Summary of Safety & Effectiveness Data

I. General Information

Device Generic Names:	Carotid Stent
Device Trade Names:	Cordis PRECISE® Nitinol Stent System (5.5 Fr and 6.0 Fr sizes, over-the-wire configuration)
Applicant's Name & Address:	Cordis Corporation 7 Powder Horn Drive P.O. Box 4917 Warren, New Jersey 07059
Premarket Approval Application (PMA) Number:	P030047
Date of Panel Recommendation:	April 21, 2004
Date of Notice of Approval To Applicant:	September 22, 2006

II. Indications for Use

The Cordis PRECISE Nitinol Stent System used in conjunction with the ANGIOGUARD™ XP Emboli Capture Guidewire is indicated for the treatment of patients at high risk for adverse events from carotid endarterectomy who require carotid revascularization and meet the criteria outlined below.

1. Patients with neurological symptoms and ≥50% stenosis of the common or internal carotid artery by ultrasound or angiogram **OR** patients without neurological symptoms and ≥80% stenosis of the common or internal carotid artery by ultrasound or angiogram, **AND**

2. Patients must have a vessel diameter of 4-9mm at the target lesion. The vessel distal to the target lesion must be within the range of 3mm and 7.5mm to allow for placement of the ANGIOGUARD XP Emboli Capture Guidewire.

III. Contraindications

The Cordis PRECISE Nitinol Stent System is contraindicated in the following patients:

1. Patients in whom antiplatelet and or anticoagulation therapy is contraindicated.
2. Patients in whom the guide catheter is unable to be placed.

3. Patients with uncorrected bleeding disorders.
4. Patients with known allergies to nitinol.
5. Lesions in the ostium of the common carotid artery.

IV. Warnings and Precautions

Warnings and Precautions can be found in the Cordis PRECISE Nitinol Stent System Instructions for Use.

V. Device Description

The Cordis PRECISE Nitinol Stent System devices are designed to deliver a flexible, self-expanding endoluminal stent to the carotid vasculature via over-the-wire (OTW) 5.5F or 6Fsheathed delivery systems. The stent is cut from a solid nitinol tube into a fine mesh ("Z" configuration) design. The delivery systems consist mainly of an inner shaft and an outer sheath with radiopaque markers, and a Tuohy Borst valve. The inner shaft terminates distally in a catheter tip and originates proximally in a luer hub designed to accept a 0.018" guidewire. The delivery systems have a nominal working length of 135 cm. The self-expanding PRECISE stent is constrained within the space between the inner shaft and the outer sheath, located between distal and proximal stent markers on the inner shaft. The stent expands to its unconstrained diameter when released from the deployment catheter into the carotid artery. Upon deployment, the stent forms an open lattice and pushes outward on the luminal surface, helping to maintain the patency of the artery.

Due to the self-expanding behavior of nitinol, the stents are indicated for placement into vessels that are 1-2mm smaller in diameter than the unconstrained diameter of the stent. PRECISE product codes are presented in **Table 1**.

Table 1 - PRECISE Catalog Codes

135 cm SDS (.018 guidewire lumen)		Stent Length (mm)		
		20	30	40
SDS Profile	Stent Diameter (mm)			
5.5F	5	P05020XC	P05030XC	P05040XC
5.5F	6	P06020XC	P06030XC	P06040XC
5.5F	7	P07020XC	P07030XC	P07040XC
5.5F	8	P08020XC	P08030XC	P08040XC
6F	9	P09020XC	P09030XC	P09040XC
6F	10	P10020XC	P10030XC	P10030XC
5.5F	6-8 (Tapered)	[redacted]	P68T30XC	[redacted]
6F	7-9 (Tapered)		P79T30XC	
6F	7-10 (Tapered)		P79T40XC	

VI. Alternative Practices and Procedures

Treatment of carotid artery disease (CAD) currently includes surgery, medical therapy, or a combination of both. The primary treatment used to prevent stroke in patients with significant CAD is surgery (endarterectomy) to remove plaque from the affected artery.

Medical therapy includes use of antiplatelet and/or anticoagulant medicine, as well as antihypertensive and antilipidemic drugs as indicated. Antiplatelet drugs include aspirin, Plavix® (clopidogrel), or Ticlid® (ticlopidine). Anticoagulants include Coumadin® (warfarin). Medical therapy can also include modification of lifestyle risk factors for stroke, such as cigarette smoking and alcohol use.

VII. Marketing History

PRECISE is marketed for carotid use in Europe, Asia Pacific, Middle East, Latin America, and South Africa. The PRECISE device has not been withdrawn from marketing for any reason relating to safety or effectiveness.

VIII. Adverse Effects of the Devices on Health

A. Observed Adverse Events - Cordis' pivotal clinical investigation (SAPPHIRE Study) included randomized arms, comparing stenting with distal protection to carotid endarterectomy (CEA), a non-randomized stent arm for patients who met the entry criteria, but were determined by the vascular surgeon not to be surgical candidates, and a non-randomized CEA arm for patients who met the entry criteria, but were determined by the interventionalist not to be candidates for stent treatment. Adverse events occurring out to 360 days in the randomized and non-randomized stent arms of the study are provided in **Table 3**. Differences in 30-day event rates in-hospital vs. out-of-hospital for major adverse events (MAE) and Transient Ischemic Attack (TIA) are also provided in **Table 3**, which follows. Please note that all bradycardia and hypotension events occurred in-hospital. Non-randomized CEA patient event rates are not provided in the table since only seven patients were enrolled in that study arm and the data are insufficient for statistical analysis. For informational purposes, the MAE rate for non-randomized CEA patients to 360 days was 14.3% (1/7).

Table 3. Adverse Events to 360 Days – Randomized and Non-Randomized Patients

30-Day Complications (In-Hospital vs. Out-of-Hospital)	Randomized Stent (N=167)		Randomized CEA (N=167)		Non-Randomized Stent (N=406)	
	In Hosp	Out of Hosp	In Hosp	Out Hosp	In Hosp	Out Hosp
MAE[1]	4.2% (7)	1.2% (2)	7.2% (12)	3.0% (5)	3.2% (13)	3.7% (15)
Death (All Cause)	0.0% (0)	1.2% (2)	1.2% (2)	1.2% (2)	1.2% (5)	1.0% (4)
Myocardial Infarction (Q or Non-Q)	2.4% (4)	0.0% (0)	4.8% (8)	1.2% (2)	1.0% (4)	0.7% (3)
Stroke	3.6% (6)	0.0% (0)	2.4% (4)	0.6% (1)	2.5% (10)	2.5% (10)
Transient Ischemic Attack (TIA)	3.6% (6)	0.0% (0)	2.4% (4)	0.0% (0)	3.2% (13)	2.2% (9)

30-Day Complications	Randomized Stent (N=167)	Randomized CEA (N=167)	P-value*	Non-Randomized Stent (N=406)
MAE[1]	4.8% (8)	9.6% (16)	0.14	6.9% (28)
Death (All Cause)	1.2% (2)	2.4% (4)	0.68	2.2% (9)
Myocardial Infarction (Q or Non-Q)	2.4% (4)	6.0% (10)	0.17	1.7% (7)
Q Wave MI	0.0% (0)	1.2% (2)	0.50	0.2% (1)
Non-Q Wave MI	2.4% (4)	4.8% (8)	0.38	1.5% (6)
Stroke	3.6% (6)	3.0% (5)	>0.99	4.9% (20)
Major Ipsilateral Stroke	0.6% (1)	1.2% (2)	>0.99	2.5% (10)
Major Non-Ipsilateral Stroke	0.6% (1)	0.6% (1)	>0.99	0.5% (2)
Minor Ipsilateral Stroke	2.4% (4)	0.6% (1)	0.37	1.7% (7)
Minor Non-Ipsilateral Stroke	0.6% (1)	0.6% (1)	>0.99	0.5% (2)
Transient Ischemic Attack (TIA)	3.6% (6)	2.4% (4)	0.75	5.4% (22)
Target Lesion Revascularization	0.0% (0)	0.0% (0)	-	0.5% (2)
Surgery	0.0% (0)	0.0% (0)		0.0% (0)
PTA	0.0% (0)	0.0% (0)		0.5% (2)
Target Vessel Revascularization not involving Target Lesion	0.0% (0)	0.0% (0)	-	0.0% (0)
Surgery	0.0% (0)	0.0% (0)		0.0% (0)
PTA	0.0% (0)	0.0% (0)		0.0% (0)
Stent Thrombosis	0.0% (0)	0.0% (0)	-	0.7% (3)
Major Bleeding[2]	9.0% (15)	10.2% (17)	0.85	12.8% (52)
Cranial Nerve Injury	0.0% (0)	4.2% (7)	0.01	0.0% (0)
Severe Hypotension	17.4% (29)	3.0% (5)	<0.01	15.0% (61)
Bradycardia	8.4% (14)	3.0% (5)	0.06	3.2% (13)
Vascular Complications[3]	5.4% (9)	N/A	-	2.5% (10)
Device/Procedure Related Adverse Events[4]	0 (0.0%)	-	-	0.0% (0)

