Summary of Safety and Probable Benefit

I. General Information

Device Generic Name:	Intracranial Stent
Device Trade Name:	CORDIS ENTERPRISE™ Vascular Reconstruction Device and Delivery System
Applicant's Name and Address:	Cordis Neurovascular, Inc. 14000 NW 57th Court Miami Lakes, FL 33014 USA
Humanitarian Device Exemption Number:	H060001
Date of Humanitarian Use Device Designation:	May 26, 2005
Date of Panel Recommendation:	N/A
Date of Good Manufacturing Practices Inspection:	August 28 to November 8, 2006
Date of Notice to the FDA:	To be completed by FDA.

II. Indications for Use

The CORDIS ENTERPRISE™ Vascular Reconstruction Device and Delivery System is intended for use with embolic coils for the treatment of wide-neck, intracranial, saccular or fusiform aneurysms arising from a parent vessel with a diameter of $\geq$ 3 mm and $\leq$ 4 mm. Wide-neck is defined as having a neck width $\geq$ 4mm or a dome-to-neck ratio < 2.

III. Contraindications

Intracranial artery stenting is generally contraindicated in the following patient types:

- Patients in whom the aneurysm size and/or parent vessel size does not fall within the indicated range.
- Patients in whom antiplatelet and/or anticoagulation therapy is contraindicated.
- Patients in whom the angiography demonstrates the anatomy is not appropriate for endovascular treatment, due to conditions such as:
    - o Severe intracranial vessel tortuosity or stenoses
    - o Intracranial vasospasm not responsive to medical therapy

IV. Warnings and Precautions

See *Warnings and Precautions* in the final labeling (*Instructions for Use*).

V. Device Description

The CORDIS ENTERPRISE™ Vascular Reconstruction Device and Delivery System is a self-expanding, neurovascular stent and delivery system. It consists of the following components:

- Vascular Reconstruction Device (VRD/Stent)
- Delivery System

A detailed description of each of the two components of the CORDIS ENTERPRISE™ Vascular Reconstruction Device and Delivery System follows:

Vascular Reconstruction Device (Stent) - The Stent has a tubular mesh structure laser cut from Nitinol. The ends of the stent are flared and feature four radiopaque tantalum markers at each end. The stent-marker assembly is covered with an insulating polymer. Upon exposure to body temperature, the stent expands to the vessel lumen diameter. In its expanded shape, the stent creates a highly flexible, closed cell structure. The stent is available in one diameter (4.5mm) and four lengths (14mm, 22mm, 28mm and 37mm).

Delivery System - The delivery system is composed of an introducer and delivery wire and is used to deliver the stent to the treatment site in the neurovasculature. The introducer consists of a polymer tube with a distal tapered end. It protects the stent and distal segment of the delivery wire from damage and creates an uninterrupted passage for the stent to be transferred to the microcatheter. The delivery wire is a ground nitinol corewire that tapers down from the proximal to distal end, providing different stiffness zones. The distal section of the delivery wire has three radiopaque markers with gaps between them, which serve different purposes. The delivery wire facilitates navigation into the distal neurovasculature. The delivery system is provided sterile with the stent pre-loaded in the introducer.

Table 1 summarizes the sizing guidelines for the CORDIS ENTERPRISE™ Vascular Reconstruction Device and Delivery System.

Table 1 – Recommended Sizing Guidelines

Unconstrained Stent Diameter (mm)	Unconstrained Stent Length (mm)	Recommended Parent Vessel Diameter (mm)	Length Foreshortening	
			%	mm
4.5	14	3 – 4	6.7	1.1
4.5	22	3 – 4	7.7	1.9
4.5	28	3 – 4	9.8	3.2

Unconstrained Stent Diameter (mm)	Unconstrained Stent Length (mm)	Recommended Parent Vessel Diameter (mm)	Length Foreshortening	
			%	mm
4.5	14	3 – 4	6.7	1.1
4.5	22	3 – 4	7.7	1.9
4.5	28	3 – 4	9.8	3.2
4.5	37	3 – 4	10.9	4.7

VI. Alternative Practices and Procedures

Wide-neck aneurysms are difficult to treat both surgically and endovascularly with clipping or coiling. Surgical clipping 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. Recent availability of neurovascular stents through the Humanitarian Device Exemption regulatory provision has provided for an additional approach to aneurysm occlusion using endovascular techniques. Stent placement across the aneurysm neck maintains blood flow through the parent artery lumen, while excluding the aneurysm sac, the stent can also serve to contain coils within the aneurysm space and prevent coil herniation into the parent vessel.

