SUMMARY OF SAFETY AND PROBABLE BENEFIT

I. GENERAL INFORMATION

Device Generic Name:	Intracranial Stent
Device Trade Name:	Wingspan™ Stent System with Gateway™ PTA Balloon Catheter
Applicant's Name and Address:	Boston Scientific SMART 47900 Bayside Parkway Fremont, CA 94538 USA
Humanitarian Device Exemption Number:	H050001
Date of Humanitarian Use Device Designation:	January 9, 2004
Date of Panel Recommendation:	N/A
Date of Good Manufacturing Practices Inspection:	October 8, 12-15, 2004
Date of Notice to the Applicant:	

II. INDICATIONS FOR USE

The Wingspan Stent System with Gateway PTA Balloon Catheter is indicated for use in improving cerebral artery lumen diameter in patients with intracranial atherosclerotic disease, refractory to medical therapy, in intracranial vessels with ≥50% stenosis that are accessible to the system.

III. CONTRAINDICATIONS

See *Contraindications* in the final labeling (*Instructions for Use*).

IV. WARNINGS AND PRECAUTIONS

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

V. DEVICE DESCRIPTION

The Wingspan Stent System with Gateway PTA Balloon Catheter is a self-expanding, neurovascular, nitinol Stent and Delivery System and Balloon Catheter that consists of the following components:

- Wingspan Stent
- Wingspan Delivery System
- Gateway PTA Balloon Catheter

A detailed description of each of the three components of the Wingspan™ Stent System with Gateway™ PTA Balloon Catheter follows:

Wingspan Stent - The Stent has a tubular mesh (zigzag struts) design. Along the length of the Stent, several individual sections self-expand as the Stent deploys. Sections are joined by 2 interconnecting struts. It is made from nitinol. There are 8 radiopaque markerbands, 4 per end, which are secured to tabs on the Stent. The Stent is available in five diameters (2.5mm to 4.5mm) and three lengths (9mm, 15mm, and 20mm).

Wingspan Delivery System - The Delivery System is used to deliver the Stent to the treatment site within the patient's artery. The Delivery System is a single lumen, over-the-wire, coaxial microcatheter. The material composition of the catheter shaft changes over the length of it to create three distinct stiffness regions: proximal, middle, and distal. The proximal end has a strain relief and standard, female Luer fitting. The Delivery System is hydrophilically coated. The Delivery System is provided sterile with the Stent preloaded. The shaft has an overall nominal working length of 135cm.

Gateway PTA Balloon Catheter - The Gateway PTA Balloon Catheter is used to pre-dilate the lesion prior to introduction of the Wingspan Stent System into the patient. The Gateway PTA Balloon Catheter contains a proximal hub, polymer tubing, Pebax balloon, and two radiopaque markerbands at the distal end. The Gateway PTA Balloon Catheter is hydrophilically coated. The Balloons are available in ten diameters (1.5mm to 4.0mm) and three lengths (9mm, 15mm, and 20mm). The Gateway PTA Balloon Catheter is provided sterile and has an overall nominal working length of 135cm.

Table 1 summarizes the sizing guidelines for the Wingspan Stent System.

Table 1: Recommended Sizing Guidelines

Wingspan Stent System Recommended Sizing Guidelines						
Labeled Stent Diameter	**Labeled Stent Length[1] (mm)**	**Self-Expanded Stent Diameter[2]**	**Recommended Vessel Diameter[3] (mm)**	**Delivery System Useable Length**	**Maximum Guidewire Diameter**	**Minimum Guide Catheter ID**
2.5 mm	9 mm	2.8 mm	>2.0 and ≤2.5	135 cm	0.014 in	0.064 in
	15 mm					
	20 mm					
3.0 mm	9 mm	3.4 mm	>2.5 and ≤3.0			
	15 mm					
	20 mm					
3.5 mm	9 mm	3.9 mm	>3.0 and ≤3.5			
	15 mm					
	20 mm					
4.0 mm	9 mm	4.4 mm	>3.5 and ≤4.0			
	15 mm					
	20 mm					
4.5 mm	9 mm	4.9 mm	>4.0 and ≤4.5			
	15 mm					
	20 mm					

[1]Select a Stent length that is at least 6mm longer than the lesion to extend a minimum of 3mm on both sides of the lesion.
[2]Stent will not expand beyond the self-expanding diameter.
[3]Select a Stent diameter based both on the sizing recommendations in this table and on the larger vessel diameter (proximal or distal reference vessel diameter).

