)	N/A
ICA – Ophthalmic	8.3% (2/24)	N/A
ICA – Anterior Choroidal Artery	0.0% (0/24)	N/A
ICA – Posterior Communicating Artery	4.2% (1/24)	N/A

ICA Bifurcation/Terminus	4.2% (1/24)	N/A
Supraclinoid Carotid Artery	12.5% (3/24)	N/A
Superior Hypophyseal	4.2% (1/24)	N/A
Basilar Apex	N/A	50.0% (3/6)
Basilar Trunk	N/A	16.7% (1/6)
Superior Cerebellar Artery	N/A	16.7% (1/6)
Anterior Inferior Cerebellar Artery	N/A	0.0% (0/6)
Posterior Inferior Cerebellar Artery	N/A	0.0% (0/6)
Vertebral Artery	N/A	0.0% (0/6)
Vertebrobasilar Junction	N/A	16.7% (1/6)
Other	0.0% (0/24)	0.0% (0/6)

Table 8. Aneurysm and Parent Artery Dimensions

	Result **N= 30 Subjects/30 Aneurysms**
Aneurysm Circulation	
Anterior circulation [% (n/N)]	80.0% (24/30)
Posterior circulation [% (n/N)]	20.0% (6/30)
Aneurysm Measurements	
Aneurysm neck width (mm)	
Mean ± SD (N)	3.9 ± 1.1 (30)
Min - Max	1.6 - 7.0
Aneurysm size (mm)[1]	
Mean ± SD (N)	5.3 ± 1.7 (30)
Min - Max	2.5 - 9.0
Dome/Neck Ratio	
Mean ± SD (N)	1.1 ± 0.2 (28)

	Result **N= 30 Subjects/30 Aneurysms**
Min - Max	0.6 - 1.5
Parent vessel diameter proximal to the aneurysm neck (mm)	
Mean ± SD (N)	2.9 ± 0.6 (30)
Min - Max	2.0 - 4.4
Parent vessel diameter distal to the aneurysm neck (mm)	
Mean ± SD (N)	2.6 ± 0.6 (30)
Min - Max	2.0 - 4.5
Parent vessel stenosis pre-implant	
Yes [% (n/N)]	0.0% (0/30)

[1] Aneurysm size calculated as a max of 3 dimensions (anterior posterior (AP) plane, lateral plane, height)

Clinical Data Analysis and Results:

The 30 subject cohort is sized to provide a characterization of the adverse event (AE) profile associated with the Neuroform Atlas Stent System 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 or pre-specified. A total of 30 subjects were implanted with the device, providing a sample size to allow for the calculation of unadjusted confidence limits for the probable benefit endpoint and assessment of the safety profile of the Neuroform Atlas Stent System. All 30 subjects were treated with the Neuroform Atlas Stent System and all were followed for 6 months, and 27/30 subjects (90%) returned for the 12 month follow-up visit. The clinical data was reviewed for safety by a Data Safety Monitoring Board (DSMB) and adjudicated by the Clinical Events Committee (CEC) for the safety and probable benefit endpoints and causality.

Table 9 presents the primary safety endpoint through 12 months follow-up for the first 30 subjects from the ATLAS clinical study used to support the HDE. There were no unanticipated adverse events (AEs) during the study. There was one subject with suspected confusion as a "manifestation of contrast induced encephalopathy," right-sided weakness, aphasia, and evidence of a small stroke on MRI exam with no residual symptoms at the time of discharge that was site-reported as related to the procedure and not to the device. NIHSS was not performed on this subject and therefore, the CEC took a

conservative approach and adjudicated the event as a major stroke that was both device- and procedure-related. There were no neurological deaths in the 30 subjects. There were two minor strokes adjudicated by the CEC (2/30 or 6.7%). One subject experienced an intra-procedural target aneurysm rupture attributed to coil packing and a minor stroke that was determined by the CEC and the study site to be related to the procedure and not related to the device. One subject with a minor stroke developed new onset aphasia 12 hours after the procedure, which resolved within 24 hours and was site determined to be unrelated to both the device and the procedure, and later CEC-adjudicated as related to both the device and the procedure.