31 to 360-Day Complications[5]	Randomized Stent (N=165)[5]	Randomized CEA (N=163)[5]	P-value*	Non-Randomized Stent (N=39[illegible][5]
MAE[1]	7.3% (12)	12.3% (20)	0.14	10.6% (42)
MAE without Non-Neurologic Deaths from 31-360 days[6]	1.2% (2)	3.7% (6)	0.17	4.0% (16)
Death (All Cause)	6.1% (10)	10.4% (17)	0.16	8.1% (32)
Myocardial Infarction (Q or Non-Q)	0.6% (1)	1.8% (3)	0.37	1.0%(4)
Q Wave MI	0.0% (0)	0.0% (0)	-	0.3% (1)
Non-Q Wave MI	0.6% (1)	1.8% (3)	0.37	0.8% (3)
Stroke	2.4% (4)	4.9% (8)	0.26	4.3% (17)
Major Ipsilateral Stroke	0.0% (0)	1.8% (3)	0.12	0.8% (3)
Major Non-Ipsilateral Stroke	0.0% (0)	0.6% (1)	0.50	0.8% (3)
Minor Ipsilateral Stroke	1.2% (2)	1.2% (2)	>0.99	2.3% (9)
Minor Non-Ipsilateral Stroke	1.2% (2)	1.8% (3)	0.68	0.5% (2)
Transient Ischemic Attack (TIA)	3.0% (5)	0.6% (1)	0.21	1.8% (7)
Target Lesion Revascularization	0.6% (1)	3.7% (6)	0.07	0.3% (1)
Surgery	0.6% (1)	0.6% (1)	>0.99	0.0% (0)
PTA	0.0% (0)	3.1% (5)	0.03	0.3% (1)
Target Vessel Revascularization not involving Target Lesion	0.0% (0)	0.0% (0)	-	0.0% (0)
	0.0% (0)	0.0% (0)	-	0.0% (0)
Surgery	0.0% (0)	0.0% (0)	-	0.0% (0)
PTA				
Stent Thrombosis	0.0% (0)	0.0% (0)	-	0.0% (0)
Major Bleeding[2]	0.0% (0)	0.0% (0)	-	0.5% (2)
Cranial Nerve Injury	0.0% (0)	0.6% (1)	-	0.0% (0)
Severe Hypotension	0.6% (1)	0.0% (0)	0.99	0.8% (3)

Bradycardia	0.0% (0)	0.0% (0)	-	0.3% (1)
Vascular Complications[3]	0.0% (0)	N/A	-	0.0% (0)
Device/Procedure Related Adverse Events[4]	0.0% (0)	0.0% (0)	-	0.0% (0)
Combined Complications to 360 Days	**Randomized Stent (N=167)**	**Randomized CEA (N=167)**	**P-value***	**Non-Randomized Stent (N=406)**
MAE [1]	12.0% (20)	19.2% (32)	0.10	15.8% (64)
MAE without Non-Neurologic Deaths from 31 days to 360 days[6]	6.0% (10)	12.6% (21)	0.06	10.3% (42)
Death (All Cause)	7.2% (12)	12.6% (21)	0.14	10.1% (41)
Myocardial Infarction (Q or Non-Q) Q Wave MI Non Q-Wave MI	3.0% (5) 0.0% (0) 3.0% (5)	7.2% (12) 1.2% (2) 6.0% (10)	0.13 0.50 0.29	2.7% (11) 0.5% (2) 2.2% (9)
Stroke	6.0% (10)	7.2% (12)	0.83	9.1% (37)
Major Ipsilateral Stroke	0.6% (1)	3.0% (5)	0.21	3.2% (13)
Major Non-Ipsilateral Stroke	0.6% (1)	1.2% (2)	1.00	1.2% (5)
Minor Ipsilateral Stroke	3.6% (6)	1.8% (3)	0.50	3.9% (16)
Minor Non-Ipsilateral Stroke	1.8% (3)	2.4% (4)	1.00	1.0% (4)
Transient Ischemic Attack (TIA)	6.6% (11)	3.0% (5)	0.20	6.9% (28)
Target Lesion Revascularization Surgery PTA	0.6% (1) 0.6% (1) 0.0% (0)	3.6% (6) 0.6% (1) 3.0% (5)	0.12 1.00 0.06	0.7% (3) 0.0% (0) 0.7% (3)
Target Vessel Revascularization not involving Target Lesion Surgery PTA	0.0% (0) 0.0% (0) 0.0% (0)	0.0% (0) 0.0% (0) 0.0% (0)	- - -	0.0% (0) 0.0% (0) 0.0% (0)
Stent Thrombosis	0.0% (0)	0.0% (0)	-	0.7% (3)
Major Bleeding[2]	9.0% (15)	10.2% (17)	0.85	13.3% (54)
Cranial Nerve Injury	0.0% (0)	4.8% (8)	0.01	0.0% (0)
Severe Hypotension	17.4% (29)	3.0% (5)	0.00	15.5% (63)
Bradycardia	8.4% (14)	3.0% (5)	0.06	3.4% (14)
Vascular Complications[3]	5.4% (9)	N/A	-	2.5% (10)
Device/Procedure Related Adverse Events[4]	0.0% (0)	0.0% (0)	-	0.0% (0)

Numbers are % (counts/sample size)

*P-value displayed refers to comparison of randomized arms.

(1) Major Adverse Events (MAE) = Death, MI or stroke to 30 days and death or ipsilateral stroke from 31-360 days.

(2) Major Bleeding: Any non-access site related bleeding resulting in a 25% or more decline in HCT or requiring transfusion

(3) Vascular Complications: Events related to bleeding or vascular injury at the percutaneous access site.

(4) There were no device or procedure related events. In 17 of 19 initial stent delivery failures, a subsequent attempt was successful. In one case, the patient was treated with CEA. In the other case, the patient was treated with balloon angioplasty alone. One stent fracture was noted from one-year ultrasound films, with no adverse effect to the patient.

(5) Rates minus patient deaths to 30 days.

(6) MAE without Non-Neurological Deaths >31 Days – The vast majority of deaths occurring from 31 days to 360 days were attributed to the co-morbidities of this high-risk population. The 'adjusted' 360 day MAE rate includes all cause death, MI and all strokes to day 30, and ***only Neurologic*** deaths and ipsilateral strokes from days 31-360.

Table 3A - Causes of Death through 360 Days*

Cause of Death	Randomized Stent	Randomized CEA	Non-Randomized Stent
Neurologic	1	3	8
Cardiac	8	10	18
Respiratory Failure	1	3	4
Cancer	2	1	5
Renal Failure	0	1	1
Multi-System Failure	0	3	2
Exsanguination	0	0	1
Unknown	0	0	2

* None of the deaths were attributed to the device or the procedure

B. Potential Adverse Events - Adverse events that may be associated with carotid artery stenting procedures include, but may not be limited to:

Air embolism
Allergic/anaphylactoid reaction
Aneurysm
Angina/coronary ischema
Arrhythmia (including bradycardia, possibly requiring need for temporary or permanent pacemaker)
Arterial occlusion/restenosis of the treated vessel
Arterial occlusion/thrombus - at puncture site
Arterial occlusion/thrombus – remote from puncture site
Arteriovenous fistula
Bacteremia or septicemia
Cerebral edema
Damage to emboli capture device
Damage to the implanted stent(s)
Death
Embolization, arterial
Embolization, stent
Emergent repeat hospital intervention
Fever
GI bleeding from anticoagulation/antiplatelet medication
Hematoma bleed – puncture site
Hematoma bleed – remote site
Hemorrhage
Hyperperfusion syndrome
Hypotension/hypertension
Infection
Intimal injury, dissection
Ischemia/infarction of tissue/organ
Local infection and pain at insertion site
Malposition (failure to deliver stent or deploy filter basket of emboli capture guidewire at intended site)
Myocardial infarction
Pain
Pseudoaneurysm
Renal failure
Restenosis of the vessel (≥50% obstruction)
Seizure
Severe unilateral headache
Stent migration
Stent Thrombosis
Stroke
Transient ischemic attack
Vasospasm

Venous occlusion/thrombosis – at puncture site
Venous occlusion/thrombosis – remote from puncture site
Vessel rupture, dissection, perforation

C. Device Delivery

Randomized Arm: Procedure success was 88.1% (140/159). Device (stent) success was 91.2% (145/159). ANGIOGUARD success was 95.6% (152/159).