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Treatment of recurrent ischemic stroke resulting from intracranial atherosclerosis currently includes medical therapy, percutaneous transluminal angioplasty (PTA), and surgery. Medical therapy includes use of antiplatelet or anticoagulants, or both, and modification of atherosclerotic risk factors. Antiplatelet drugs include aspirin, clopidogrel, or dipyridamole. Anticoagulants include warfarin. Alternative treatments used to re-establish blood flow through the brain are accomplished either by mechanically opening the atherosclerotic blockage or by surgically bypassing the affected artery.

VII. MARKETING HISTORY

The Wingspan Stent System has not yet been marketed in any country.

The Gateway PTA Balloon Catheter is currently marketed by Boston Scientific in Japan. The Gateway PTA Balloon Catheter is a similar device to the Maverick™ PTA Balloon Catheter, which is currently marketed in the US (P860019/S162).

VIII. ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Observed Adverse Effects

A clinical study was conducted on 45 patients with intracranial atherosclerotic disease at 12 international sites. Data are presented on 44 patients through 30 days post-stent placement and on 42 patients who have reached the 6-month follow-up visit. **Table 2** summarizes the adverse events observed in the clinical study.

Table 2 –Adverse Events

	N=45		Time of Occurrence		
Event	**N**	**%**	**Procedure[1]**	**<30 days**	**>30 days**
Infection	9	20.0	0	7	2
TIA	7[2]	15.6	0	1	6
Stroke	5	11.1[3]	0	2[4]	3[5]
Hematoma	6	13.3	3	2	1
Vasospasm	5	11.1	5	0	0
Hemorrhagic Event	4	8.9	0	2	2
Hypertension	4	8.9	3	0	1
Peripheral vascular diseases	4	8.9	0	0	4
Neurological symptoms	3	6.7	1	1	1
Pain	3	6.7	0	3	0
AMI	2	4.4	0	1	1
Angina	2	4.4	0	2	0
Arrhythmia	2	4.4	1	0	1
Creatinine increase	2	4.4	0	1	1
Hematuria	2	4.4	0	2	0
Hypoglycemia/hyperglycemia	2	4.4	1	1	0
Asymptomatic Thromboembolic Event	1	2.2	1	0	0
Bradycardia (35 min)	1	2.2	0	1	0
Broken middle-foot left/V-fracture	1	2.2	0	0	1
Chronical antrum gastritis	1	2.2	0	0	1
Death	1	2.2	0	1	0
Elevated bilirubin, GOT, GPT[6]	1	2.2	0	1	0
Fever	1	2.2	1	0	0
Hiatus hernia	1	2.2	0	0	1
Hypervolemia	1	2.2	1	0	0
New distal in-stent stenosis[7]	1	2.2	0	0	1
Pulmonary edema	1	2.2	0	1	0
Respiratory failure[8]	1	2.2	1	0	0
Seizure	1	2.2	0	1	0
Syncope	1	2.2	0	1	0

(1) Procedural events were those occurring within 24 hours of the procedure (day 0).
(2) Seven TIAs occurred in 6 patients.
(3) Five strokes occurred in four patients. Four strokes were adjudicated as ischemic stroke, and one as a hemorrhagic stroke.
(4) Both events were adjudicated as major ipsilateral stroke. One of these was a hemorrhagic stroke, and the patient later died. The other was an ischemic stroke from which the patient recovered.
(5) All three events were ischemic strokes. One event was adjudicated as ipsilateral and minor. The remaining two events were adjudicated as contralateral, one major and the other minor.
(6) Due to unknown reasons
(7) This patient was implanted with a coronary stent after experiencing TIA but without CT scan evidence of a new infarction. Angiographic results indicated an in-stent stenosis of >90% distal to the previously treated lesion.
(8) Due to epiglottic edema caused by an unknown allergic reaction.