Table 9. Primary Safety Endpoint at 12 months Follow-up

Endpoint	**% Subjects (n/N)**	**95% Conf. Interval**[1]
Any major ipsilateral stroke or neurologic death[2]	3.3% (1/30)	[0.1% - 17.2%]
Major ipsilateral stroke[2]	3.3% (1/30)	[0.1% - 17.2%]
Neurologic death	0.0% (0/30)	[0.0% - 11.6%]

[1] Clopper-Pearson Exact Confidence Interval

[2] One reported stroke with minor neurological symptoms of aphasia and right sided weakness lasted < 48 hours and was designated as a major stroke as an NIHSS was not performed.

As shown in Table 10, 30 procedure/device-related AEs occurred in 12 subjects (12/30 or 40.0%). The most frequently site reported procedure-related AEs were categorized as nervous system disorders (N=20) and, of these, 19/20 were non-serious and 1/20 was serious due to intra-procedural target aneurysm rupture attributed to coil packing. Of the 19 non-serious AEs included, there were 11 reports of headaches in 10 subjects (10/30 or 33.3%), one report of migraine with aura (1/30 or 3.3%), one report of ophthalmoplegic migraine (1/30 or 3.3%), and one report of mental confusion (1/30 or 3.3%) that was deemed by the site to be related to the contrast media used in the procedure. The second most commonly reported procedure-related AEs in nervous system disorders were 6 cerebral vasoconstriction events occurring in 5 subjects (5/30 or 16.7%). Three subjects (3/30 or 10.0%) experienced 4 access site-related AEs (application site hematoma (2) and catheter site hemorrhage (2)) categorized as general disorders and administration site conditions. In addition, two subjects (2/30 or 6.7%) experienced eye disorders (diplopia, visual impairment), one subject (1/30 or 3.3%) experienced procedural complication (arterial restenosis), and one subject (1/30 or 3.3%) experienced two respiratory disorders (cough, laryngitis). All events listed in Table 10**Table** were classified by the site as having a Related, Probable, or Possible relationship to the study procedure.

Table 10. Site Reported Procedure /Device Related AEs by Medical Dictionary for Regulatory Activities (MedDRA) Codes

	Serious AE		**Non-Serious AE**		**All AEs**	
MedDRA System Organ Class/Preferred Term	**Events Related to Procedure/ Atlas Device**	**Subjects with Events [n (% Based on N=30)]**	**Events Related to Procedure/ Atlas Device**	**Subjects with Events [n (% Based on N=30)]**	**Events Related to Procedure/ Atlas Device**	**Subjects with Events [n (% Based on N=30)]**
Any AE	1	1 (3.3%)	29	11 (36.7%)	30	12 (40.0%)
Eye disorders	0	0	2	2 (6.7%)	2	2 (6.7%)
Diplopia	0	0	1	1 (3.3%)	1	1 (3.3%)
Visual impairment	0	0	1	1 (3.3%)	1	1 (3.3%)

	Serious AE		Non-Serious AE		All AEs	
MedDRA System Organ Class/Preferred Term	**Events Related to Procedure/ Atlas Device**	**Subjects with Events [n (% Based on N=30)]**	**Events Related to Procedure/ Atlas Device**	**Subjects with Events [n (% Based on N=30)]**	**Events Related to Procedure/ Atlas Device**	**Subjects with Events [n (% Based on N=30)]**
General disorders and administration site conditions	0	0	4	3 (10.0%)	4	3 (10.0%)
Application site hematoma	0	0	2	2 (6.7%)	2	2 (6.7%)
Catheter site hemorrhage	0	0	2	2 (6.7%)	2	2 (6.7%)
Injury, poisoning and procedural complications	0	0	1	1 (3.3%)	1	1 (3.3%)
Arterial restenosis	0	0	1	1 (3.3%)	1	1 (3.3%)
Nervous system disorders	1	1 (3.3%)	20	11 (36.7%)	21	12 (40.0%)
Cerebral vasoconstriction	0	0	6	5 (16.7%)	6	5 (16.7%)
Confusional state	0	0	1	1 (3.3%)	1	1 (3.3%)
Headache	0	0	11	10 (33.3%)	11	10 (33.3%)
Migraine with aura	0	0	1	1 (3.3%)	1	1 (3.3%)
Ophthalmoplegic migraine	0	0	1	1 (3.3%)	1	1 (3.3%)
Ruptured cerebral aneurysm	1	1 (3.3%)	0	0	1	1 (3.3%)
Respiratory, thoracic and mediastinal disorders	0	0	2	1 (3.3%)	2	1 (3.3%)
Cough	0	0	1	1 (3.3%)	1	1 (3.3%)
Laryngitis	0	0	1	1 (3.3%)	1	1 (3.3%)