Non-Randomized Arm: Procedure success was 87.9% (355/404). Device (stent) success was 89.6% (363/405). ANGIOGUARD success was 91.6% (372/406).

IX. Summary of Non-Clinical Laboratory Studies

There are two versions of the Cordis PRECISE Nitinol Stent System. The 5.5F system, which delivers 5, 6, 7, & 8mm diameter x 20, 30, & 40mm long straight stent sizes, and a 6-8mm diameter x 30mm long tapered stent size, and the 6F system, which delivers 9 & 10mm diameter x 20, 30, & 40mm long straight stents and 7-9mm & 7-10mm diameter x 30mm long tapered stent sizes.

Section IX(A) of this summary provides non-clinical data to support all sizes of the Cordis PRECISE Nitinol Stent Systems.

A. Cordis PRECISE - The following summarizes pre-clinical studies supporting the Cordis PRECISE Nitinol Stent System. During the course of clinical testing, minor delivery system design modifications were made. Also, 5mm diameter stent sizes and tapered stent sizes were added to the study. The sponsor performed appropriate testing to address each change/addition.

5.5F PRECISE Product (Bench) Testing/Evaluations

5.5F PRECISE Reliability Analysis/Product Performance Qualification (PPQ) Testing - 5.5F PRECISE was qualified and met the requirements outlined in **Table 4** via reliability analysis. Straight stent sizes were included in the qualification. Additional PPQ testing was conducted after a minor change to the raw tubing size used for 5-8mm stents (final dimensions remained the same). Results met acceptance criteria noted in **Table 4** for characteristics that could be affected by the change (SDS preparation, visuals, deployment, uniformity & outer diameter (OD), length & flare, radial resistive and chronic outward forces (RRF and COF).

5.5F PRECISE PPQ Testing (Minor Manufacturing Change) – Additional PPQ testing of relevant characteristics (visual inspection, marker band placement, deployment) was conducted to address minor manufacturing changes. Requirements outlined in **Table 4** were met. Marker band placement criteria were slightly modified (see current requirements in **Table 4**) and additional testing verified acceptability of the new marker band placement requirements.

5.5F PRECISE 6-8x30mm Tapered Stent Testing - Design verification testing of tapered 5.5F PRECISE Stents was conducted. Characteristics that could be impacted by use of a tapered stent (deployment, visuals, uniformity & OD, length & flare, RRF and COF) were evaluated. Results concluded the tapered stent met established performance criteria (per **Table 4**).

6F PRECISE Product (Bench) Testing

6F PRECISE PPQ Testing/Reliability Assessment – 6F PRECISE OTW was qualified and met requirements outlined in **Table 4** via PPQ testing and reliability assessment. Straight stent sizes were included in the qualification. Additional PPQ testing was conducted to address a minor manufacturing change. The marker band placement specification requirement was slightly increased. Results met acceptance criteria outlined in **Table 4** for those characteristics that could be affected by the manufacturing and marker band placement requirement changes (visual inspection, current marker band placement, delivery system preparation, stent pre-deployment).

6F PRECISE Test Report for Tapered Stents: Design verification of tapered PRECISE stents used in the 6F delivery system was conducted. Characteristics that could be impacted by use of a tapered stent (deployment, visuals, uniformity and OD, length & flare, RRF and COF) were evaluated. Results concluded the tapered stents met requirements (per **Table 4**) and the criteria specific to the tapered stent design (below).

OD: 7-9x30mm Tapered Stent – 7.0mm Distal, 9.0mm Proximal
7-10x30mm Tapered Stent – 7.0mm Distal, 10.0mm Proximal
All OD's must be within +0.75mm/-0.50mm

Flare: Stent ends must be parallel to or outside the tapered profile and must not protrude into the lumen of the stent.

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Table 4
5.5F and 6F PRECISE Acceptance Criteria

Test	5.5F PRECISE Acceptance Criteria	6F PRECISE Acceptance Criteria
Visual	Carton free of gross damage (crushed areas, severely bent areas and torn or cut areas); No rips, tears, or puncture in pouches; Body of SDS contained within dispenser; Labeling matches router; No SDS surface damage, kinks, bends, marks, cuts, exposed braid wire, melted or collapsed tubing, loose contamination, or any other forms of damage; Hubs inspected for cracks or any other gross damage; Tip inspected at 10X for ragged edges, voids or other gross damage; & Inner member tip/brite tip junction cannulated.	Carton and tray free of gross damages; No rips, tears, open seals, channels, or punctures in pouches; Body of SDS contained within dispenser; No SDS surface damage, kinks, bends, marks, cuts, exposed braid wire, melted or collapsed tubing, loose or imbedded/affixed contamination; Hubs inspected for cracks or any other gross damage; Inner member tip inspected for ragged edges, voids, or other gross damage; Inner member tip/brite tip junction cannulated; ID Band for proper stent size or non-uniformity of ID band shrinkage and clear-legible print.
SDS Dimensional (nominal)	Overall length: 161.5; Usable length: 135 cm; Trailing end OD: .062"; Leading end OD: .070" Tip OD: Pass a .073" hole with ≤ .075 lbs. pressure Marker Band Placement: 20mm Previous ≤22.8mm Current ≤23.3mm; 30mm ≤34.6mm ≤35.1mm; 40mm ≤46.4mm ≤46.9mm	Overall length: 161.5; Usable length: 135 cm; Trailing end OD: .066"; Leading end OD: .079" Tip OD: Pass a .073" hole with ≤.075 lbs. pressure Marker Band Placement: 20mm Previous ≤22.1mm Current ≤22.6mm; 30mm ≤32.8mm ≤33.3mm; 40mm ≤43.4mm ≤43.9mm
Expanded Stent Length & Flare (nominal)	Lengths: 5x20mm – 21.3mm; 6x20mm – 20.9mm; 7x20mm – 20.4mm; 8x20mm – 19.9mm; 5x30mm – 32.8mm; 6x30mm – 32.2mm; 7x30mm – 31.5mm; 8x30mm – 30.6mm; 5x40mm – 44.4mm; 6x40mm – 43.5mm; 7x40mm – 42.6mm; 8x40mm – 41.4mm Stent Flare: OD of the ends (flare) shall be larger than the stent OD	Lengths: 8x20mm – 20.5mm 9x30mm – 30.2mm 10x40mm – 39.0mm Stent Flare: OD of the ends (flare) shall be larger than the stent OD
SDS Preparation	Confirmation of fluid flow from guidewire lumen distal tip, from rear of hemostasis valve, & from outer member distal tip for delivery system lumen. Guidewire should move easily and without difficulty.	
Stent Deployment Force	≤5.0 lb.	
Deployed Stent Visual	No damaged or broken struts.	
Deployed Stent Uniformity	[x-y] absolute value diameter measurements not greater than 1.25mm at any single location.	
Deployed Stent OD	Nominal diameter	
RRF/COF	Radial Resistive Force (RRF) – Greater than 0.90 N/cm Chronic Outward Force (COF) – Less than 0.75 N/cm	

Test	5.5F PRECISE Acceptance Criteria	6F PRECISE Acceptance Criteria
Hypotube/Wire Lumen/Tip Pull	>0.67 lb.	
Hub/Hypotube Pull	≥2.2 lbs.	
Outer Member Hub Pull	≥5.0 lbs.	
Brite Tip/TT1 Fuse Joint Pull	≥2.2 lbs.	
TT2/Body Fuse Joint Pull	≥5.0 lbs.	
TT2/TT1 Fuse Joint Pull	≥3.4 lbs.	≥5.0 lbs.
Body Elongation	≥5.0 lbs. at the 0.2" displacement point	≥5.0 lbs. at 5% strain
Body/TT2 Elongation	≥3.4 lbs. at 0.15" displacement point	≥5.0 lbs. at 5% strain
Hypotube/Coil/Coil Sleeve/Stop Compression	Inner member must be capable of compressing ≥3.75 lbs. without separation.	Inner member must be capable of compressing ≥5.00 lbs. without separation. Stop pull force must be ≥ 0.7 lb.