VII. Marketing History

The CORDIS ENTERPRISE™ Vascular Reconstruction Device and Delivery System is currently marketed in Europe (CE-Mark) and has not been withdrawn from the market for safety reasons.

VIII. Adverse Effects of the Device on Health

Observed Adverse Effects

Twenty-eight subjects were entered into the clinical feasibility study and treated with a CORDIS ENTERPRISE™ Vascular Reconstruction Device. A Clinical Events Committee (CEC) reviewed all adverse event listings and adjudicated all serious adverse event summaries that were reported by the investigators during the course of the study. An adverse event was defined as any untoward medical occurrence in a subject compared to pre-existing conditions that occurred during the clinical investigation. A serious adverse event was defined as any adverse event that:

- Led to a death

- Led to a serious deterioration in the health of the subject that:
  1. Results in a life-threatening illness or injury;
  2. Results in a permanent impairment of a body structure or a body function;
  3. Requires inpatient hospitalization or prolongation of hospitalization;
  4. Results in a medical or surgical intervention to prevent permanent impairment to a body structure or a body function; or led to
  5. Fetal distress, fetal death or a congenital abnormality or birth defect

Fifty-seven adverse events that were considered to be at least possibly procedure or device related occurred in 20 subjects. The majority (68.4%) of these events occurred by 30 days. Table 2 summarizes all device or procedure related adverse events, including Serious Adverse Events.

Table 2: Adverse Events[1]

Device or Procedure Related Adverse Events	Number of Occurrences	Number of Subjects (%)	Time of Occurrence		
		N = 28	Procedure	1 - 30 days	31 days - 6 months
Headache	8	5 (17.9%)	1	2	5
Insertion site hematoma/bleeding	5	5 (17.9%)	5	0	0
Laboratory abnormality	5	4 (14.3%)	0	1	4
TIA	3	3 (10.7%)	1	2	0
Mid, Low back pain	3	3 (10.7%)	2	1	0
Floaters, blurry vision	3	2 (7.1%)	0	2	1
Left, Right-sided weakness	2	2 (7.1%)	0	1	1
Intracerebral hemorrhage[2]	2	2 (7.1%)	0	2	0
Aneurysm recanalization	2	2 (7.1%)	0	0	2
Not feeling right	2	1 (3.6%)	0	2	0
Nausea	2	2 (7.1%)	1	1	0
Fever	2	2 (7.1%)	1	1	0
Edema	2	2 (7.1%)	1	1	0
Cerebral infarct	1	1 (3.6%)	0	1	0
Cranial nerve II deficit	1	1 (3.6%)	0	1	0
Stenosis of stented segment	1	1 (3.6%)	0	0	1
Cranial nerve palsy	1	1 (3.6%)	0	1	0
Failure deliver stent	1	1 (3.6%)	1	0	0
Panic attack	1	1 (3.6%)	0	0	1
Confusion	1	1 (3.6%)	0	1	0
Neck pain	1	1 (3.6%)	1	0	0
Arm cramps	1	1 (3.6%)	1	0	0
Upset stomach	1	1 (3.6%)	1	0	0
Pain at insertion site	1	1 (3.6%)	1	0	0
Hip pain	1	1 (3.6%)	1	0	0
Cold hands and feet	1	1 (3.6%)	1	0	0
Eyes fixed unable to focus	1	1 (3.6%)	0	0	1
Visual field decrease	1	1 (3.6%)	0	0	1
Facial numbness	1	1 (3.6%)	0	1	0

Database closure 07/13/2005

[1] Includes both non-serious adverse events and CEC adjudicated serious adverse events

[2] One subject died post-operatively, resulting in a death rate of 3.6% (1/28)

Based on the Clinical Events Committee adjudication, seven patients experienced one or more serious adverse events for an estimated rate of 25.0% (Table 3).

Table 3: Adjudicated Serious Adverse Events Related to Procedure or Device

Device or Procedure Related	All Patients (N = 28)	95% Confidence Interval
Any Procedure or Device Related Event	25.0% (7/28)	[10.7%, 44.9%]
Intracerebral Hemorrhage[1]	7.1% (2/28)	[0.9%, 23.5%]
Aneurysm Recanalization	7.1% (2/28)	[0.9%, 23.5%]
TIA (Transient Ischemic attack)	7.1% (2/28)	[0.9%, 23.5%]
Cerebral Infarct	3.6% (1/28)	[0.1%, 18.3%]
Cranial Nerve II Deficit	3.6% (1/28)	[0.1%, 18.3%]
Cranial Nerve Palsy	3.6% (1/28)	[0.1%, 18.3%]
Groin Hemorrhage	3.6% (1/28)	[0.1%, 18.3%]

[1] One of these subjects died post-operatively, resulting in a death rate of 3.6% (1/28) with a 95% confidence interval of [0.1%, 18.3%]. A CORDIS ENTERPRISE™ Vascular Reconstruction Device and coils were successfully deployed to treat the aneurysm without any reported technical complications. The death was classified as secondary to the subject's presenting intracerebral hemorrhage.