The primary probable benefit endpoint was defined by the rate of aneurysm angiographic occlusion of 100% (Raymond Class I) in the absence of re-treatment or significant parent artery stenosis (> 50%) at 12 months as adjudicated by an independent Core Laboratory. DSA images were collected on 27 of the 30 treated subjects at the 12-month follow-up visit. For the three subjects who did not have evaluable 12-month DSA data, the last observation was carried forward (LOCF) (see Table 11). Based on the Core Laboratory imaging assessment, there was 100% occlusion and no evidence of significant parent artery stenosis (i.e., narrowing > 50%) or re-treatment in 83.3% of the treated subjects (25/30) at 12 months.

Table 11. Core Laboratory Imaging Results Imputed by LOCF

Raymond Class	**Immediately Post-Procedure % (n/N)**	**6 Months % (n/N)**	**12 Months % (n/N)[1]**
Complete (100% Occlusion)	60.0% (18/30) [40.6%,77.3%]	81.3% (13/16) [54.4%, 96.0%]	86.7% (26/30) [69.3%, 96.2%]
With Stenosis ≤ 50%	60.0% (18/30) [40.6%, 77.3%]	81.3% (13/16) [54.4%, 96.0%]	83.3% (25/30) [65.3%, 94.4%]
With Stenosis > 50%	0.0% (0/30) [0.0%, 11.6%]	0.0% (0/16) [0.0%, 20.6%]	3.3% (1/30) [0.1%, 17.2%]

Residual Neck	26.7% (8/30) [12.3%, 45.9%]	12.5% (2/16) [1.6%, 38.3%]	0.0% (0/30) [0.0%, 11.6%]
Residual Aneurysm	10.0% (3/30) [2.1%, 26.5%]	0% (0/16) [0.0%, 20.6%]	10.0% (3/30) [2.1%, 26.5%]
Not assessable[2]	3.3% (1/30) [0.1%, 17.2%]	6.3% (1/16) [0.2%, 30.2%]	3.3% (1/30) [0.1%, 17.2%]
Parent Artery Stenosis w/LOCF for 12 Months Follow-Up			
0-25%	100.0% (30/30) [88.4%, 100%]	87.5% (14/16) [61.7%, 98.4%]	93.3% (28/30) [77.9%, 99.2%]
26-50%	0.0% (0/30) [0.0%, 11.6%]	12.5% (2/16) [1.6%, 38.3%]	3.3% (1/30) [0.1%, 17.2%]
51-70%	0.0% (0/30) [0.0%, 11.6%]	0% (0/16) [0.0%, 20.6%]	0.0% (0/30) [0.0%, 11.6%]
71-99%	0.0% (0/30) [0.0%, 11.6%]	0% (0/16) [0.0%, 20.6%]	3.3% (1/30) [0.1%, 17.2%]
100%	0.0% (0/30) [0.0%, 11.6%]	0% (0/16) [0.0%, 20.6%]	0.0% (0/30) [0.0%, 11.6%]

[1] Three missing subjects in 12 month follow-up were imputed by using LOCF.
[2] Image type or image quality preclude reliable interpretation by Core Laboratory.

Additional secondary endpoints analyzed to support the safety of the Neuroform Atlas Stent System include assessment of the NIHSS scores at baseline and the 12 month follow-up visit. As shown in Table 12, the mean baseline NIHSS score in the 30 subject cohort was 0.2 ± 0.5. At the 12-month follow-up visit, NIHSS scores were obtained on 25 of the 27 subjects who had clinic visits. The mean NIHSS score among these 25 subjects was 0.2 ± 0.4. NIHSS scores were not available at 12 months for 5 subjects due to missed visits (n=3) or missed NIHSS assessments (n=2). The NIHSS stroke scale generally remained unchanged at the 12 month follow-up visit based on the evaluable data.