Potential Adverse Effects

Potential adverse events that were not observed in the clinical study but that may be associated with the use of the Wingspan Stent System with Gateway PTA Balloon Catheter or with the procedure include:

Cerebral aneurysm	Stent migration	Vessel perforation
Coagulopathy	Stent misplacement	Vessel rupture
Emboli (air, tissue, or thrombotic tissue)	Stent occlusion	Vessel thrombosis
Intimal dissection	Stent embolization	Vessel trauma requiring surgical
Pseudoaneurysm	Stent thrombosis	repair or intervention

IX. SUMMARY OF PRECLINICAL STUDIES

Biocompatibility Testing

Biocompatibility testing of the Stent alone, the Wingspan Stent System, and the Gateway PTA Balloon Catheter was conducted. The following tests were performed in accordance with ISO 10993-1, USP, and Good Laboratory Practice (GLP) Regulations, 21 CFR 58

- Acute Intracutaneous Reactivity (Irritation)
- Acute Systemic Toxicity
- Sensitization (Guinea Pig Maximization)
- Cytotoxicity—MEM Elution
- Hemolysis—Direct Contact
- Pyrogenicity—Material Mediated
- Lee and White Coagulation
- *In Vitro* Hemocompatibility Assay
- Complement Activation
- Genotoxicity
- Mouse Lymphoma

Sterility

The Wingspan Stent System with Gateway PTA Balloon Catheter is sterilized using ethylene oxide (EO). The EO cycle was validated to a sterility assurance level of 10^{-6} per ISO 11135.[1] The System was tested and met specifications after a minimum of two sterilization exposures.

[1] AAMI/ANSI/ISO 11135:1994, Medical Devices – Validation and Routine Control of Ethylene Oxide Sterilization.

Shelf Life

For the Wingspan Stent System, a 1-year shelf life was validated using an accelerated aging study of finished devices and packaging in accordance with ISO 11607.[2] Package integrity testing included pouch seal integrity, label integrity, dye penetration, and ship testing. Device functionality testing included System functionality testing, Stent characteristic testing, and Delivery System characteristic testing. Both package integrity and device testing met specifications to support a 1-year expiration date.

For the Gateway PTA Balloon Catheter, a 1-year shelf life has been established using real time and accelerated aging studies and extreme conditioning of finished devices and packaging. Package integrity testing included pouch seal integrity, label integrity, dye penetration, pouch burst, and ship testing. Device functionality testing was performed. Both package integrity and device functionality testing met specifications to support a 1-year expiration date.

Magnetic Resonance Imaging (MRI) Compatibility

The Stent was shown to be MRI compatible in MRI systems operating at field strengths of up to 3.0 Tesla. MRI laboratory evaluation demonstrated that no significant image distortion or heating was created by the presence of the Stents at scanning sequences commonly used during MRI procedures for the given test. Therefore, the Stent is compatible and safe in MRI systems operating at 3.0 Tesla or less.

Mechanical Testing

All mechanical testing was performed on the finished, sterile Wingspan Stent System and the Gateway PTA Balloon Catheter, as well as on individual components of the System. All system functionality testing and individual component testing passed the acceptance criteria. A summary of functional testing is provided in **Table 3**.

Table 3 – Functional Testing Summary

Test	Samples		Acceptance Criteria	Results
	Size (mm)	N		
Wingspan Stent System Preparation	4.5 x 20	30 ea	Wingspan Stent System must be acceptably flushed	All samples tested were acceptably flushed during preparation
Wingspan Stent System Guide Catheter Compatibility	4.5 x 20	30 ea	The Delivery System must track through a 6F guide catheter	All samples tested were successfully tracked through a 6F guide catheter
Wingspan Stent System Trackability over Guidewire	4.5 x 20	30 ea	The Wingspan Stent System must track over the guidewire	All samples tested tracked successfully over the guidewire
Stent Accessibility of Target Deployment	4.5 x 20	30 ea	The Wingspan Stent System must be capable of advancing to and positioning the Stent across	All samples tested were successfully positioned at the target deployment zone

[2] ISO 11607, Packaging for Terminally Sterilized Medical Devices.