Potential Adverse Events

Potential adverse events that were not observed in the clinical study but that may be associated with the use of the CORDIS ENTERPRISE™ Vascular Reconstruction Device and Delivery System or with the procedure include:

Allergic reaction including, but not limited to contrast, Nitinol metal and medications
Arrhythmia
Arteriovenous fistula
Coil migration/prolapse into normal vessels adjacent to the aneurysm
Dissection
Emboli (air, tissue or thrombotic)
Emergent neurosurgery
Incomplete aneurysm occlusion
Infection
Injury to normal vessels or tissue
Ischemia
Occlusion of side branch
Myocardia infarction
Neurological deficit
Infection at insertion site
Perforation
Pseudoaneurysm
Renal Failure
Rupture, vessel or aneurysm
Seizures
Stent migration/embolization
Stent thrombosis/occlusion
Stroke
Total occlusion of treated segment
Vasospasm
Vessel thrombosis

IX. Summary of Pre-clinical Studies

Biocompatibility Testing

Biocompatibility Testing for all materials used to manufacture the CORDIS ENTERPRISE™ Vascular Reconstruction Device and Delivery System was conducted or justified. The following tests were performed in accordance with ISO 10993 Part 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 Practices):

- Cytotoxicity
- Sensitization
- Intracutaneous Toxicity
- Acute Systemic Toxicity
- Genotoxicity / Mutagenicity
- Implantation – 6 Month
- Hemolysis
- Pyrogenicity
- *In Vitro* Hemocompatibility (Partial Thromboplastin Time and Platelet and Leukocyte Count)
- Physico-Chemical Aqueous Extraction

All the materials used to manufacture the CORDIS ENTERPRISE™ Vascular Reconstruction Device and Delivery System met all the biocompatibility tests as specified by ISO 10993 Part 1 and the General Memorandum #G95-1 on Biological Evaluation of Medical Devices.

Sterility

The CORDIS ENTERPRISE™ Vascular Reconstruction Device and Delivery System is sterilized using ethylene oxide (EtO). The EtO cycle was validated to a sterility assurance level of 10^{-6} per ISO 11135. The system was tested and met specifications after two sterilization cycles.

Shelf Life

A one-year shelf life was verified for the CORDIS ENTERPRISE™ Vascular Reconstruction Device and Delivery System using a six (6) month real time aging study of the finished, sterile device, and consideration of information of other similar products. Device testing included stent, delivery wire, introducer and stent system functionality testing. Device testing met specifications to support a one-year expiration date. A one-year shelf life was verified for the packaging. Packaging integrity testing included product migration verification, temperature monitor label verification, package challenge test, pouch seal integrity test and package seal strength.

Magnetic Resonance Imaging (MRI)

The CORDIS ENTERPRISE™ Vascular Reconstruction Device has been shown to be MR Conditional in MRI systems operating at field strengths of 3.0 T or less using ASTM F2503-05. MR imaging quality may be diminished if the area of interest is in the same area as the CORDIS ENTERPRISE™ Vascular Reconstruction Device.

Mechanical Testing

All mechanical testing was conducted on finished, sterile devices and components. All testing performed on the device, its components, and the packaging verified that all design inputs were met. Testing results met the acceptance criteria. Provided in **Tables 4, 5 and 6** is a listing of the testing conducted on the CORDIS ENTERPRISE™ Vascular Reconstruction Device and Delivery System.

Table 4 – Stent Testing

Characterization Testing	
Material Composition	
Material Certification	
Shape Memory and Superelasticity	
Corrosion Resistance (Potentiodynamic and Galvanic)	
Dimensional and Functional Attributes	
Dimensional Verification	Chronic Outward Force and Radial Resistive Force
Expansion Uniformity	Mechanical Properties of Stent Tubing (Raw Material and Stent Finished Component)
Foreshortening	Stress Analysis (Finite Element Analysis [Fatigue Strain and Kink Radius Calculations])
Cell Inscribed Circle Verification	Pulsatile Fatigue Test (400MM Cycles)
Percent Open Area Calculation	Coating Durability / Accelerated Coating Durability
Stent Integrity	Magnetic Resonance Imaging (MRI) Testing at 3.0T
Additional Testing	
Quantitative Analytical Determination for Residual Cyclohexane	