Table 12. NIHSS Scores from Baseline through 12 Month Follow-Up

NIHSS	**Pre-Implant**	**Two-Month Follow-Up**	**Six-Month Follow-Up**	**Twelve-Month Follow-up**[1]
Mean ± SD (N)	0.2 ± 0.5 (30)	0.1 ± 0.3 (14)	0.1 ± 0.4 (7)	0.2 ± 0.4 (25)
Median (Q1 - Q3)	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)
Min - Max	0.0 - 2.0	0.0 - 1.0	0.0 - 1.0	0.0 - 1.0

[1]At the time of database closure, NIHSS scores were not available for 5 subjects due to missed visits (3) or visits with no NIHSS scores obtained (2).

In addition, mRS assessments were obtained on all 30 subjects at baseline and at the 6 month follow-up visit to further support the safety profile of the Neuroform Atlas Stent System. Per protocol, the mRS assessments were to be conducted by an independent, unblinded assessor and in person at the 6 month and 12 month follow-up visits. The majority of subjects (29/30 or 96.7%) had baseline mRS scores ranging from 0-2. At the 6 month follow-up, the proportion of all 30 subjects with mRS scores of 0-2 remain unchanged compared to the baseline mRS. The mRS data shows that at 6 months post-procedure, only 1 subject exhibited a worsening of the mRS score compared to their baseline mRS. At the 12 month follow-up visit, mRS scores were available for 25 out of the 30 subjects. The majority of these subjects had mRS scores of 0 (23/25; 92%). Two

subjects (2/25; 8%) had a mRS score of 1. The mRS scores from baseline to 12 month follow-up is shown in Table 13.

Table 13. mRS Scores from Baseline through 12 Month Follow-Up

Modified Rankin Scale (mRS) Score	**Pre-Implant [% (n/N)]**	**Post-Implant [% (n/N)]**	**2 Month Follow-Up[1] [% (n/N)]**	**6 Month Follow-Up [% (n/N)]**	**12 Month Follow-Up[2] [% (n/N)]**
0 - No symptoms	70.0% (21/30)	70.0%[3] (21/30)	79.3% (23/29)	76.7% (23/30)	92.0% (23/25)
1 - No significant disability	23.3% (7/30)	23.3% (7/30)	20.7% (6/29)	16.7% (5/30)	8.0% (2/25)
2 - Slight disability	3.3% (1/30)	6.7%[3] (2/30)	0.0% (0/29)	3.3% (1/30)	0.0% (0/25)
3 - Moderate disability	3.3% (1/30)	0.0% (0/30)	0.0% (0/29)	0.0% (0/30)	0.0% (0/25)
4 - Moderately severe disability	0.0% (0/30)	0.0% (0/30)	0.0% (0/29)	3.3% (1/30)	0.0% (0/25)
5 - Severe disability	0.0% (0/30)	0.0% (0/30)	0.0% (0/29)	0.0% (0/30)	0.0% (0/25)
6 - Dead	0.0% (0/30)	0.0% (0/30)	0.0% (0/29)	0.0% (0/30)	0.0% (0/25)
mRS [0-2]	96.7% (29/30)	100.0% (30/30)	100.0% (29/29)	96.7% (29/30)	100.0% (25/25)

[1] One subject (202-002) missed the 2-month follow-up visit. This subject's mRS scores at baseline and the 6-month follow-up were 2 and 1, respectively.
[2] At the time of database closure, mRS scores were not available for 2 of the 27 subjects who completed 12-month visits.
[3] After database closure, one subject with a post-implant mRS score of 0 was queried. Retrospective medical record review revealed that the post-implant mRS score was 2. The data in this table has been changed accordingly.

To further support the probable benefit of the Neuroform Atlas Stent System, the technical success of the device procedure and implantation was assessed as a secondary endpoint. The results demonstrate that technical success of delivering and deploying the Neuroform Atlas Stent to the intended target location was achieved in all 30 subjects (see Table 14).

Table 14. Procedural Technical Success

Procedural Outcomes	**Results [% (n/N)]**
Procedural Technical Success (per subject)[1]	100.0% (30/30)
Number of Subjects with One Stent Successfully Implanted	90.0% (27/30)
Number of Subjects with Two Stents Successfully Implanted	10.0% (3/30)
Neuroform Atlas Stent Implantation Success (per device)	97.1% (33/34)
Neuroform Atlas Stent Implantation Failure (per device)[2]	2.9% (1/34)

[1] Procedural technical success is defined as the proportion of subjects in whom the stent was successfully delivered to, and deployed at, the target location.
[2] One subject had one Neuroform Atlas Stent System removed due to difficult delivery and stent was not deployed; a second stent was delivered and deployed successfully.

