Summary of Safety and Probable Benefit

I. General Information

Device Generic Name:	Intracranial Stent
Device Trade Name:	LVIS (Low profile Visualized Intraluminal Support) and LVIS Jr Device
Applicant Name:	Microvention Inc. 1313 Valencia Avenue Tustin, California 92780 USA
Humanitarian Device Exemption Number:	H130005
Humanitarian Use Device (HUD) Designation Number:	#09-0222
Date of Humanitarian Use Device Designation:	February 19, 2010
Date of Panel Recommendation:	None
Date of Good Manufacturing Practices Inspection:	April 20, 2013
Date of Notice of Approval to Applicant:	July 25, 2014

II. Indications for Use

The LVIS Device is intended for use with bare platinum embolic coils for the treatment of unruptured, wide neck (neck ≥ 4 mm or dome to neck ratio < 2), intracranial, saccular aneurysms arising from a parent vessel with a diameter ≥ 2.5 mm and ≤ 4.5 mm.

III. Contraindications

Use of the LVIS device is contraindicated under these circumstances:

- Patients in whom anticoagulant, anti-platelet therapy or thrombolytic drugs are contraindicated;
- Patients with known hypersensitivity to metal, such as nickel-titanium and metal jewelry; Patients with anatomy that does not permit passage or deployment of the LVIS device;
- Patients with an active bacterial infection; and

- Patients with a pre-existing stent in place at the target aneurysm.

IV. Warnings and Precautions

The Warnings and Precautions can be found in the Instructions for Use labeling for the LVIS device.

V. Device Description

The LVIS device consists of a self-expanding nickel-titanium, single wire braid, compliant closed cell implant that can be deployed and retrieved by a single operator. The LVIS device is packaged sterile as a single unit with a pusher (delivery system) to release the implant and with an introducer sheath.

The device consists of a:
a. self-expanding nickel titanium stent
b. delivery pusher and introduction sheath

The nitinol implant has a tubular woven mesh, closed cell structure, with flared ends. A set of radiopaque wires (tantalum) are woven into the implant in helical configuration. In addition, the implant has up to 4 radiopaque (RO) markers at each end to aid in stent placement under fluoroscopy. Stents range from expanded diameters of 3.5, 4.5, and 5.5 mm and lengths of 15-32 mm.

The delivery system is composed of an introducer and a delivery pusher. The introducer consists of a polymer tube with a tapered distal end. The introducer is used to protect the stent in the package and helps facilitate introduction into the microcatheter hub.

The delivery pusher is composed of a tapered proximal to distal core wire (mandrel). The distal end of the pusher has three radiopaque markers. The two proximal markers are used as part of the delivery mechanism. The distal marker is used to indicate the distal end of the mandrel and the distal end of the implant when it is fully crimped. A stainless steel outer coil is wound on the outside of the tapered portion of the mandrel. The proximal end of the stainless steel outer coil is secured to the proximal end of the tapered portion of the mandrel and the distal end is secured to the most proximal radiopaque marker. The delivery pusher is designed to secure the implant by mechanical means and release the implant at the lesion.

The LVIS devices are deliverable through a 0.021" ID microcatheter whereas the LVIS Jr. devices are deliverable through a 0.017" ID microcatheter. The LVIS and LVIS Jr. devices utilize the same fundamental design and some variations were incorporated to accommodate the smaller profile microcatheter for the LVIS Jr.

VI. Alternative Practices and Procedures

Wide neck aneurysms are difficult to treat both surgically and endovascularly with clipping or coiling. Often aneurysms reside in locations not amenable to surgical clipping and this technique may be difficult or impossible if there is no true neck present. Coiling involves endovascular placement of 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 is sometimes limited to parent artery occlusion, if there is adequate collateral flow or by a balloon-assisted technique. Availability of neurovascular stents through the Humanitarian Device Exemption regulatory provision has provided for an additional approach to aneurysm occlusion using endovascular techniques. Recently, a device, intracranial aneurysm flow diverter, has been made available, but the device is limited to large or giant wide-necked aneurysms in the internal carotid artery from the petrous to the superior hypophyseal segments. If left untreated, aneurysms can rupture, causing death or significant morbidity.