Table 5 - Delivery System Testing

Delivery Wire
Material Characterization
Dimensional Verification
Distal Coil – Distal Joint Attachment Strength / Delivery Wire Tip Tensile Strength
Proximal Coil – Distal Joint Attachment Strength
Tip Linear Stiffness

Turns to Failure
Introducer
Material Characterization
Dimensional Verification

Table 6 - Vascular Reconstruction Device and Delivery System Testing (Stent System)

Stent System
Stent Push Force in Introducer
Stent Push Force in Microcatheter
Stent-Delivery Wire Engagement Strength
Deployment Forces
Stent Marker Attachment Strength / Delivery Wire Engagement Gap Tensile Strength
Particulate Matter
Pyrogen Testing
Bioburden Testing

Based on the results of the above-mentioned pre-clinical testing, the CORDIS ENTERPRISE™ Vascular Reconstruction Device and Delivery System can be safely deployed and implanted.

Animal Testing

A non-GLP chronic animal study was conducted with an earlier version of the CORDIS ENTERPRISE™ Vascular Reconstruction Device to evaluate chronic performance characteristics of the device in an *in vivo* setting at 30, 90 and 180 days. The device was implanted in 32 rabbits (27 rabbit explanted) in which Elastase-induced wide neck aneurysms were created originating from the common carotid artery. Animals were sacrificed for analysis at 30 days (9 animals), 90 days (9 animals) and 180 days (9 animals). Excised vessels were submitted for histology / histopathology, luminal patency and morphometric analysis. The study also assessed the technical feasibility of the device and delivery system, the degree of angiographic aneurysm occlusion and the ability of the vascular reconstruction device to support the coil mass.

The findings showed that at 30 days, 90 days and 180 days the stent produced minimal inflammation and only mild injury to the vessel. The stents were completely endothelialized within 30 days and intimal smooth muscle maturation was evident.

With respect to angiographic assessment, the study found that at explant the animals exhibited an average of 93% aneurysm occlusion at 30 days, 95 % at 90 days and 98% at 180 days.

Four acute porcine studies were conducted on the final device to assess the performance attributes of the CORDIS ENTERPRISE™ Vascular Reconstruction Device and Delivery

System. These studies assessed the technical feasibility of the system and verified that the user requirements were met and the device performed as intended.

A GLP six (6) month safety animal study was conducted on the CORDIS ENTERPRISE™ Vascular Reconstruction Device and Delivery System to examine the tissue response elicited by polymer coated coupons when implanted into the cerebral cortex of a rabbit. Implantation produced slight procedural trauma that resulted in very low levels of parenchyma reaction including hemosiderosis, fibrosis, and isolated low levels of inflammation. The polymer coated and control (bare) coupons did not produce any brain tissue response beyond the response to the slight mechanical trauma of coupon insertion. There were no differences in tissue response elicited by polymer-coated, and uncoated coupons when implanted into the cerebral cortex of the rabbit. In conclusion, the CORDIS ENTERPRISE control and test coupons did not produce necrosis in rabbit brains.

Based on the results of the above-mentioned animal studies, the CORDIS ENTERPRISE™ Vascular Reconstruction Device and Delivery System can be safely deployed and implanted.

X. Summary of Clinical Information

This was a prospective, non-randomized, feasibility study conducted at five institutions in the United States. The goal of the study was to demonstrate the safety and feasibility of the CORDIS ENTERPRISE™ Vascular Reconstruction Device and Delivery System. Subjects were eligible if they presented with a ruptured (Hunt and Hess Grade I – III) or non-ruptured intracranial wide neck saccular aneurysm that was deemed by the attending interventional neuroradiologist to be an acceptable candidate for endovascular coil embolization. Wide neck was defined as having a neck width ≥ 4 mm or a dome-to-neck ratio < 2.

The study included four periods: screening period, treatment period, thirty-day follow-up and six-month follow-up. Subjects were evaluated with an independent neurological assessment and cerebral angiography preoperatively, with a cerebral angiography immediately postoperatively, 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.

The endpoints of the study were 1) an adverse event assessment post-procedure, at discharge, at thirty days and six months after treatment, 2) neurological status assessed by an independent neurologist at discharge, at thirty days and six months after treatment compared to the baseline evaluation and 3) technical feasibility for all subjects with a deployed stent to evaluate the percent aneurysm occlusion immediately post-procedure and at six months after treatment, to evaluate for successful stent placement with satisfactory coil mass position post-procedure, and to assess for coil mass position at six months after treatment.