Stent-Specific Testing

The testing presented in **Table 5**, which follows, was conducted to demonstrate properties and characteristics of PRECISE stents.

Table 5 – Stent-Specific Testing

Test/Evaluation	5-8mm PRECISE Stents (Including Tapered Stents)	9 and 10mm diameter PRECISE Stents (Including Tapered Stents)
Mechanical & Thermal Properties	Nitinol tubing was assessed to demonstrate no critical changes to mechanical properties. Data analysis confirmed that tubing data follow expected shape memory and super-elastic behavior similar to wire (see 9 & 10mm results). There was an expected increase in plateau strength with decrease in nominal Af, with no critical changes in tensile strength or ductility.	Nitinol stent material was assessed for mechanical & shape memory properties for use in its intended application. Assessment conducted on nitinol wire heat-treated to achieve nominal Af of 6F PRECISE. Results demonstrated satisfactory tensile properties. tensile strain properties, tensile thermal properties, compression, visual transformation and transformation temperatures of nitinol wire.
Finite Element Analyses	Multiple analyses were conducted: -FEA considered strain & safety 5.5F PRECISE stents (5-8mm diameters x 20, 30, and 40mm lengths) & analyzed worst-case condition of the 8x30mm stent in 6mm vessel to obtain mean and pulsatile fatigue parameters. Additional analysis was conducted for resistance to neck flexure & static bending strains. Safety factor was >1. -An analysis of 6-8x30 tapered stent was conducted. For each strain contribution, the 8x30mm PRECISE stent analysis can be used to estimate fatigue behavior of the tapered stent. -FEA conducted providing additional evidence that largest (8mm) diameter has the worst fatigue resistance and is therefore supportive of all 5.5F PRECISE stent sizes.	6F PRECISE Stents are identical to the SMART Stent in design, material, and dimensions and will experience the same *in-vivo* mean and alternating strains. Hence, FEA conducted on SMART supports 6F PRECISE stents. -Strain and safety of 6-10mm diameter stents in focal and bent configurations under pulsatile loading with 1 & 2mm of over-sizing was considered. Conditions represent higher forces than seen in carotid artery environment. Under these worst-case conditions, the safety factor was >1. -FEA conducted on 6F PRECISE Stents to calculate fatigue strains and safety factors based on carotid physiological conditions. FEA confirmed that under these conditions. stent has a safety factor >3. FEA also confirmed that largest diameter stent has worst-case fatigue characteristics.
Balloon Tacking	Testing of similar design SMART Stents demonstrated that post-deployment balloon tacking does not compromise stent or balloon. Stents were successfully tacked and after taking the balloon to burst, the stent is not adversely affected. 5.5F PRECISE stent testing confirmed that the minor dimensional differences of the stent do not negatively impact a balloon. Tacking was performed on the 8mm diameter stent because it has the largest amount of open area (to best expose the balloon to the stent edges). The stent did not compromise balloon performance when balloon tacking is performed after stent deployment.	Testing was conducted to assess balloon burst inside the 6F PRECISE stent; to confirm that balloon performance is not compromised by the presence of the stent; and to demonstrate that the balloon does not damage the stent. 10x40mm stents were tested because they have the largest open area (to best expose the balloon to the stent edges). Results confirmed that balloon tacking of the stent after deployment can be conducted without compromising the stent or the performance of the balloon.

Test/Evaluation	5-8mm PRECISE Stents (Including Tapered Stents)	9 and 10mm diameter PRECISE Stents (Including Tapered Stents)
Stent Corrosion	Nitinol corrosion properties were compared to 316L stainless steel. -Nitinol discs and stents show superior pitting resistance. -Corrosion rates are similar. -Lifetime of nitinol stents is significantly longer than 10 years. -Nitinol repassivation capacity is superior to 316L stainless steel. Tested stents were made from the same material & with similar processes as PRECISE Stents. Corrosion properties are not dependent on stent size. Hence, data support PRECISE Stents.	
MRI Compatibility	Literature review provided evidence that nitinol is MRI safe with minimal artifacts. Also, 5.5F PRECISE stents were tested per ASTM F2182-02A, F2213-02 and F2052. Results concluded that stents have <1°C temperature increase with exposure to RF application of a 1.5 Tesla MR scanner, no magnetically induced torque displacement forces were detected in a 1.5 Tesla environment, and stents are MR safe and compatible in a 1.5 Tesla MR scanner environment.	
AF Temperature Verification	Methods for verifying stent Af temperature conclude that stent Af temperature is accurately maintained through process controls and testing.	
Stent Recoil	Nitinol exerts residual outward force. There is no elastic recoil as with balloon-expandable stents.	
Stent Expansion	Nitinol stents are not plastically deformed during expansion and do not give rise to crack initiation.	
Flaw Size Detection	An analysis of SMART Stents determined the smallest surface imperfection detected during inspection. The same inspection methodology is used for PRECISE Stents. Since SMART and PRECISE are constructed of the same material and under similar processes, the results of the analysis are applicable to all PRECISE Stents.	
Crush Fatigue	5.5F PRECISE stents and SMART Stents (identical to 6F PRECISE Stents in design, material & dimensions) were crushed between two metal plates through 1,000 cycles; each cycle representing a worst-case condition in that the stent was crushed to within 2mm (nearly a complete closure) as opposed to being crushed in a complaint vessel without rigid support. Results demonstrated crush fatigue resistance.	
Pulsatile Fatigue	400 million cycle pulsatile fatigue testing was conducted on 5.5F and 6F PRECISE Stents and on SMART Stents (identical to 6F PRECISE Stents in design, material & dimensions). Results confirmed satisfactory fatigue characteristics to 400 million cycles.	
Length vs. Diameter	Calculations of changes in stent length as a function of stent diameter were conducted at diameters representing largest recommended vessel diameter (worst-case) for the particular stent in question. The method was verified against actual measurements in an earlier foreshortening analysis. Results demonstrated that foreshortening ranges from 1.2% to 6.2% for 5.5F PRECISE Stents and 4.1% to 8.0% for 6F PRECISE Stents, depending on diameter.	
Dimensional Verification	Inspection data demonstrated that all stent sizes meet dimensional specifications.	
Open Area	Analytical assessments determined stent open area to range from 83-89% for 5.5F PRECISE Stents and 85-88% for 6F PRECISE Stents.	
Stent Kinking	Testing confirmed stent resistance to kink or buckling while in a bent configuration & documented cross-sectional area as a function of bend radius. Results showed that stents do not kink and maintain cross-sectional area extremely well while constrained in a curvilinear shape.	

PRECISE Biocompatibility Testing

Biocompatibility testing was conducted on all the materials of construction of PRECISE after processing through all of the manufacturing steps, including sterilization. All testing, with the exception of Aqueous Extraction testing, was conducted in accordance with ISO 10993-1, the FDA Blue Book Memorandum dated May 1, 1995, and 21 CFR §58 (Good Laboratory Practices). The results of the testing demonstrate that all the materials are biocompatible and, hence, safe for human use.

PRECISE Shelf Life Testing

Product Shelf Life - Product testing was conducted to support a two-year expiration date on the Cordis PRECISE Nitinol Stent System. The results demonstrate that the PRECISE

systems comply with product specifications, quality characteristics, functional and safety requirements after two years of accelerated aging.

Package Shelf Life – Package testing supporting two-year package expiration date and package integrity for the S.M.A.R.T. product family, which includes PRECISE, was conducted. Testing was conducted on packaging containing S.M.A.R.T. product. This represents worst-case conditions as the product tested is heavier and has a higher profile. The tested packaging is slightly larger than that used for PRECISE, with only minor dimensional differences. Pouch sealing methods, seal width, and package materials are the same. After three cycles of sterilization, transportation testing, environmental conditioning, and two-year accelerated aging, the package was tested for visuals, package integrity, seal integrity, and pouch peel-ability. Results demonstrated that the packaging maintains integrity after two-years accelerated aging. Earlier aging testing to three years supports the thermal indicator that appears on the package. The results confirm stability of the thermal indicator to three years. Subsequent testing confirmed the transition temperature of the thermal indicator to be 60°C +/- 1°C.