Test	Samples		Acceptance Criteria	Results
	Size (mm)	N		
Zone			the target deployment zone	
Stent Deployability	4.5 x 20	30 ea	The Wingspan Stent System must deploy the Stent at the target deployment zone	All samples tested were successfully deployed at the target deployment zone
Wingspan Stent System Particulate (during Stent deployment)	4.5 x 20	29 ea	Wingspan Stent System must be free of significant number of particulate during Stent deployment: ≤ 6000 particles of ≥ 10μm size ≤ 600 particles of ≥ 25μm size	100% (n=29) of Wingspan Stent Systems tested were free of significant particulate for particles ≥10μm and ≥25μm
Ease of Delivery System Removal	4.5 x 20	30 ea	The Delivery System must not interfere with the deployed Stent	All samples tested did not interfere with the Stent upon removal of the Delivery System after deployment
Delivery System Integrity after Use	4.5 x 20	30 ea	System must remain intact after use	All samples tested remained intact after use
Delivery System Coating Lubricity	4.5 x 20	30 ea	Outer Body must have a friction force of ≤0.08 lb after the fifth movement cycle	All samples tested had Outer Body coating a friction force of ≤0.08 lb after the fifth movement cycle
Balloon Profile	1.5-4.0x20 2.0-4.0x30 (19 sizes)	5 ea	The balloon profiles must not exceed the maximum allowable deflated balloon profiles of <0.033in max (1.5 x 20) through <0.043in max (4.0 x 20)	All samples tested met specification
Balloon Catheter Shaft Tensile Strength	2.0x20 3.0x20 4.0x20	15 ea	Catheter Shaft tensile strength must be ≥1.12 lb	All samples tested had tensile strengths ≥1.12 lb
Balloon Deflation Time	1.5-4.0x20 2.0-4.0x20 (19 sizes)	15 ea	Balloon must deflate in <21 sec	All samples tested had average deflation times <21 sec
Balloon Catheter Distal Tip Tensile Strength	1.5x20	30 ea	The distal tip is required to withstand a tensile force of ≥0.3 lb	All samples tested were ≥0.3 lb
Balloon Burst Strength	1.5x9 2.0x9 1.5x15 1.5-4.0x20 2.0x30 4.0x30 (15 sizes)	15 ea	Balloon burst pressure must be above the rated burst pressure (12atm or 14atm, based on size) with no loss of guidewire movement during pressurization; 95%/99.9%	All samples tested met specification

Animal Testing

The Stent was tested in 45 New Zealand rabbits in accordance with Good Laboratory Practices (GLP). Two separate studies were performed. A pilot GLP study was performed in 20 animals using the Wingspan Stent System, and a parallel control safety GLP study was performed on 25 animals using the Wingspan Stent System and Gateway PTA Balloon Catheter. The intent of the pilot study was to evaluate the appropriate

sizing of the Stent to the vessel diameter. The intent of the safety study was to compare the Wingspan Stent to a control Stent; both Stents were placed after vessel dilation using the Gateway PTA Balloon Catheter.

In every case, the Wingspan Stent System reached the intended treatment site for both the pilot study and the safety study. For the safety study, in all cases the Gateway PTA Balloon Catheter was successfully inflated to dilate the treatment site and deflated prior to stenting. There were no instances of acute vessel perforation or occlusion. There was no angiographic evidence of vessel stenosis in the immediate post-implant or follow-up angiograms. Histology performed included light microscopy, gross tissue evaluation, SEM, and morphometry.

For the pilot study, arteries examined at 32 days and 180 days post Stent implant had minimal to mild neointimal hyperplasia, minimal to mild vessel wall injury, and minimal to mild inflammatory reaction with variable degrees of mineral precipitation, particularly in the regions of the Stent struts at 180 days. For the safety study, arteries examined at 30 days post Balloon dilation and Stent implant had minimal to mild neointimal hyperplasia, minimal to mild vessel wall injury, and minimal to mild inflammatory reaction. Arteries examined at 90 days and 180 days post Balloon dilation and Stent implant arteries had minimal to mild neointimal hyperplasia, minimal to mild and, rarely, moderate vessel wall injury, minimal to mild inflammatory reaction, and variable degrees of arterial wall mineralization. At 180 days, transverse and longitudinal sections revealed varying degrees of injury to the arterial wall as a result of high radial expansion of the deployed Stent. Neointimal hyperplasia occurred, but relatively wide luminal patency remained.