Patient Data

Thirty subjects were enrolled into the study. Baseline data for these patients are presented in Table 7: Patient Demographic, Table 8: Medical History, Table 9: Neurological History and Table 10: Previous Neurological Surgical Procedures.

Table 7: Patient Demographics

Subject Characteristics	Total (N=30)
Gender	
Male	7 (23.3%)
Female	23 (76.7%)
Age (years)	
Mean	57.8
Range (min, max)	22.0 – 77.0
Standard deviation	13.9
Age Group (years)	
≤ 39	2 (6.7%)
40-49	6 (20.0%)
50-59	8 (26.7%)
60-69	6 (20.0%)
≥ 70	8 (26.7%)

Table 8: Medical History

Subject Characteristics	Total (N=30)
Medical History	
(non-exclusive, N, % or mean ± SD)	
Hypertension	20 (66.7%)
Cardiovascular Disease	12 (40.0%)
Musculoskeletal Disease	8 (26.7%)
Psychological	8 (26.7%)
Chronic Pulmonary Disease	7 (23.3%)
Gastrointestinal Disease	7 (23.3%)
Immunologic	6 (20.0%)
Endocrine / Metabolic Disease	5 (16.7%)
Diabetes	3 (10.0%)
Renal Disease	3 (10.0%)
Hepatic / Pancreatic Disease	2 (6.7%)
Lymphatic	2 (6.7%)
Connective Tissue Disorder	1 (3.3%)
Hypersensitivity or Contrast Material	1 (3.3%)
Peripheral Vascular Disease	1 (3.3%)
Other	20/29 (69%)

Table 9: Neurological History

Subject Characteristics	Total (N-30)
Neurological History	
(non-exclusive, N, % or mean ± SD)	
Pounding/Pulsatile Headaches	13 (43.3%)
Altered Mental Status	8 (26.7%)
Cranial Nerve Palsy	5 (16.7%)
Seizures	5 (16.7%)
Subarachnoid Hemorrhage	5 (16.7%)
CVA (stroke)	4 (13.3%)
Deterioration	3 (10.0%)
TIA	2 (6.7%)
Other	7 (23.3%)

Table 10: Previous Neurological Surgical Procedures

Subject Characteristics	Total (N=30)
Previous Neurological Surgical Procedures	
Intracranial Embolization	7 (23.3%)
Intracranial Radiosurgery	1 (3.3%)
Intracranial Clipping	1 (3.3%)

Two of the 30 subjects met angiographic exclusion criteria during the pre-procedure angiography and were not treated with a CORDIS ENTERPRISE™ Vascular Reconstruction Device. One parent vessel diameter was too large; one aneurysm neck too wide. Of the 28 subjects who were entered into the clinical study and treated with a CORDIS ENTERPRISE™ Vascular Reconstruction Device, the aneurysms were most commonly located in the internal carotid/ophthalmic location (57.1 %). Five aneurysms (17.9%) were located in the vertebrobasilar system. Table 11 summarizes the locations of the treated aneurysms.

Table 11: Aneurysm Location

Aneurysm Location	Total (N=28)	
	N	%
Carotid/Ophthalmic	16	57.1
Distal 1/3 Basilar (including apex)	4	14.3
Posterior Communicating	3	10.7
Cavernous Carotid	1	3.6
Carotid Bifurcation	1	3.6
Middle Cerebral	1	3.6
Posterior Cerebral	1	3.6
Vertebral	1	3.6

Aneurysm and Parent Artery Dimensions

An independent angiographic core laboratory was used to assess the aneurysm and parent artery dimensions. Table 12 contains the pre-procedure, post-procedure and six months aneurysm dimensions. Table 13 contains the parent artery dimensions. At pre-procedure, the mean aneurysm dome height and width were 8.2 mm and 8.6 mm, respectively. The mean neck width was 5.3 mm, and mean dome width-to-neck ratio was 1.43. The mean proximal/distal diameter of the parent vessel pre-procedure was 3.4/3.0, and 3.3/2.9 at six months.

Unaccounted for data include N/A (not available) or N/D (not determinable) assessments. N/A was assigned by the core laboratory if the measure was not appropriate, such as in the case of measuring neck width for a fusiform aneurysm. N/D was assigned when the core laboratory was unable to perform the measurement due to poor image quality or complex aneurysm shape resulting in visual overlap with the parent artery, or if the measurement could not be determined due the presence of coils from a previous embolization procedure.