PRECISE Sterilization EtO Residual Qualification

PRECISE is sterilized by ethylene oxide (EtO) sterilization. The sterilization validation provides documented evidence that the device, in the packaging evaluated, may be sterilized to a 10^{-6} Sterility Assurance Level (SAL) in the Cordis ethylene oxide sterilization process, validated per ISO 11135. EtO residual evaluations demonstrated that residual levels were below FDA maximum permissible levels for devices contacting blood and for implantable devices and were also below ISO specified levels.

PRECISE ANIMAL TESTING

Chronic Studies - Two chronic canine studies were conducted with similar design S.M.A.R.T. Stents, which are constructed of the same material and have the same performance requirements as PRECISE stents. S.M.A.R.T. stent dimensions are identical to 6F PRECISE Stents, and have only minor dimensional differences from 5.5F PRECISE stents. Hence, long-term safety results are applicable to PRECISE Stents. Separate acute animal studies (presented in **Table 6**) were conducted to evaluate PRECISE for stent deliver-ability and system performance.

The chronic studies evaluated early and late patency rates, healing response of the vessel to the device, endothelialization, changes in stent diameter with time, and overall function of the stent and delivery system. In one study, twelve canines were implanted with four stents each (into carotid, subclavian, and iliac arteries), with angiographic and other assessments at 2, 4, 13, and 26 weeks. In the other study, fifteen canines were implanted with a S.M.A.R.T. Stent in the left iliac artery, and evaluations were made at 48 hours, four weeks, and six and 12 months. The results showed the stent was successfully deployed, complete endothelialization occurred, patency was maintained without inflammation for up to 12 months, and stent diameters did not change significantly. Some slight media thinning observed at six months was not present at 12 months, and simply reinforces the Instructions for Use regarding correct stent sizing.

Acute Studies - Acute porcine studies conducted on PRECISE are presented in **Table 6**, which follows.

Table 6 – Acute PRECISE Studies in Porcine

Device	Implant Site	Assessments	Results
PRECISE (5.5F) 8x40mm stents (N=4)	Left & right subclavian, right carotid & left iliac	SDS/Stent performance (trackability, tip retrieval through stent, placement accuracy, deployment force, completeness of deployment, architecture & uniformity, radiopacity, & guidewire movement.	All attributes rated Good or Excellent
PRECISE 5.5F 6-8x30mm Tapered (N=12)	Left subclavian, left carotid & left femoral	Acute placement accuracy, 30-day stent migration, acute stent length & 30-day stent length	➢ Successful deployment ➢ No significant differences in stent length acutely and 30 days ➢ No stent migration when deployed in porcine anatomy closely matching intended human carotid bifurcation & placed in the recommended manner.
PRECISE 6F 10x40mm (N=3) 10x30mm (N=2) 7-10x30mm Tapered (N=2)	Left maxillary, left Maxillary, 1st Branch off right subclavian, left carotid	Preparation, ease of insertion, trackability, pushability, marker band radiopacity, flexibility, contrast flow, deployment force, placement accuracy, tip retrieval through stent, withdrawal over guidewire, withdrawal through guide catheter/sheath, stent radiopacity, deployment completeness, architecture, uniformity, balloon crossing & post-dilation, guidewire movement through stent, wall apposition of tapered stent	Acceptable results.

X. Summary of Clinical Studies

A. Objectives

The primary objective of the pivotal clinical study (SAPPHIRE) was to compare the safety and effectiveness of the Cordis PRECISE Nitinol Stent Systems, used in conjunction with the ANGIOGUARD XP Emboli Capture Guidewire, to carotid endarterectomy (CEA) in the treatment of carotid artery disease in patients at increased risk for adverse events from CEA. Study hypotheses examined whether the major adverse event (MAE) rate of randomized stent patients was not inferior to randomized CEA patients. Safety evaluations included assessments of major clinical events occurring during the procedure, prior to discharge, within 30 days, six months, one year and every 12 months thereafter for a total of three years; access site vascular complications; independent neurological assessments at 24 hours, 30 days, six months and one year post procedure. Effectiveness evaluations included assessments of successful stent deployment at the target lesion; less than 30% residual diameter stenosis at the completion of the procedure as measured by carotid angiography; and restenosis (≥50%) as determined by carotid ultrasound at 30 days, six months and one year post procedure and every 12 months thereafter for a total of three years.

B. Study Design

The pivotal SAPPHIRE study was a multi-center, prospective, randomized, triangular sequential trial comparing patients at increased risk for adverse events from CEA who received a stent to a surgical (CEA) control. The safety and effectiveness of the Cordis PRECISE Nitinol Stent System, used in conjunction with the ANGIOGUARD XP Emboli Capture Guidewire, in the treatment of *de novo* or restenotic obstructive carotid artery disease in these patients was evaluated.

The study also included a non-randomized stent arm, which included those patients who met entry criteria but who were determined by the surgeon at the study site to be at too high a risk for adverse outcomes from surgery and therefore inappropriate for randomization. Likewise, patients meeting the entry criteria, but determined by the interventionalist to be unacceptable candidates for stenting and therefore not randomizable, had the option of entering a non-randomized surgical arm.

SAPPHIRE entry criteria were identical for all patients. All patients were evaluated to determine whether they met the entry criteria by a multi-disciplinary team consisting of a neurologist, interventionalist, and vascular surgeon. Patients meeting the criteria were either randomized to treatment by stent or CEA, or placed into the non-randomized stent or CEA arms, based on the medical judgment of the interventionalist and surgeon as noted above. Patients who were entered into this study were either asymptomatic with a $\geq$80% diameter stenosis or symptomatic with a $\geq$50% diameter stenosis. Symptomatic patients were defined as those patients who have one or more TIAs, characterized by distinct focal neurological dysfunction or monocular blindness with clearing of signs and symptoms within 24 hours or one or more completed strokes with persistence of symptoms or signs for more than 24 hours. In addition, **ALL** patients must also have had at least one anatomic or co-morbid risk factor placing them at high-risk for adverse events from CEA. These risk factors are as follows:

- Congestive Heart Failure (Class III/IV), and/or known severe left ventricular dysfunction <30%
- Open-heart surgery within 6 weeks
- Recent myocardial infarction (>24 hours and <4 weeks)
- Unstable angina (CCS class III/IV)
- Synchronous severe cardiac and carotid disease requiring open heart surgery and carotid revascularization
- Severe pulmonary disease to include any of the following:
  - Chronic oxygen therapy
  - Resting P02 of $\leq$ 60 mmHg
  - Baseline hematocrit $\geq$ 50%
  - FEV1 or DLCO $\leq$ 50% of normal
- Contralateral carotid occlusion
- Contralateral laryngeal palsy
- Post-radiation treatment
- Previous CEA recurrent stenosis
- High cervical ICA lesions
- CCA lesions below the clavicle
- Severe tandem lesions

- Abnormal stress test

The primary endpoint was a composite of MAE including death, any stroke, or myocardial infarction (MI), in the first 30 days following treatment and death or ipsilateral stroke between 31 days and 12 months. An independent Clinical Events Committee adjudicated all MAE's and other events. Endpoints were analyzed on an intent-to-treat basis.

A total of 747 patients were enrolled in the SAPPHIRE study at 29 centers in the United States. The randomized population was comprised of 334 patients (167 stent/167 CEA), 310 of who were treated per protocol. The primary reasons why the remaining 24 patients were not treated were: 1) Eleven patients withdrew consent; 2) Six patients were found not to meet inclusion criteria subsequent to randomization; 3) Five patients' conditions deteriorated and they became too high a risk for any treatment; and 4) Two patients were randomized to surgery that was never performed. The non-randomized stent arm was comprised of 406 patients and the non-randomized CEA arm was comprised of seven patients. Follow-up evaluations were scheduled at 30 days, 6 months and one-year post procedure, and annually thereafter for three years. Patient follow-up and accountability at 30 days and 360 days are presented in **Table 9**, as these were the primary data analysis timepoints.

Imaging data provided in this summary are based on findings from two independent centralized Core Laboratories, which reviewed ultrasound and angiographic films. A third independent laboratory analyzed trapped material contained in a percentage of all ANGIOGUARD XP filter baskets. A Clinical Events Committee (CEC) adjudicated all clinical events and an independent Data Safety Monitoring Board (DSMB) monitored safety.