No adverse hematologic, histologic, thrombogenic, or morphologic responses were observed in either study. There was no angiographic evidence of parent vessel stenosis or flow abnormalities during implantation or follow-up.

X. SUMMARY OF CLINICAL INFORMATION

This study was a prospective, multi-center, single-arm trial of 45 patients enrolled at 12 international centers. Patients were considered eligible if they had presented with evidence of recurrent stroke, refractory to medical therapy and thought to be secondary to intracranial stenosis $\geq$50% for the purpose of the study inclusion criteria, recurrent stroke was defined as patients with stroke history, treated with medical therapy, who remain symptomatic at enrollment screening. The study did not include a control group because no alternative standard therapy was readily available for this disease state. The results from this study were compared with historical controls based on literature published in peer-reviewed journals pertaining to a similar cohort of patients. The objective of the study was to evaluate the safety and feasibility of the Wingspan Stent System with Gateway PTA Balloon Catheter for the treatment of symptomatic atherosclerotic lesions in the intracranial arteries. Patients were evaluated with a neurological examination and cerebral angiography preoperatively, with a cerebral angiography immediately postoperatively, with a neurological examination prior to hospital discharge and at 30-day follow-up, and with a neurological examination and cerebral angiography at 6 months post-procedure.

The primary safety endpoint was composite ipsilateral stroke/death at 30 days. Changes in the target vessel were evaluated angiographically. Procedure success was defined as Stent success without stroke or death at discharge. Safety was evaluated by the incidence of adverse events at discharge, 30-day follow-up, and 6-month follow-up.

The study was considered complete, with respect to the primary endpoint, after 30 evaluable patients completed the 30-day follow-up evaluation. However, all enrolled patients were to have a follow-up digital subtraction angiogram and neurological exam at 6 months. Evaluable patients were those who met eligibility requirements for primary endpoint assessment and who received a Stent.

Patient Data Available

Of the 45 patients enrolled, 44 were treated with the Wingspan Stent System with Gateway PTA Balloon Catheter and were considered evaluable patients. All 45 patients were followed through discharge. One patient was enrolled but not treated due to problems with access through the patient's tortuous anatomy. One patient died ten days post-procedure from cerebral hemorrhage, and 44 were followed through 30-day follow-up. Of these, 42 patients were followed through 6 months with clinical and neurological examinations, and 40 patients were followed through 6 months with post-operative angiographic assessment of the treated lesions. Patient demographics are listed in **Table 4**, patient neurological history is listed in **Table 5**, and patient medical history is listed in **Table 6**.

Table 4 – Patient Demographics

Patient Characteristics	N=45
Age (Years)	
Mean ± SD	66 ± 8
Median	65
Range (min, max)	47 , 81
Male	73.3% (33/45)
Ethnicity	
Caucasian	73.3% (33/45)
Asian	26.7% (12/45)

Table 5 – Neurological History

Neurological History	N=45	
	N	%
Stroke	43	95.6
Transient Ischemic Attacks	13	28.9
Other Neurological Diseases	35	77.8

Table 6 – Medical History

Medical History	N=45	
	N	%
Hypertension	41	91.1
Hypercholesterolemia/Hyperlipidemia	26	57.8
Smoking	24	53.3
Diabetes	24	53.3
Angina/Coronary Artery Disease	10	22.2
Peripheral Artery Disease	6	13.3
Arrhythmia	4	8.9
Congestive Heart Failure	3	6.7
Renal Failure	2	4.4
Myocardial Infarction	1	2.2
Liver Dysfunction	1	2.2

Table 7 summarizes the data from the investigators regarding lesion locations. A total of 44 intracranial atherosclerotic lesions were treated in 45 patients. Twenty-three (51.1%) of the lesions were located in the anterior circulation, and 22 (48.9%) were located in the posterior circulation.