Table 12: Aneurysm Dimensions

Parameters Measured	Pre-Procedure (N = 28)[1,2]	95% Confidence Interval	Post-Procedure (N = 28)[1,2]	95% Confidence Interval	Six Months (N = 28)[1,3]	95% Confidence Interval
Dimensions of Aneurysm						
Neck Width (mm)						
Mean±SD (n)	5.3 ± 1.6 (23)	[4.6, 6.0]	5.5 ± 1.7 (18)	[4.6, 6.3]	5.2 ± 1.8 (21)	[4.4, 6.0]
Range (min., med., max.)	(2.9, 5.0, 8.7)		(2.8, 5.1, 9.1)		(2.0, 5.1, 8.3)	
Maximum Dome Height (mm)						
Mean±SD (n)	8.2 ± 4.9 (28)	[6.3, 10.1]	9.0 ± 5.0 (23)	[6.7, 9.9]	8.4 ± 4.1 (22)	[6.6, 10.3]
Range (min., med., max.)	(2.6, 6.5, 25.0)		(2.7, 8.0, 24.8)		(2.6, 8.3, 17.9)	
Maximum Dome Width (mm)						
Mean±SD (n)	8.6 ± 4.0 (27)	[7.0, 10.2]	8.9 ± 4.8 (27)	[6.8, 9.8]	8.5 ± 3.9 (25)	[6.9, 10.1]
Range (min., med., max.)	(3.2, 7.0, 18.0)		(3.1, 7.2, 24.1)		(2.6, 7.8, 17.5)	
Dome Width: Neck Width Ratio						
Mean±SD (n)	1.43 ± 0.40 (23)	[1.26, 1.61]	1.37 ± 0.34 (18)	[1.20, 1.54]	1.50 ± 0.41 (20)	[1.31, 1.69]
Range (min., med., max.)	(1.0, 1.3, 2.8)		(1.01, 1.28, 2.37)		(1.0, 1.4, 2.4)	

Numbers are % (numerator/denominator) or mean ± 1 SD.

[1] Unaccounted for data include observations classified as N/A= Not Available or N/D = Not Determinable.

[2] Twenty-eight subjects were available for post-procedure measures. Two of the 30 enrolled subjects were not entered into the study due to a pre-procedure angiographic exclusion criteria and therefore are not included in the post-procedure measurements.

[3] Twenty-seven subjects were available in follow-up. Two of the 30 enrolled subjects were not entered into the study due to a pre-procedure angiographic exclusion criterion and 1 subject died after the procedure.

Table 13: Parent Artery Dimensions

Parameters Measured	Pre-Procedure (N = 28) [1,2]	95% Confidence Interval	Post-Procedure (N = 28) [1,2]	95% Confidence Interval	Six Months (N = 28) [1,3]	95% Confidence Interval
Dimensions of Parent Artery						
Proximal Diameter (mm)						
Mean±SD (n)	3.4 ± 0.7 (28)	[3.1, 3.6]	3.4 ± 0.7 (28)	[3.1, 3.6]	3.3 ± 0.8 (27)	[3.0, 3.6]
Range (min., med., max.)	(1.7, 3.3, 4.7)		(1.8, 3.3, 4.9)		(1.9, 3.3, 4.9)	
Distal Diameter (mm)						
Mean±SD (n)	3.0 ± 0.8 (28)	[2.7, 3.3]	3.0 ± 0.8 (28)	[2.7, 3.2]	2.9 ± 0.7 (27)	[2.6, 3.1]
Range (min., med., max.)	(1.9, 2.9, 4.8)		(1.9, 2.9, 4.8)		(1.7, 2.8, 4.1)	

Numbers are % (numerator/denominator) or mean ± 1 SD.

[1] Unaccounted for data include observations classified as N/A= Not Available or N/D = Not Determinable.

[2] Twenty-eight subjects were available for post-procedure measures. Two of the 30 enrolled subjects were not entered into the study due to a pre-procedure angiographic exclusion criterion and therefore are not included in the post-procedure measurements.

[3] Twenty-seven subjects were available in follow-up. Two of the 30 enrolled subjects were not entered into the study due to a pre-procedure angiographic exclusion criterion and 1 subject died after the procedure.

Procedure Success Measures (Technical Feasibility Endpoints)

Twenty-seven of 28 subjects entered into the study received the CORDIS ENTERPRISE™ Vascular Reconstruction Device (VRD/Stent) and were followed for 6 months. One subject died post-operatively. Two subjects received two stents.

Technical success was judged based on angiographic core lab assessment. Successful stent placement with satisfactory coil mass position immediately post-procedure was 100%. Successful stent placement was defined as stable stent placement with complete coverage across the aneurysm neck and parent artery patency, while satisfactory coil mass position was defined as the stent maintaining coil position within the sac with parent artery patency. Maintenance of coil mass position was 95.8% at six months. The protocol-defined procedural success measures are provided in Table 14.