Table 9 – SAPPHIRE Patient Follow-Up and Accountability

	0 days	30 days	360 days
# Patients Alive at Time Interval			
Randomized stent	167	165 (99.0%)	155 (93.0%)
Randomized CEA	167	163 (98.0%)	146 (87.4%)
Non-randomized stent	406	397 (98.1%)	365 (90.0%)
Clinical Evaluation			
Randomized stent	167 (100%)	158 (96.0%)	145 (94.0%)
Randomized CEA	167 (100%)	145 (89.1%	125 (86.0%)
Non-randomized stent	406 (100%)	389 (98.1%)	342 (94.1%)
Angiographic Evaluation (Core Lab)			
Randomized stent	149 (89.2%)	N/A	N/A
Randomized CEA	N/A	N/A	N/A
Non-randomized stent	386 (95.1%)	N/A	N/A
Ultrasound Evaluation (Core Lab)			
Randomized stent	142 (85.0%)	N/A	125 (81.0%)
Randomized CEA	141 (84.4%)	N/A	101 (69.2%)
Non-randomized stent	341 (84.0%)	N/A	287 (79.0%)
Neurological Evaluation			
Randomized stent	165 (99.0%)	148 (90.0%)	126 (81.3%)
Randomized CEA	155 (93.0%)	131 (80.4%)	96 (66.1%)
Non-randomized stent	398 (98.0%)	361 (91.0%)	293 (80.3%)

Table 10 presents patient characteristics of the patients enrolled in the SAPPHIRE randomized arm and non-randomized stent arm of the SAPPHIRE trial.

Table 10 - Baseline Demographics and Clinical Characteristics - Randomized and Non-Randomized Stent Patients*

Patient Characteristics	Randomized Stent	Randomized CEA	P-Value**	Non-Randomized Stent
Age (Years)	72.5 ± 8.3	72.3 ± 9.1	0.86	71.4 ± 9.8
% Male	66.9% (111/166)	67.1% (108/161)	1.00	64.3% (261/406)
Diabetes	25.3% (42/166)	27.5% (44/160)	0.71	30.8% (125/406)
Coronary Artery Disease (CAD)	85.8% (133/155)	75.5% (111/147)	0.03	68.9% (259/376)
Previous PTCA (Coronary)	34.8% (56/161)	23.4% (37/158)	0.03	21.2% (83/392)
Previous CABG	43.4% (72/166)	30.8% (49/159)	0.02	31.5% (128/406)
Previous Q-Wave or Non Q-Wave MI	29.7% (46/155)	35.3% (54/153)	0.33	33.4% (122/365)
Angina at a Low Workload or Unstable Angina	24.1% (20/83)	14.7% (11/75)	0.16	31.5% (41/130)
Congestive Heart Failure	17.5% (29/166)	17.4% (28/161)	1.00	18.2% (74/406)
Coexistent Severe CAD Requiring Carotid and Coronary Revascularization	15.9% (26/164)	16.5% (26/158)	1.00	12.8% (51/400)
Systolic Blood Pressure	151.7 ± 26.0	153.5 ± 26.9	0.54	148.2 ± 27.2
History of Dyslipidemia	78.5% (128/163)	76.9% (123/160)	0.79	73.9% (289/391)
Previous CEA/Recurrent Stenosis	22.6% (37/164)	22.2% (35/158)	1.00	37.7% (151/401)
Post-Radiation Treatment	4.3% (7/164)	5.7% (9/158)	0.61	16.2% (64/401)
Prior CEA	28.3% (47/166)	26.7% (43/161)	0.80	45.2% (183/405)
Contralateral Carotid Occlusion	23.6% (39/165)	25.3% (40/158)	0.80	16.3% (65/400)
History of Stroke	27.1% (45/166)	23.8% (38/160)	0.53	32.3% (129/399)
History of TIA	31.1% (50/161)	34.0% (53/156)	0.63	34.5% (138/400)
High Cervical ICA Lesions	4.3% (7/164)	4.4% (7/158)	1.00	12.7% (51/401)
CCA Lesions Below the Clavicle	0.0% (0/164)	0.0% (0/158)	-	3.0% (12/401)
Other Co-morbid Risk Factors Precluding CEA	0.0% (0/164)	0.0% (0/160)	-	7.9% (32/404)
Renal Insufficiency	6.0% (10/166)	7.5% (12/160)	0.66	7.4% (30/405)
Current Cigarette Use	16.9% (27/160)	16.4% (26/159)	1.00	13.5% (54/399)
Patients >80 years	19.3% (32/166)	20.5% (33/161)	0.78	19.2% (78/406)

* The denominator represents the total number of responses to a question in the case report form.
**P-value displayed refers to comparison of randomized arms.

C. Study Results

The 360-day MAE rate, defined as death, stroke, or MI (Q wave or non-Q wave), to 30 days and death or ipsilateral stroke from 31 days to 360 days was 12.0% for the randomized stent patients compared with 19.2% for the control group. These results demonstrate non-inferiority (p=0.004) of carotid stenting to carotid endarterectomy with the pre-specified non-inferiority delta of 3%. The MAE rate at 360 days for the non-randomized stent patients was 15.8%. Principal safety and effectiveness results to 360 days are presented in **Table 11**, which follows. The cumulative percentage of MAE through 360 days for the randomized and non-randomized stent patients is presented in **Figure 1**, which follows. **Figures 2 and 3** present the cumulative percentage of MAE through 360 days for randomized asymptomatic and symptomatic patients.

Table 11 - Principal Safety & Effectiveness Results To 360 Days (Intent to Treat)

Safety Measures & Other Clinical Events to 360 Days	**Randomized Stent (N=167)**	**Randomized CEA (N=167)**	**P-Value***	**Non-Randomized Stent (N=406)**
MAE [1]	12.0% (20/167)	19.2%(32/167)	0.10	15.8% (64/406)
Death (All Cause)	7.2% (12/167)	12.6% (21/167)	0.14	10.1% (41/406)
Stroke	6.0% (10/167)	7.2% (12/167)	0.83	9.1% (37/406)
Major Ipsilateral Stroke	0.6% (1/ 167)	3.0%(5/167)	0.21	3.2% (13/406)
Minor Ipsilateral Stroke	3.6% (6/ 167)	1.8% (3/167)	0.50	3.9% (16/406)
Myocardial Infarction (Q or Non-Q)	3.0% (5/167)	7.2% (12/167)	0.13	2.7% (11/406)
TIA	6.6% (11/167)	3.0% (5/167)	0.20	6.9% (28/406)
Major Bleeding [2]	9.0% (15/ 167)	10.2% (17/167)	0.85	13.3% (54/406)
Cranial Nerve Injury	0.0% (0/167)	4.8% (8/167)	0.01	0.0% (0/406)
Severe Hypotension	17.4% (29/167)	3.0% (5/167)	<0.01	15.5% (63/406)
Bradycardia	8.4% (14/167)	3.0% (5/167)	0.06	3.4% (14/406)
Vascular Complications [3]	5.4% (9/167)	N/A	-	2.5% (10/406)
Device/Procedure Related Adverse Events [4]	0.0% (0)	0.0% (0)	-	0.0% (0)
Efficacy Measures	**Randomized Stent (N=167)**	**Randomized CEA (N=167)**	**P-Value**	**Non-Randomized Stent (N=406)**
Lesion Success [5]	91.8% (145/158)	N/A	N/A	90.4% (368/407)
Procedure Success [6]	88.1% (140/159)	N/A	N/A	87.9% (355/404)
Device Success [7]	91.2% (145/159)	N/A	N/A	89.6% (363/405)
ANGIOGUARD Success [8]	95.6% (152/159)	N/A	N/A	91.6% (372/406)
Post-Procedure In-Lesion Minimal Lumen Diameter (MLD in mm) Mean±SD (N) Range (min, max)	3.9±0.8 (147) (2.1,7.3)	N/A	N/A	3.8±0.8 (385) (2.0, 8.1)
Post-Procedure In-Lesion Percent Diameter Stenosis (%DS) [9] Mean±SD (N) Range (min, max)	17.2±11.3(147) (1.5, 49.3)	N/A	N/A	18.5± 12.6 (385) (-12.1, 64.7)
Post-Procedure In-Stent Minimal Lumen Diameter (MLD in mm) Mean±SD (N) Range (min, max)	4.3±0.9 (147) (2.1, 7.9)	N/A	N/A	4.1±0.8 (381) (2.2, 8.1)
Post-Procedure In-Stent Percent Diameter Stenosis (%DS)[10] Mean±SD (N) Range (min, max)	8.3+16.7 (147) (-42.0, 46.6)	N/A	N/A	10.9±14.2 (381) (-34.9, 43.8)
Binary Ultrasound In-Vessel Restenosis at 360 days [11]	19.7% (24/122)	31.3% (30/96)	0.06	27.7% (78/282)
Binary Ultrasound In-Stent Restenosis at 360 days [11]	15.6% (19/122)	13.5% (13/96)	0.70	18.4% (52/282)
Cumulative % of TLR at 360 days** [12]	0.6%	4.3%	0.04	0.8%
Cumulative % of MAE[1] at 360 days**	12.2%	20.1%	0.05	16.0%

Numbers are % (counts/sample size).