Pediatric Extrapolation

In this premarket application, existing clinical data was leveraged to determine that the HUD will not expose pediatric patients to an unreasonable or significant risk of illness or injury and the probable benefit to health from use of the device outweighs the risk of injury or illness from its use while taking into account the probable risks and benefits of currently available devices or alternative forms of treatment of the proposed device in adolescents ≥ 18 years of age. The 30 subjects used to support the HDE ranged from 31-79 years old. This data can be leveraged to support the use of the device in adults ≥ 22 years old and adolescents ≥ 18 years old because the disease, anatomy, and the effects of the device should be sufficiently similar in adults compared to adolescents ≥ 18 years of age.

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 27 investigators and sub-investigators of which none were full-time or part-time employees of the sponsor and 1 investigator had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: 0.
- Significant payment of other sorts: 1 investigator.
- 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.

XII. RISK PROBABLE BENEFIT ANALYSIS

A. Probable Benefit Conclusions

Immediately following implantation of the Neuroform Atlas Stent, complete (100%) aneurysm occlusion was obtained in 18 out of 30 treated subjects (60%) as adjudicated by an independent Core Laboratory using DSA. By 12 months follow-up, 26 out of 30 subjects achieved complete aneurysm occlusion, which means that their aneurysm has no residual neck and has been completely occluded from cerebral blood flow entering the aneurysm sac. At 12 months follow-up, there was 1 subject with significant parent artery stenosis (> 50%), which resulted in a primary probable benefit endpoint of 83.3% (25/30) of subjects who achieved complete occlusion of their target aneurysm without re-treatment and significant parent artery stenosis at 12 months post-procedure. In addition, the procedural technical success demonstrated that 100% (30/30) of subjects had successful delivery, deployment, and placement of the Neuroform Atlas Stent at the target location.

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory and animal studies as well as data collected from the first 30 subjects treated in the ATLAS clinical study conducted to support HDE approval as described above. The primary safety endpoint results demonstrated that there were no neurological deaths and only 1 major ipsilateral stroke (1/30; 3.3%). There were two minor strokes adjudicated by the CEC (2/30 or 6.7%). One subject experienced an intra-procedural target aneurysm rupture attributed to coil packing and a minor stroke that was determined to be related to the procedure and not related to the device. One subject with a minor stroke developed new onset aphasia 12 hours after the procedure, which resolved within 24 hours and was determined to be unrelated to both the device and the procedure. All of AEs observed in the 30 subjects were reported as non-serious and all resolved with no residual effects.

Furthermore, additional clinical assessments of the NIHSS and mRS were analyzed to support the safety profile of the Neuroform Atlas Stent System as secondary endpoints. The average NIHSS scores available at 12 months follow-up did not change compared to the average baseline NIHSS scores. The mRS scores were available for all 30 treated subjects at 6 months follow-up, which showed that the majority of subjects (29/30; 96.7%) had the same mRS or an improved mRS score compared to their baseline mRS prior to treatment, and only 1 subject (1/30; 3.3%) had a worsening mRS at 6 months compared to their baseline mRS. At the 6 month follow-up visit, 96.7% (29/30) of subjects had a good mRS outcome of 0-2.

C. Probable Benefit-Risk Conclusions

The probable benefits of the device are also based on data collected from the first 30 subjects treated in the ATLAS clinical study conducted to support HDE approval as described above. The analysis of the primary probable benefit endpoint showed that 83.3% (25/30) of subjects achieved complete occlusion of their target aneurysm without re-treatment and significant parent artery stenosis at 12 months post-procedure. This result demonstrates that the Neuroform Atlas Stent System is able to successfully assist in retaining neurovascular embolization coils within the aneurysm sac for wide-neck, intracranial, saccular aneurysms arising from a parent vessel with a diameter of ≥ 2 mm and ≤ 4.5 mm that are not amenable to treatment with surgical clipping to achieve 100% occlusion of the intracranial aneurysm to prevent blood flow from entering the aneurysm sac for a majority of treated subjects. In addition, there was a low rate of serious adverse events as defined in the primary safety endpoint of neurological deaths and major ipsilateral stroke (i.e., 3.3%; 1/30). All of the AEs observed in the study resolved within 12 months follow-up. In addition, the mRS score, which assesses functional independence and disability, showed that only 1 subject had a worsening mRS at 6 months follow-up compared to their baseline mRS score as a result of treatment with the Neuroform Atlas Stent System. After treatment with the Neuroform Atlas Stent System, the majority of subjects had a favorable clinical outcome assessed using the mRS score of 0-2 (29/30; 96.7%).