Table 14: Procedure Success Measures

Parameters Measured	Post-Procedure (N = 28) [1, 2]	95% Confidence Interval	Six months (N = 28) [1, 3]	95% Confidence Interval
Procedure Success Measures				
Proximal Parent Artery Coverage (mm)				
Mean±SD (n)	10.0 ±3.5 (26)	[8.6, 11.4]	- ± - (0)	[- , -]
Range (min., med., max.)	(3.6, 9.9, 20.3)		(- , - , -)	
Distal Parent Artery Coverage (mm)				
Mean±SD (n)	7.5 ± 2.8 (26)	[6.4, 8.7]	- ± - (0)	[- , -]
Range (min., med., max.)	(1.3, 7.0, 13.6)		(- , - , -)	
Stable Stent Placement with Complete Neck Coverage	100.0% (26/26)	[86.8%, .%]	- (- / -)	[- , -]
Maintenance of Coil Mass Position	100.0% (23/23)	[85.2%, .%]	95.8% (23/24)	[78.9%, 99.9%]
Procedure Success [4]	95.5% (21/22)	[77.2%, 99.9%]	- (- / -)	[- , -]

Numbers are % (numerator/denominator) or mean ± 1 SD.

[1] Unaccounted for data include observations classified as N/A= Not Available or N/D = Not Determinable.

[2] Twenty-eight subjects were available for post-procedure measures. Two of the 30 enrolled subjects were not entered into the study due to a pre-procedure angiographic exclusion criterion and therefore are not included in the post-procedure measurements.

[3] Twenty-seven subjects were available in follow-up. Two of the 30 enrolled subjects were not entered into the study due to a pre-procedure angiographic exclusion criterion and 1 subject died after the procedure.

[4] Successful stent placement with satisfactory coil mass position angiographically assessed immediately post procedure without the occurrence of procedural serious adverse events. The duration of the procedure was defined as the time the stent delivery system was introduced into the infusion catheter until the time the guiding catheter was removed from the subject.

The independent core lab assessment of mean percent aneurysm occlusion for the different follow-up time points in the study is presented in Table 15. The mean post-procedure percent aneurysm occlusion was 87.9%, becoming 92.0% at six months. The mean values were further categorized by percent occlusion.

Table 15: Percent Aneurysm Occlusion – Independent Core Laboratory

Parameters Measured	Post-Procedure (N = 28[1])	95% Confidence Interval	6 Months (N = 28[3])	95% Confidence Interval
Occlusion of Aneurysm				
Mean ± SD (n)	87.9%± 14.4 (24[2])	[81.8%, 94.0%]	92.0%± 13.9 (25[4])	[86.2%, 97.7%]
Range (min.,med.,max.)	(30.0%, 95.0%, 95.0%)		(33.0%, 95.0%, 100.0%)	
Percent Occlusion				
100%	0.0% (0/24)	[- , 14.2%]	36.0% (9/25)	[18.0%, 57.5%]
95%-99%	58.3% (14/24)	[36.6%, 77.9%]	28.0% (7/25)	[12.1%, 49.4%]
<95%	41.7% (10/24)	[22.1%, 63.4%]	36.0% (9/25)	[18.0%, 57.5%]

[1] Twenty-eight subjects were available for post-procedure measures. Two of the 30 enrolled subjects were not entered into the study due to pre-procedure angiographic exclusion criteria and therefore are not included in the post-procedure measurements.

[2] Four subjects did not have a percent aneurysm occlusion measurement due to N/A = Not Available or N/D = Not Determinable.

[3] Twenty-seven patients were available in follow-up. Two of the 30 enrolled subjects were not entered into the study due to a pre-procedure angiographic exclusion criteria and 1 subject died after the procedure.

[4] Three subjects did not have a percent aneurysm occlusion measurement due to N/A = Not Available or N/D = Not Determinable.

Neurological Assessments (Neurological Status Endpoint)
Neurological Assessments were performed pre-procedure, at discharge, 30 days, and six months post procedure. The mean NIH Stroke score was 1.4 pre-procedure and 0.3 at six months. The majority of subjects (75.9%) were rated Grade 0 or Grade 1 on the modified Rankin scale pre-procedure, and 80.7% of subjects were Grade 0 or Grade 1 at six months. One subject was enrolled with acute subarachnoid hemorrhage. The Hunt & Hess score for this subject had degraded from a Grade III to Grade IV just prior to the procedure. The subject expired after the procedure as a result of intracerebral hemorrhage. For the clinical neurological examinations which included vision, motor, sensory, speech, mutation, and cranial nerve deficit, most subjects experienced either no change or improved status from pre-procedure assessment to 6 months.