VII. Marketing History

The LVIS device has been marketed in the following countries:

Argentina, Australia, Austria, Baltics Belarus, Belgium, Bulgaria, Canada, Chile, Columbia, Czech, Cyprus, Denmark, Ecuador, El Salvador, Finland, France, Georgia, Germany, Honduras, Hong Kong, Iran, Ireland, Italy, Jordan, Libya, Malaysia, Maroc, Mexico, New Zealand, Peru, Poland, Romania, Russia, Serbia, Singapore, Slovenia, Spain, Sweden Switzerland, Tobago, Turkey, Ukraine, United Kingdom, Uruguay, Venezuela, and Vietnam.

It has not been withdrawn from the market for safety reasons.

VIII. Adverse Effects of the Device on Health

Twenty eight subjects were entered into the clinical study and treated with the LVIS Intraluminal Support Device. A Data Safety Monitoring Board (DSMB) reviewed and adjudicated all adverse events reported during the course of the study. The DSMB adjudicated the events for their relationship to the study device and the index procedure, including adjudication of the events for seriousness.

There were no unanticipated adverse events during the study. No serious adverse events were classified as definitely or probably related to the study device. One event was adjudicated as possibly related to the study device. One event (same event) was classified as probably related to the procedure.

Device or Procedure Related Serious Adverse Event (adjudicated):

Description	Number of occurrences	Number of subjects (%), N = 28	Relationship to Device	Relationship to Procedure	Time of occurrence

Stroke or TIA	1	1 (3.6%)	Possibly	Probably	31 days – 6 months

Non-device or Non-procedure Related Serious Adverse Events (adjudicated):

Description	Number of occurrences	Number of subjects (%), N=28	Time of occurrence
Vasovagal Response	1	1 (3.6%)	1 - 30 days
Anemia	1	1 (3.6%)	31 days - 6 months
Respiratory Distress	1	1 (3.6%)	Procedure
Non-target aneurysm repair	3	2 (7.2%)	1 – 30 days (1) 31 days – 6 months (2)
Non-target aneurysm retreatment	1	1(3.6%)	31 days – 6 months
Target aneurysm retreatment	1	1 (3.6%)	>6 months
Thoracic aneurysm dissection	1	1 (3.6%)	31 days – 6 months

IX. Summary of Preclinical Studies

The LVIS device underwent rigorous mechanical, functionality, biocompatibility, and animal testing to evaluate its suitability for its intended use. The device was tested and determined to have a 3-year shelf life. The device is sterilized via electron beam irradiation with a sterility assurance level that exceeds 10^{-6}. The device was found to be acceptable for use in humans based on preclinical testing results.

The following tables summarize the preclinical tests that performed for the device:

Mechanical Testing

Implant (Stent)
Material Characterization
Shape Memory and Superelasticity
Corrosion Resistance (Potentiodynamic and Galvanic)
Dimensional Verification
Percent Metal Surface Area
Foreshortening
Stent Integrity
Radial Outward Force
Tensile Bond Strength
Stress Analysis (Finite Element Analysis)

Accelerated Durability Testing – Pulsative Fatigue (10 year equivalent)
Particulate Matter Evaluation
Magnetic Resonance Imaging at 3.0 and 1.5 T
Radiopacity

Delivery System
Pusher
Material Characterization
Dimensional Verification
Delivery, Deployment, Retraction
Bond Strength
Flexibility and Kink Test
Introducer
Material characterization
Dimensional Verification

Biocompatibility Testing

Biocompatibility testing for all materials used to manufacture the LVIS Intraluminal Support Device was conducted or justified. The following tests were performed in accordance with ISO 10993-1 and the General Program Memorandum # G95-1 on Biological Evaluation of Medical Devices and in compliance with the applicable requirements of 21 CFR Part 58 (Good Laboratory Practice):