*P-value displayed refers to comparison of randomized arms.

**Cumulative percentage estimates are by Kaplan-Meier methods with standard error estimates by Peto formula.

(1) Major Adverse Events (MAE) = Death, MI or stroke to 30 days and death or ipsilateral stroke from 31-360 days.

(2) Major Bleeding. Any non-access site related bleeding resulting in a 25% or more decline in HCT or requiring transfusion.

(3) Vascular Complications: Events related to bleeding or vascular injury at the percutaneous access site

(4) There were no device or procedure related events. In 17 of 19 initial stent delivery failures, a subsequent attempt was successful. In one case, the patient was treated with CEA. In the other case, the patient was treated with balloon angioplasty alone. One stent fracture was noted from one-year ultrasound films, with no adverse effect to the patient.

(5) Lesion Success = The attainment of a final residual stenosis of <30% using any percutaneous method. If no in-stent measurements were available, in-lesion measurements were used, and if no QCA was available, visual estimates were used.

(6) Procedure Success = The attainment of a final residual stenosis of <30% and no in-hospital MAE. If no in-stent measurements were available, in-lesion measurements were used, and if no QCA was available, visual estimates were used

(7) Device Success = The attainment of a final residual stenosis of <30% using only the assigned device. If no in-stent measurements were available, in-lesion measurements were used, and if no QCA was available, visual estimates were used

(8) ANGIOGUARD Success = Successful deployment and retrieval of the ANGIOGUARD device.

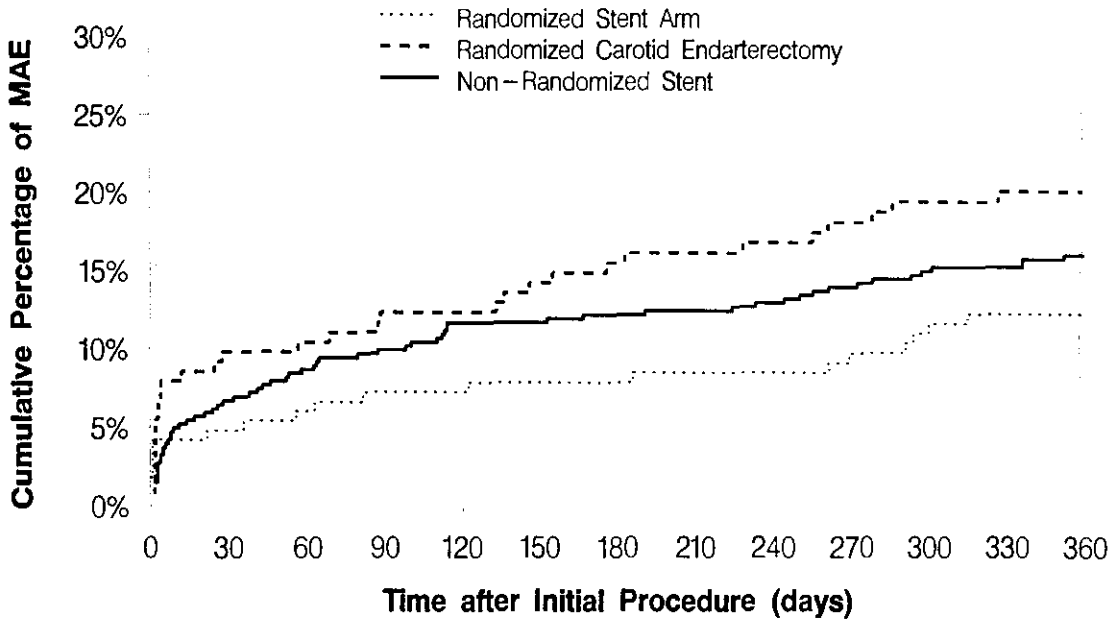
(9) In-lesion % DS Measurement: Defined as the % diameter stenosis either within the stented segment or within 5mm proximal or distal to the stent edges.

(10) In-stent % DS Measurement: Defined as the % diameter stenosis within the stented segment

(11) Binary Restenosis is defined by Ultrasound as % diameter stenosis >50%.

(12) TLR = Target Lesion Revascularization

Figure 1
Cumulative Percentage of MAE* at 360 days

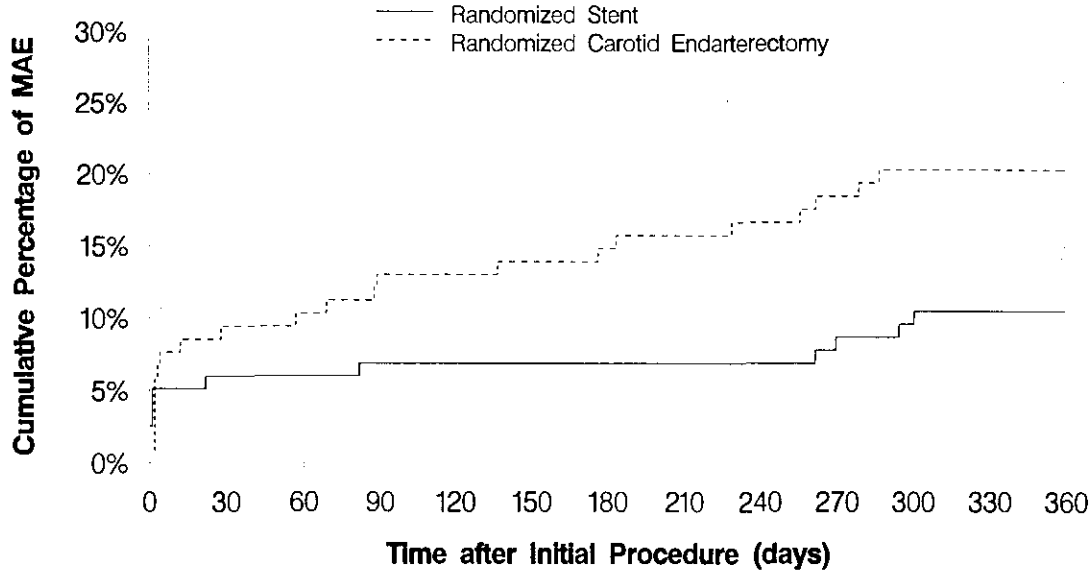


	Time After Procedure (Days) – Randomized Patients			
	0	30	180	360
Stent				
N at Risk	167	158	152	143
% w/Events	1.8	4.2	7.9	12.2
CEA				
N at Risk	167	146	136	118
% w/Events	0.6	9.8	15.5	20.1
Test Between Groups				
Log-Rank P-Values	0.053			

	Time After Procedure (Days) – Non-Randomized Patients			
	0	30	180	360
Stent				
N at Risk	406	382	352	329
% w/Events	1.5	6.9	12.2	16.0

* Major Adverse Events (MAE) = Death, MI or stroke to 30 days and death or ipsilateral stroke from 31-360 days.