Table 7 – Lesion Location

Location	N=45	
	N	%
Carotid petrous artery	5	11.1
Carotid cavernous artery	4	8.9
Carotid ophthalmic artery	1	2.2
Posterior communicating artery	1	2.2
Supraclinoid carotid artery	1	2.2
Carotid bifurcation	1	2.2
Middle cerebral artery (M1)	10	22.2
Vertebral artery	13	28.9
Basilar trunk	9	20
Total	**45**	**100**

Primary Safety Endpoints

The results of the study indicated that the Gateway PTA Balloon Catheter could be inflated safely to dilate the lesion, and the Stent could be deployed safely across the target lesion (44/45 lesions, 97.8% successfully accessed). The primary endpoints for safety were composite ipsilateral stroke or death at 30 days. The data are presented below for the evaluable patient populations (N=44) in **Table 8**.

Table 8 – Primary Endpoints: Stroke or Death (Evaluable Patients)

Endpoints (30 Day)*	(N=44)	
	N	%
Death or Ipsilateral stroke** (composite)	2	4.5
Major Ipsilateral stroke#	2	4.5
Death	1	2.3

* Results were based on adjudication by the Clinical Events Committee (CEC)

** Ipsilateral stroke is defined as events that occurred in the same hemisphere of the target lesion

Major stroke is defined as NIHSS ≥15, MRS ≥4, or BI ≤60, where NIHSS is the National Institute of Health Stroke Scale, MRS is Modified Rankin Scale, and BI is Barthel Index

Secondary Endpoints

The secondary endpoints in this study include incidence of parent vessel dissection, symptomatic restenosis, Stent migration, access site complications requiring treatment, and clinical outcomes of stroke and death at 6 months. No parent vessel dissections or Stent migration were reported at immediate post-implant or at 6-month follow-up. There were four reported incidents of access site complications requiring treatment. Five patients developed seven access site-related adverse events, but only four events required treatment.

Table 9 summarizes the secondary endpoints for safety of composite ipsilateral stroke or death at 6-month follow-up. A total of 42 patients had 6-month follow-up and are included in this analysis.

Table 9 – Incidence of Stroke or Death at 6-Month Follow-Up (Clinical Follow-Up)

Endpoints at 6 Months (Evaluable Patients)*	(N = 42)**	
	N	%
Death or ipsilateral stroke (composite)	3	7.1
Ipsilateral stroke#	3	7.1
Major ipsilateral stroke+	2	4.8
Minor ipsilateral stroke	1	2.4
Contralateral stroke	1	2.4
Major contralateral stroke+	1	2.4
Minor contralateral stroke	0	0.0
Death	1	2.4
All-cause stroke	4	9.5
Major all-cause stroke+	3	7.1
Minor all-cause stroke	1	2.4

* Results were based on adjudication by the Clinical Events Committee CEC

** At 6 months, 2 of the 44 patients were lost to follow-up

Ipsilateral stroke is defined as events that occurred in the same hemisphere of the target lesion

+ Major stroke is defined as NIHSS ≥15, MRS ≥4, or BI ≤60 where NIHSS is the National Institute of Health Stroke Scale, MRS is Modified Rankin Scale, and BI is Barthel Index

Table 10 below compares the angiographic results between treatment and 6-month follow-up. At trial's end, 40 patients were examined angiographically at 6 months.

Table 10 – Angiographic Treatment Results at 6-Month Follow-Up

Measure	Baseline (N=45)	Post PTA (N=44)	Post Stent (N=44)	6 Months* (N=40)
Reference Vessel Diameter (mm)				
Mean ± SD	3.1 ± 0.8	3.2 ± 0.8	3.2 ± 0.8	3.1 ± 0.8
Median	3.1	3.2	3.2	3.1
Range (min, max)	(1.3 , 4.8)	(1.3 , 4.8)	(1.3 , 4.8)	(1.3 , 4.8)
MLD at Target Lesion (mm)**				
Mean ± SD	0.8 ± 0.6	1.6 ± 0.6	2.1 ± 0.5	2.2 ± 0.8
Median	0.8	1.6	2.0	2.1
Range (min, max)	(0.0 , 2.0)	(0.5 , 2.9)	(1.3 , 3.2)	(0.4 , 4.0)
Gain in MLD from Baseline (mm)				
Mean ± SD		-0.8 ± 0.6	-1.3 ± 0.6	-1.4 ± 0.7
Median		-0.7	-1.2	-1.4
Range (min, max)		(-3.0 , 0.2)	(-3.5 , -0.2)	(-3.5 , -0.0)
% Stenosis				
Mean ± SD	74.9 ± 9.8	50.0 ± 16.2	31.9 ± 13.6	28.0 ± 23.2
Median	75.0	53.0	33.0	30.0
Range (min, max)	(57.0 , 99.0)	(0.0 , 79.0)	(-8.0 , 49.0)	(-33.0 , 81.0)
Change in % Stenosis from Baseline				
Mean ± SD		24.8 ± 19.5	43.0 ± 18.6	47.8 ± 25.6
Median		22.5	39.0	42.0
Range (min, max)		(-5.0 , 88.0)	(18.0 , 107.0)	(2.0 , 116.0)
≥50% Stenosis	100% (45/45)	54.5% (24/44)	0.0% (0/44)	7.5% (3/40)