Implant Results:

Test Method	Standard	Results
Cytotoxicity MEM Elution Test – L-929	ISO 10993-5	No biological reactivity was observed in the L929 mammalian cells at 48 hours post exposure to the test article extract.
Sensitization Kligman Maximization Test - ISO	ISO 10993-10	The test extract did not increase the rectal temperature of any of the animals by more than 0.5 degrees Celsius.
Irritation Intracutaneous Injection Test - ISO	ISO 10993-10	The test extract and the negative control must exhibit similar edema and erythema scores.
Hemocompatibility Hemolysis	ISO 10993-4	The UFO HC of the test extract was less than 5% Hemolysis.
Hemocompatibility Prothrombin Time (PT) Assay	ISO 10993-4	The test and control extracts did not vary more than 1 second.
Hemocompatibility Unactivated Partial Thromboplastin Time Assay (UPTT)	ISO 10993-4	The UPTT of the plasma exposed to test article extract did not significantly decreased when compared to untreated and negative controls.

Test Method	Standard	Results
Hemocompatibility Complement Activation Assay (Indirect)	ISO 10993-4	The plasma exposed to test article extract exhibited no significant increase in C3a or SC5b-9 when compared to untreated and negative control after 90 minutes exposure.
Hemocompatibility Complement Activation Assay (Direct)	ISO 10993-4 No deviations	The plasma exposed to test article exhibited no significant increase in C3a or SC5b-9 when compared to untreated and negative control after 90 minutes exposure.
Hemocompatibility Thrombogenicity in Dogs	ISO 10993-4	No significant thrombosis with a grade of 0.
Systemic Toxicity Systemic Injection	ISO 10993-11	The test article did not show significantly greater biological activity than the control.
Systemic Toxicity Rabbit Pyrogen Test (material mediated)	ISO 10993-11	The test article did not increase the rectal temperature of any of the animals by more than 0.5 degrees Celsius.
Genetic Toxicology Salmonella Typhimurium & Escherichia Coli Reverse Mutation Assay (Ames Test)	ISO 10993-3	A statistically significant increase in the number of relevant colonies were not be observed with either of the test article extracts as compared to the negative controls in both non-activated and activated conditions.
Genetic Toxicology Mouse Lymphoma Mutagenesis Assay	ISO 10993-3	No significant increase in the frequency of homozygous mutants in cells exposed to the NaCl or PEG extracts of the test articles compared to the respective controls.
Genetic Toxicology Rodent Bone Marrow Micronucleus Assay (90 Animals)	ISO 10993-3	Test article extracts did not show a statistically significant increase in micronucleated erythrocytes as compared to the negative controls 24 and 48 hours after dosing.
Intramuscular Implantation 7-day Muscle Implantation	ISO 10993-6	The test article did not demonstrate any remarkable difference as compared to the control implants when implanted for 1 week.
Intramuscular Implantation 13 Week Muscle Implantation	ISO 10993-6	The test article did not demonstrate any remarkable difference as compared to the control implants when implanted for 13 week.
Intramuscular Implantation 26 Week Muscle Implantation	ISO 10993-6	The test article did not demonstrate any remarkable difference as compared to the control implants when implanted for 26 week.

Delivery System Results:

Test Method	Standard	Acceptance Criteria
Cytotoxicity L-929 MEM Elution Test – ISO	ISO 10993-5	No biological reactivity was observed in the L929 mammalian cells at 48 hours post exposure to the test article extract.
Sensitization Kligman Maximization Test - ISO	ISO 10993-10	The test extract did not increase the rectal temperature of any of the animals by more than 0.5 degrees Celsius.
Irritation Intracutaneous Injection Test - ISO	ISO 10993-10	The test extract and the negative control exhibited similar edema and erythema scores.
Hemocompatibility Hemolysis – Rabbit Blood	ISO 10993-4	The UFO HC of the test extract was less than 5% Hemolysis.