Additional factors to be considered in determining probable risks and benefits for the Neuroform Atlas Stent System included the limitations of the single arm clinical study design, which limits the ability to directly compare the safety and probable benefit of the Neuroform Atlas Stent System to alternative treatments due to different patient selection criteria, clinical test conditions, and aneurysm characteristics. In addition, the first 30 subjects treated in the ATLAS clinical study that was used to support the HDE is not a sufficient sample size to have statistical power for hypothesis testing of the primary safety and probable benefit endpoints, and the results are presented using descriptive statistics only and provide a general conclusion of the safety and probable benefit profile of the Neuroform Atlas Stent System. Furthermore, the mRS assessments were conducted by an unblinded assessor at the 6 month and 12 month follow-up visits, which can introduce bias into this measurement. However, the uncertainty introduced by these limitations is considered to be acceptable based on the observed clinical study results from the 30 subjects. The clinical results achieved with the Neuroform Atlas Stent System demonstrated a similar safety profile when compared to those reported for the Multi-Center European Trial of the Neuroform Microdelivery Stent that was the basis for HDE approval of the first generation Neuroform device (H020002)[1]. Within the context of the adverse event rates reported in the medical literature for HDE approved Neuroform Stents and comparable treatment alternatives, and Neuroform Atlas Stent System outside the U.S. (OUS) clinical experience[2], there is no scientific evidence to demonstrate that patients will be exposed to an unreasonable or significant risk of injury from use of the Neuroform Atlas Stent System as compared to other means of treatments for wide-neck, intracranial, saccular aneurysms. The availability of the Neuroform Atlas Stent System will allow patients with a severe condition to have access to an additional treatment option.

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 who are ≥ 18 years of age, the Neuroform Atlas Stent System used with neurovascular embolization coils for the treatment of wide neck, intracranial, saccular aneurysms arising from a parent vessel with a diameter of ≥ 2 mm and ≤ 4.5 mm that are not amenable to treatment with surgical clipping, and wide neck aneurysms are defined as having a neck ≥ 4 mm or a dome-to-neck ratio of < 2, 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 from the first 30 subjects of the ATLAS clinical study showed that 83.3% (25/30) of subjects achieved complete occlusion of their target aneurysm without re-treatment and significant parent artery stenosis at 12 months post-procedure as adjudicated by an independent Core Laboratory. This result demonstrates that the Neuroform Atlas Stent System is able to successfully assist in retaining neurovascular embolization coils within the aneurysm sac for wide-neck, intracranial, saccular aneurysms arising from a parent vessel with a diameter of ≥ 2 mm and ≤ 4.5 mm that are not amenable to treatment with surgical clipping to achieve 100% occlusion of the intracranial aneurysm to prevent blood flow from entering the aneurysm sac for a majority of treated subjects. In addition, there was a low rate of serious adverse events as defined in the primary safety endpoint of neurological deaths and major ipsilateral stroke (i.e., 3.3%; 1/30). All of the AEs observed in the study resolved within 12 months follow-up. Furthermore, the mRS score, which assesses functional independence and disability, showed that only 1 subject had a worsening mRS at 6 months follow-up compared to their baseline mRS score as a result of treatment with the Neuroform Atlas Stent System. After treatment with the Neuroform Atlas Stent System, the majority of subjects had a favorable clinical outcome assessed using the mRS score of 0-2 (29/30; 96.7%).

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 Neuroform Atlas Stent System 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 November 2, 2017.

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

1. Neuroform Microdelivery Stent System, Summary of Safety and Probable Benefit, H020002.

2. King B, Vaziri S, Singla A, et al. "Clinical and angiographic outcomes after stent-assisted coiling of cerebral aneurysms with Enterprise and Neuroform stents: A comparative analysis of the literature." *J Neurointervent Surg* 2014;0:1-5.