* Of the 44 evaluable patients, 40 patients were available for angiographic follow-up
** MLD – Minimum Lumen Diameter

A comparison of the stroke rates in the SSYLVIA study to those in the Wingspan study are summarized in **Table 11**. The SSYLVIA study was a prospective, single arm study of angioplasty and balloon expandable stenting of intracranial atherosclerotic disease in patients with a history of stroke or TIA. From the small number of patients studied, it appears that the Wingspan study results are similar to those reported for the SSYLVIA study.

Table 11 –Stroke Rate Comparison (SSYLVIA[1] vs. Wingspan)

Clinical Study	Follow-Up	All Stroke	Death	All Stroke and Death	Ipsilateral Stroke
SSYLVIA n=61	Mean: 216 days (n=48 at 6 months)	13.1% (8/61)	6.6% (4/61)	13.1% (8/61)	11.5% (7/61)
Wingspan n=45	Mean: 174 days (n=42 at 6 months)	9.5% (4/42)	2.4% (1/42)	9.5% (4/42)	7.1% (3/42)

XI. RISK/PROBABLE BENEFIT ANALYSIS

Recurrent stroke attributable to intracranial atherosclerosis refractory to medical therapy is associated with a poor prognosis. The poor prognosis is related to additional strokes and clinical events due to atherosclerosis. Mechanisms for these additional strokes include reduced blood flow secondary to decrease in arterial diameter and arterial to arterial embolism based on plaque morphology. The probable benefit of this device is an increase in diameter of atherosclerotic arteries.

Extensive mechanical testing was performed on the Wingspan Stent with Gateway PTA Balloon Catheter as a system, as well as on the individual components. All tests met the stated acceptance criteria. The system was demonstrated to be biocompatible. Animal model testing provided evidence that the Gateway PTA Balloon Catheter could be safely inflated, and the Wingspan Stent System could be safely deployed and implanted in the animal model. There was no angiographic evidence of parent vessel stenosis or flow abnormalities observed in the acute or chronic follow-up evaluations in the animal model.

The Wingspan clinical study treated 45 patients with symptomatic atherosclerotic lesions in intracranial arteries who were refractory to medical therapy. The lesions were pre-dilated and stented. Clinical follow-up (42 patients) and angiographic follow-up (40 patients) were performed at 6 months. The type and frequency of observed adverse events including stroke are consistent with or lower than similar neurovascular procedures.

Therefore, it is reasonable to conclude that the probable benefit to health from using the Wingspan Stent System with Gateway PTA Balloon Catheter for treating intracranial stenosis 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 Wingspan Stent System with Gateway PTA Balloon Catheter will not expose patients to an unreasonable or significant risk of illness or injury, and the probable benefit to health from using the System for improving cerebral artery lumen diameter in patients with intracranial atherosclerotic disease, refractory to medical therapy, in intracranial vessels with $\geq$50% stenosis that are accessible to the system outweighs the risks of illness or injury, and issued an approval order on _____.

XIV. APPROVAL SPECIFICATIONS

Indications for Use: See *Instructions for Use* (Attachment 1)

Information for the Patient: See *Patient Brochure* (Attachment 2)

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the *Instructions for Use* (Attachment 1).

XV. REFERENCES

1. Food and Drug Administration, CDRH SSYLVIA Study NEUROLINK® System Summary of Safety and Probable Benefit page. Available at: http://www.fda.bov/cdrh/pdf/H010004b.pdf . Accessed January 19, 2005.