Test Method	Standard	Acceptance Criteria
Hemocompatibility Thrombogenicity Study in Dogs – ISO (In-Vivo)	ISO 10993-4	No significant thrombosis with a grade of 0.
Hemocompatibility Prothrombin Time Assay – ISO	ISO 10993-4	Within normal range of human plasma.
Hemocompatibility Unactivated Partial Thromboplastin Time Assay -UPTT	ISO 10993-4 No deviations	The UPTT of the plasma exposed to test article extract should not significantly decrease when compared to untreated and negative controls.
Hemocompatibility Complement Activation Assay (Indirect)	ISO 10993-4	The plasma exposed to test article extract did not significantly increase in C3a or SC5b-9 when compared to untreated and negative control after 90 minutes exposure.
Hemocompatibility Complement Activation Assay (Direct)	ISO 10993-4	The plasma exposed to test article did not significantly increase in C3a or SC5b-9 when compared to the untreated and negative control after 90 minutes exposure.
Systemic Toxicity Systemic Injection Test – ISO	ISO 10993-11	The test article did not show significantly greater biological activity than the control.
Systemic Toxicity Rabbit Pyrogen Test (material mediated) - ISO	ISO 10993-11	The test article did not increase the rectal temperature of any of the animals by more than 0.5 degrees Celsius.

All the materials used to manufacture the LVIS device met all biocompatibility tests as specified by ISO 10993-1 and the General Memorandum #G9501 on Biological Evaluation of Medical Devices.

Sterility

The LVIS Intraluminal Support Device is sterilized using electron beam irradiation. The sterilization method was validated to a sterility assurance level of 10^{-6} per ISO11137. The device was tested and met specifications for sterilization.

Shelf Life

The 3 year shelf life was verified for the LVIS Intraluminal Support Device on accelerated aged devices per ASTM F-1980. The samples were preconditioned for simulated shipping and sterilization. The dimensional and functional attributes were tested and met acceptance criteria. In addition, packaging integrity testing (pouch) was verified and met acceptance criteria.

Magnetic Resonance Imaging (MRI)

The LVIS Intraluminal Support Device has been shown to be MR Conditional in MRI systems operating field strengths of 3.0 and 1.5T or less per ASTM F-2503.

Animal Testing

A GLP animal study was conducted on an earlier version of the device to evaluate acute and chronic performance characteristics of the device in an in vivo animal model at 0, 30, 90, and 180 days. The device was implanted in 20 rabbits in which elastase-induced aneurysms were created. Animals were sacrificed for analysis at 30 days (N=5), 90 days (N=7), and 180 days (N=7). Prior to sacrifice, the animals were angiographically assessed for stent performance, parent vessel patency, and aneurysm occlusion. Excised vessels were evaluated for histology – histopathology and vessel patency. One animal died 120 hrs post procedure due to an air embolus.

Minimal inflammation was found and judged to be comparable to similar devices. At 180 days, evaluation showed good results with moderate neointimal hyperplasia. Three stents migrated proximally into aortic arch but this was attributed to parent vessel too large for the device and the short proximal landing zone of the elastase aneurysm.

The results of the animal studies showed satisfactory performance and safety for use in human clinical studies.

X. Summary of Clinical Information

This was a prospective, non-randomized, feasibility study conducted at six institutions in the United States. The goal of the study was to demonstrate the safety and probable benefit of the LVIS Intraluminal Support Device. Subjects were eligible if they presented with an unruptured, wide-necked, intracranial, saccular aneurysms arising from a parent vessel ≥ 2.5 mm and ≤ 4.5 mm. Wide-necked was defined as having a neck > 4 mm or dome to neck ratio < 2 mm. The age of eligible subjects ranged from 18 and 80 years of age.