Summary
The clinical feasibility study, conducted under IDE #G030248, demonstrated a reasonable safety profile of the CORDIS ENTERPRISE™ Vascular Reconstruction Device and Delivery System to facilitate endovascular coil embolization of wide neck saccular intracranial aneurysms, and provided the ability to occlude aneurysm illustrating that the size of the aneurysm could be maintained through 6-months.

XI. Risk/Probable Benefit Analysis

Wide-neck aneurysms are very difficult to treat by surgical clipping and coiling. Surgical clipping requires a defined neck which is, by definition, not found in wide-necked aneurysms. And, aneurysms with wide necks can not often structurally retain embolization coils and complications such as protrusion of the coil into the parent artery may occur. Parent vessel permanent occlusion is dependent upon adequate collateral blood flow and may or may not be a feasible alternative. Recent availability of neurovascular stents through the Humanitarian Device Exemption regulatory provision has provided for an additional approach to treating these difficult-to-occlude aneurysms. The CORDIS ENTERPRISE™ Vascular Reconstruction Device serves the specific purpose of retaining a coil mass within the aneurysm sac in scenarios where the shape of the aneurysm does not do so naturally (i.e. aneurysms with a wide neck).

The CORDIS ENTERPRISE™ Vascular Reconstruction Device and Delivery System clinical feasibility study treated 28 patients with wide-neck, intracranial, saccular or fusiform aneurysms. Clinical follow-up (27 patients) and angiographic follow-up (27 patients) was performed at 6 months. The type and frequency of observed adverse events are consistent with similar neurovascular procedures.

In terms of the clinical benefit of the CORDIS ENTERPRISE™ Vascular Reconstruction Device and Delivery System, coil mass position was maintained in 95.8% (23 of 24) of patients and 64% (16 of 25) of patients had ≥ 95% occlusion at the 6-month follow-up, as measured by an independent core laboratory. The average percent occlusion at 6 months was 92%. Aneurysm occlusion of ≥ 90% is generally considered successful by the clinical community. In terms of neurological assessment from baseline to the 6-month evaluation, the percent of patients rated Grade 0 or Grade 1 on the modified Rankin scale increased from 75.9% (22/29) to 80.7% (21/26) and the mean NIH Stroke score was reduced from 1.4 (29) to 0.3 (26). A Rankin score of "0" indicates no neurological disability, and an NIH stroke score of "0" is an indication of being completely normal.

Extensive mechanical testing was performed on the CORDIS ENTERPRISE™ Vascular Reconstruction Device and Delivery System, as well as on the individual components. All tests met the acceptance criteria. Animal studies with acute assessments observed that the CORDIS ENTERPRISE™ Vascular Reconstruction Device could be deployed, recaptured and implanted in maxillary arteries. Animal studies with long term, or chronic, assessments provided evidence that the CORDIS ENTERPRISE™ did not elicit any brain tissue response in addition to a response to the mechanical trauma of coupon insertion. There were no differences in tissue response elicited by polymer-coated or uncoated coupons when implanted into the cerebral cortex of the rabbit. In conclusion, the CORDIS ENTERPRISE™ control and test coupons did not produce necrosis in rabbit brains. Refer to Section IX for details.

Therefore, it is reasonable to conclude that the probable benefit to health from using the CORDIS ENTERPRISE™ Vascular Reconstruction Device and Delivery System with embolic coils for wide-neck aneurysms outweighs the risk of illness or injury when used in accordance with the Instructions for Use and when taking into account the probable risks and benefits of currently available alternative forms of treatment.

XII. Panel Recommendation

Review of this HDE application was performed by FDA. It was determined that the preclinical and clinical issues raised by the HDE did not require review by the Neurological Devices Advisory Committee.

XIII. CDRH Decision

CDRH determined that, based on the data submitted in the HDE, the CORDIS ENTERPRISE™ Vascular Reconstruction Device and Delivery System will not expose patients to an unreasonable or significant risk of illness or injury, and the probable benefit to health from using the System with embolic coils for the treatment of wide-neck, intracranial, saccular or fusiform aneurysms arising from a parent vessel with a diameter of $\geq$ 3 mm and $\leq$ 4 mm outweighs the risks of illness or injury, and issued an approval order on ________.

XIV. Approval Specifications

Indications for Use: See *Instructions for Use*

Information for the Patient: See *Patient Brochure*

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

XV. References

None