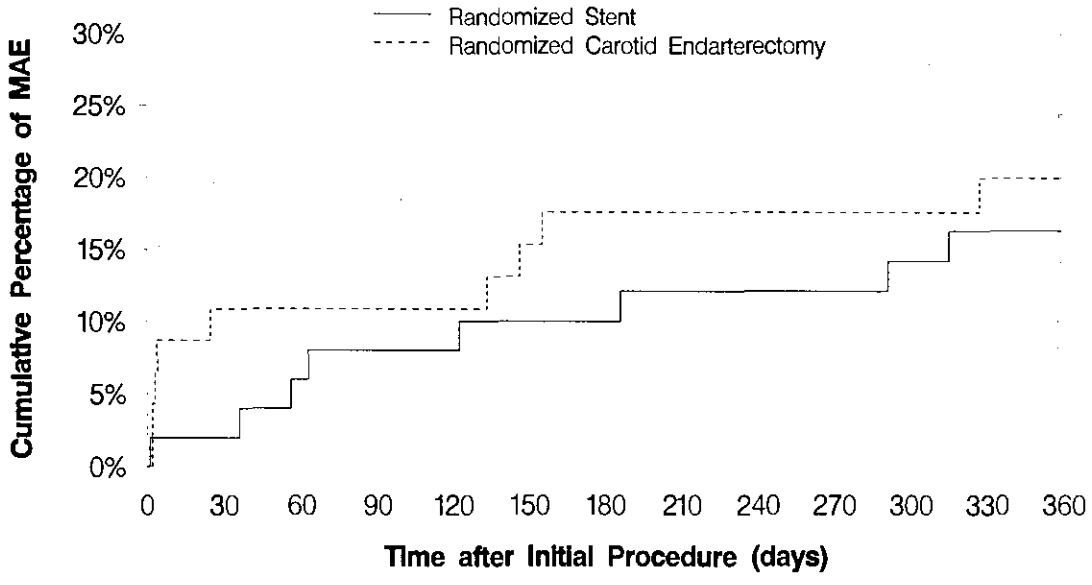
Figure 2
Cumulative Percentage of MAE* at 360 days – Asymptomatic Randomized Stent and CEA Patients



	Time after initial procedure (days)		
	0	**30**	**360**
Stent			
N at risk	117	109	100
% with events	2.6%	6.0%	10.5%
CEA			
N at risk	119	103	84
% with events	0.8%	9.4%	20.3%
Test Between Groups			
Log Rank P-value	0.044		

* Major Adverse Events (MAE) = Death, MI or stroke to 30 days and death or ipsilateral stroke from 31-360 days.

Figure 3
Cumulative Percentage of MAE at 360 Days – Symptomatic Randomized Stent & CEA Patients



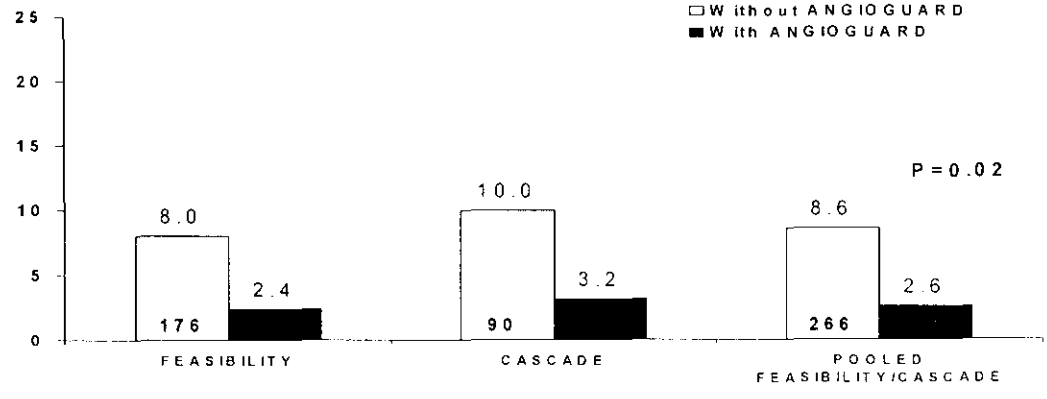
	Time After Procedure (Days)		
	0	**30**	**360**
Stent			
N at risk	50	49	42
% with events	0.0%	2.0%	16.3%
CEA			
N at risk	46	42	32
% with events	0.0%	10.9%	20.0%
Test Between Groups			
Log Rank P-value	0.582		

* Major Adverse Events (MAE) = Death, MI or stroke to 30 days and death or ipsilateral stroke from 31-360 days.

Basket Content Analysis - A pathology core lab analyzed the contents of 294 ANGIOGUARD XP filter baskets from the non-randomized Stent Arm of the SAPPHIRE trial, which determined that 59.5% (175/294) of the baskets evaluated contained material that had been captured during the carotid stenting procedure. Physicians reported that there was visible material present in 56% of the 393 baskets inspected in the non-randomized stent arm and in 72.2% of the 158 baskets inspected in the randomized stent arm.

30-Day Stroke Rate of Carotid Artery Stenting with and without ANGIOGUARD XP Emboli Capture Guidewire - Two non-randomized studies utilizing the PRECISE stent (and its predecessor, the SMART stent) were conducted in Europe (CASCADE) and in the US (US Feasibility Study). Thirty-one (31) of the 131 patients in CASCADE and 85 of 261 patients in the US Feasibility study were treated with stenting in conjunction with the ANGIOGUARD embolic protection device while the remaining patients were treated with stenting alone. Because the number of patients in each trial is small, an exploratory analysis was performed in which 30-day stroke data from these two trials were combined. 30-day stroke rates for patients treated by stenting alone and for patients treated by stenting with distal embolic protection were analyzed in a post-hoc analysis; combined rates of 30-day stroke were 8.6% for the 266 patients treated with stenting alone and 2.6% for the 116 patients treated by stenting with distal embolic protection. In this analysis, the difference between these two rates (an absolute reduction of 6% and a relative reduction of 70%) with a p-value of 0.02.

Figure 4:30-Day Stroke Rate of Carotid Artery Stenting with and without the ANGIOGUARD XP Emboli Capture Guidewire



XI. Conclusions Drawn from the Studies

The pre-clinical studies indicate that the Cordis PRECISE Nitinol Stent Systems used in conjunction with the ANGIOGUARD XP Emboli Capture Guidewire meet or exceed safety and performance specifications. Multi-center clinical data reached the following conclusions:

Randomized Study Arm: The incidence of death, stroke, or MI at 30 days plus death or ipsilateral stroke at 360 days (MAE) in the carotid stent group was 12.0% (20/167) compared with 19.2% (32/167) in the surgical group. In comparing treatment arms for MAE at 360 days, the stent arm was non-inferior to the CEA arm within the designated 3% delta.

Non-Randomized Study Arm: The incidence of death, stroke and MI at 30 days plus death or ipsilateral stroke at 360 days (MAE) was 15.8% (64/406). In a test of the primary endpoint against the Objective Performance Criteria (OPC), despite the fact that the rate was numerically less than the OPC plus the delta, the p value was found to be 0.2899. In a test of the MAE rate when post 30-day non-neurological deaths are not included, the p value was found to be <0.0001. The causes of these non-neurological deaths are well documented, and consist of cardiac deaths, cancer deaths, renal failure, and respiratory failure.

The sponsor compared the non-randomized stent arm and the randomized CEA arm by conducting a propensity score analysis that accounted for baseline imbalances due to the non-randomized (i.e., more observational) nature of group membership. The analysis found the treatment difference (non-randomized stent minus CEA) in 360 day MAE was –5.3%, with an adjusted 95% confidence interval of –13.4% to 3.0%. Thus, after adjusting for the higher risk of patients in the non-randomized stent arm, 360-day MAE outcomes were non-inferior to the CEA arm of the randomized study within a 3% delta.

The results of the pre-clinical and clinical studies provide valid scientific evidence and reasonable assurance that the Cordis PRECISE Nitinol Stent System used in conjunction with the ANGIOGUARD XP Emboli Capture Guidewire is safe and effective for the above listed intended use.

XII. Panel Recommendation

At an advisory meeting held on April 21, 2004, the Circulatory System Devices Panel recommended that Cordis's PMA for the Precise® nitinol Stent System be approved subject to submission of, and approval by, the Center for Devices and Radiological Health (CDRH) of the following:

(1) refinements to the indication statement in the Instructions for Use (IFU)

(2) addition of a warning statement regarding possible increased risk of adverse events if the procedure is performed without the Angioguard

(3) refinements to the patient label

(4) protocols for two post-approval studies: one following the patients enrolled in the IDE out to 3 years, and another study with independent neurological assessment out to 12 months

XIII. CDRH Decision

CDRH concurred with the Circulatory System Device Panel's recommendation of April 21, 2004. FDA worked with the sponsor to refine the physician and patient labels, and the protocol for the post-approval studies. The sponsor agreed to conduct two separate post-approval studies. One study will evaluate the long-term safety and effectiveness of the device in the original study cohort through three years of implantation. The second study will evaluate safety and effectiveness of the device in at least 1000 U.S. patients at up to 100 geographically disbursed sites with high, moderate and low volumes of potential patient participation through 12 months of follow-up.

The applicant's manufacturing facilities were inspected and found to be in compliance with the Quality System Regulation (21 CFR 820). FDA issued an approval order on September 22, 2006.

XIV. Approval Specifications

Instructions for Use: See the labeling

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

Postapproval Requirements: See approval order.