The study included four periods: screening, treatment, 30 day follow-up, and 6 month follow-up. Subjects were evaluated by independent neurological assessment and cerebral angiography preoperatively, with a cerebral angiography immediately post-operatively, with a neurological examination prior to hospital discharge and at 30 days follow-up, and with a neurological examination and cerebral angiography at 6 months follow-up.

The primary endpoints of the study were for safety (any major stroke or death within 30 days, or major ipsi-lateral stroke or neurological death within 6 months) and probable benefit (successful aneurysm treatment with the study device as defined by aneurysm angiographic occlusion of ≥ 90% at six months).

Secondary endpoints to be assessed were device and procedure related SAEs, successful delivery of the study device, parent artery patency at 6 months, stent migration at 6 months, significant (> 50%) stenosis of the treated artery at 6 months, and unplanned embolization coiling within 6 months.

Patient Data:

Thirty six subjects were enrolled into the study, but 5 of the 36 subjects were not treated. After enrollment, treatment did not occur due to the following reasons: (1) subject changed mind, (2) subject was found with metal allergy – exclusion criteria, (3) subject enrolled after study closed, (4) subject with GI bleed prior to procedure, and (5) during procedure found stent was not required.

Due to non-treatment, the 5 subjects were discontinued from the study which left 31 remaining subjects in the cohort.

Of the 31 subjects enrolled and treated, one subject was implanted with an alternative stent with embolic coils, due to failed deployment of the study device. As a result, a total of 30 subjects were implanted with the study device.

Baseline data for the 31 treated subjects are provided below:

***Subject Demographics** (N= 31):*

Subject Characteristic	**Result % (n)**
Gender	
Male	26% (8)
Female	74% (23)
Age (yrs)	
Mean	58.6
Range (min, max)	38, 74
Standard deviation	10.6
Age Group (years)	
18 ≤ 22	0%
≤39	6% (2)
40-49	16% (5)
50-59	26% (8)
60-69	35% (11)
≥70	16% (5)

***Medical History** (N=31):*

Subject Characteristics	**Result % (n)**
Vascular Risk Factors	
Hypertension	52% (16)
Cardiovascular disease	23% (7)
Diabetes	10% (3)
History of AVM	0% (0)
Peripheral vascular disease	0% (0)
Family history of aneurysm	13% (4)
Tobacco use	55% (17)
Alcohol use	13% (4)
Substance Abuse (cocaine, methamphetamine, etc.)	0% (0)
History of Stroke	
Ischemic	6% (2)

Hemorrhagic	3% (1)
Any prior stroke	10% (3)
Neurological Surgery	
Prior Treatment of target aneurysms	6% (2)

***Aneurysm Location** (N=31):*

Location	**n**	**%**
Anterior Communicating artery	1	3%
Basilar Tip	1	3%
Basilar Trunk	1	3%
Carotid ophthalmic	6	19%
Carotid Cavernous	2	6%
Middle Cerebral Artery	4	13%
Posterior Communication Artery	5	16%
Posterior Inferior Cerebellar Artery (PICA)	2	6%
Superior Cerebellar Artery	1	3%
Superior Hypophyseal	8	26%

Aneurysm and parent artery dimensions were assessed by an independent angiographic core laboratory.

***Aneurysm and Parent Artery Dimensions** (N=31):*

Characteristic	**Result** % (n) or (mean ±std, min-max)
Dome Height (mm)	7.2 ± 3.8 2.0 – 16.4
Dome Width (perpendicular to height) (mm)	6.7 ± 3.1 3.3 – 13.0
Neck (mm)	4.6 ± 1.8 2.1 – 9.1
Dome to neck ratio <2 >2	 68% (21) 32% (10)
Parent artery distal diameter (Landing Zone) (mm)	3.1 ± 0.8 1.5 – 4.4
Parent artery proximal diameter (Landing Zone) (mm)	3.6 ± 0.8 1.4 – 4.8

Procedure Success Measures (Endpoints):

Thirty of 31 subjects entered into the study received the LVIS Intraluminal Support Device and were followed for 6 months. Two subjects did not have angiography performed at 6 months.

Primary Endpoints:

Safety

The primary safety endpoint was any major stroke or death within 30 days, or major ipsi-lateral stroke or neurological death within 6 months. During the study, no report of this type was received thus the primary safety endpoint was met.

Primary Safety Endpoint

	Results (N=31)	**Upper CI Limit**
Primary Safety Event	0% (0)	9.2%
Major Stroke w/in 30 days	0% (0)	-
Death w/in 30 days	0% (0)	-
Major ipsi-lateral stroke w/in 6 months	0% (0)	-
Neurological Death w/in 6 months	0% (0)	-

Probable Benefit

Technical success was judged based on angiographic core lab assessment. The primary study endpoint for probably benefit was defined by aneurysm angiographic occlusion of $\geq$ 90% at 6 months.

Primary Endpoint

Probable Benefit – successful treatment at 6 months	**Results (N=29)**
Aneurysm Angiographic Occlusion of ≥90%	89.7% (26) 95% 1-sided limit: 78.4%

The LVIS results in this study yielded a success rate of 90% at six months. Based upon this, the LVIS device met the probable benefit criteria set in the clinical protocol.

The independent core lab assessment of the mean percent aneurysm occlusion for the different time points in the study is presented below. The mean initial (post procedure) percent aneurysm occlusion was 87% and at 6 months it was 95%.

Aneurysm Occlusion – Independent Core Lab

	Initial (N=30[1])	6 Months (N=28)
Occlusion of Aneurysm		
Mean ±std	87% ±18.6	95% ±19.0
Range (min, max)	(0%, 100%)	(0%, 100%)
Percent Occlusion Category		
100%	17% (5)	75% (21)
90-99%	50% (15)	18% (5)
<90%	33% (10)	7% (2)

[1] One (1) subject did not have an assessment of occlusion.

Secondary Endpoints:

In addition to the primary endpoints, several secondary endpoints were also evaluated at time points and no significant issues were noted regarding the secondary endpoints.

Secondary Endpoints

	Result % (n/N)	95% CI
Device and Procedure Related SAEs	3.2% (1/31) [Stroke/TIA probably device related]	0.1%, 16.7%
Successful Delivery of the LVIS Device - if the stent was placed without issue	97% (30/31) [subject had alternative stent]	83%, 99.9%
Parent Artery Patency at 6 Months (per site assessment)	100% (29/29)[1]	0%, 11.9%
Stent Migration at 6 Months (per core lab)	0% (0/26)	0%, 13.2%
Significant (>50%) Stenosis of the treated artery at 6 months (per core lab)	100% Patent 100% (27) >50% stenosis 0% (0) Complete Occlusion 0% (0) Could not assess (1)	Not applicable
Unplanned Embolization Coiling through 6 months	3.3% (1/30)	0%, 17.2%

[1] One (1) subject had the assessment made by CTA, not angiography (denominator 29 instead of 28)

Neurological Assessments:

Neurological assessments were performed at baseline and 6 months. The majority of subjects had NIH Stroke Scale of Grade 0 at baseline (90%) and at 6 months (96%). The mean NIH Stroke Scale was 0.3 (baseline) and 0.25 (6 months). The NIH Stroke Scale for all subjects remained unchanged or improved after 6 months from baseline. In addition, the modified Rankin Scale assessments of Grade 0 were 84% of subjects at baseline and 87% at 6 months. For all subjects the mRS remained unchanged or improved after 6 months from baseline.

Summary:

The clinical feasibility study, conducted under IDE G110014, demonstrated the satisfactory safety profile of the LVIS Intraluminal Support Device to facilitate endovascular coil embolization of unruptured, wide necked, intracranial, saccular aneurysms, and provided the ability to occlude the aneurysm and be maintained through 6 months.

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 clinical study included 12 investigators of which none were full-time or part-time employees of the sponsor and 6 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: none
- Significant payment of other sorts: 6 investigators
- Proprietary interest in the product tested held by the investigator: none
- Significant equity interest held by investigator in sponsor of covered study: none

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

XII. Risk/Probable Benefit Analysis

Wide-necked aneurysms are very difficult to treat by surgical clipping and coiling. Surgical clipping requires a defined neck which is not typically found in wide-necked aneurysms. Aneurysms with wide necks cannot structurally retain embolization coils and complications such as protrusion of the coil into the parent artery may occur. Another alternative treatment is permanent parent artery occlusion which is dependent on adequate collateral blood flow and may not always be a feasible option. Recent availability of neurovascular stents through the Humanitarian Device Exemption provision has provided an additional approach to treat these difficult to occlude aneurysms. The LVIS Intraluminal Support Device functions to retain the coil mass within the aneurysm sac in scenarios where the shape of the aneurysm does not do so naturally (i.e. wide necked).

The LVIS Intraluminal Support Device clinical feasibility study treated 31 subjects with unruptured, wide-necked, intracranial, saccular aneurysms. Clinical follow-up (30 subjects) and angiographic follow up (28 subjects) were performed at 6 months

post procedure. The type and frequency of observed adverse events is consistent with similar neurovascular procedures.

At 6 months follow up, the clinical benefit of the LVIS was established as angiographic aneurysm occlusion of ≥90% was achieved for 92.9% (26 of 28) of subjects. The mean percent occlusion at six months was 95%. Aneurysm occlusion of ≥90% is generally considered successful by the clinical community.

With regards to the neurological assessment from baseline to 6 months, the percent of subjects rated Grade 0 on the mRS increased from 84% (26/31) to 87% (26/30). The mean NIH Stroke Score was reduced from 0.3 (31) to 0.25 (27).

Extensive mechanical testing was performed on the LVIS Intraluminal Support Device. All testing met acceptance criteria. Animal studies with acute assessments observed that the LVIS device could be deployed, retrieved, and implanted in the animal arterial models. Chronic animal studies provided support that the LVIS device did not impact brain tissue in addition to mechanical trauma due to implantation. The animal studies concluded that the LVIS device was well tolerated and healing advanced in parent vessels, with a tissue response similar to other stented vessels of similar duration.

Therefore, it is reasonable to conclude that the probable benefit to health using the LVIS Intraluminal Support Device with embolic coils for wide-necked aneurysms outweighs the risk of illness or injury when used in accordance with the Instruction for Use and when taking into account the probable risks and benefits of currently available alternative forms of treatment.

XIII. Panel Recommendation

This HDE was not reviewed by the Neurological Devices Panel. The panel has previously reviewed two other similar neurovascular stents (Neuroform Microdelivery Stent System – H020002, and the Enterprise Vascular Reconstruction Device – H060001). This HDE does not raise any unanticipated safety issues. Therefore, it was determined that this application need not be submitted to the advisory panel.

XIV. CDRH Decision

CDRH determined that based on the data submitted in the HDE, the LVIS Intraluminal Support 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 with embolic coils for the treatment of unruptured, wide-necked, intracranial, saccular aneurysms arising from a parent vessel of ≥ 2.5 mm to ≤ 4.5 mm outweighs the risk of illness and injury, and issued an approval order on July 25, 2014..

Although the age range of treated subjects in the clinical study was 38-74 years, consultations with FDA neurosurgeons supported lowering the age limit to 18 was

appropriate because the intracranial vascular anatomy in 18 year old subjects without congenital syndromes or systemic diseases is similar to that of adult subjects. The safety considerations regarding endovascular access, navigability, delivery and retrieval are similar. Consequently, the indicated age range for this HDE hence can be ≥ 18 years and ≤ 80 years until further testing is completed supporting a lowered age range.

XV. Approval Specifications

Directions for Use: See the Physician's Labeling (Instructions for Use)

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