

SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. General Information

Device Generic Name: Iliac Stent

Device Trade Name: S.M.A.R.T.TM Nitinol Stent System; and
S.M.A.R.T.TM ControlTM Nitinol Stent System

Applicant's Name and Address: Cordis Corporation
14201 NW 60th Avenue
Miami Lakes, FL 33014

Premarket Approval (PMA) Application Number: P020036

Date of Panel Recommendation: None

Date of Notice of Approval to Applicant: August 12, 2003

II. Indications for Use

The S.M.A.R.T.TM Nitinol Stent System (hereinafter called the SMART stent system) and the *S.M.A.R.T.TM ControlTM Nitinol Stent System* (hereinafter called the SMART Control stent system) are indicated for improving luminal diameter in patients with symptomatic atherosclerotic disease of the common and/or external iliac arteries up to 126 mm in length, with a reference vessel diameter of 4 to 9 mm, and angiographic evidence of a patent profunda or superficial femoral artery.

III. Contraindications

There are no known contraindications at this time.

IV. Warnings and Precautions

The warnings and precautions can be found in the labeling for the SMART stent system and the SMART Control stent system (Attachment 1).

V. Device Description

A. SMART stent system

The SMART stent system includes a self-expanding stent (SMART stent) made of Nitinol (nickel-titanium alloy) material and a 7 French (2.3 mm) sheathed delivery system. The stent is laser cut from a solid nitinol tube into a fine mesh ("Z" configuration) design. The stent expands to its unconstrained diameter when released from the deployment catheter into the iliac 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 1-2 mm smaller in diameter than the unconstrained diameter of the stent.

The stent is available in the sizes indicated in the following table (Table 1) listing catalog numbers for the 80 cm and 120 cm lengths of the stent delivery system (SDS):

Table 1. Catalog Numbers for Cordis SMART stent system

| 80 cm SDS | | Stent Length (mm) | | | |
|---------------------|----|-------------------|----------|----------|----------|
| | | 20 | 40 | 60 | 80 |
| Stent Diameter (mm) | 6 | N06020SL | N06040SL | N06060SL | N06080SL |
| | 7 | N07020SL | N07040SL | N07060SL | N07080SL |
| | 8 | N08020SL | N08040SL | N08060SL | N08080SL |
| | 9 | N09020SL | N09040SL | N09060SL | N09080SL |
| | 10 | N10020SL | N10040SL | N10060SL | N10080SL |

| 120 cm SDS | | Stent Length (mm) | | | |
|---------------------|----|-------------------|----------|----------|----------|
| | | 20 | 40 | 60 | 80 |
| Stent Diameter (mm) | 6 | N06020ML | N06040ML | N06060ML | N06080ML |
| | 7 | N07020ML | N07040ML | N07060ML | N07080ML |
| | 8 | N08020ML | N08040ML | N08060ML | N08080ML |
| | 9 | N09020ML | N09040ML | N09060ML | N09080ML |
| | 10 | N10020ML | N10040ML | N10060ML | N10080ML |

The delivery system of the SMART stent system comprises an inner shaft and a 7Fr outer sheath, which are locked together with a Touhy Borst valve. The inner shaft terminates distally in a catheter tip and originates proximally in a luer hub designed to accept a 0.035 inch (0.89 mm) guidewire. The self-expanding 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 delivery system has a nominal working length of either 80 cm or 120 cm. The SMART stent system is designed to be delivered through an appropriately sized catheter sheath introducer.

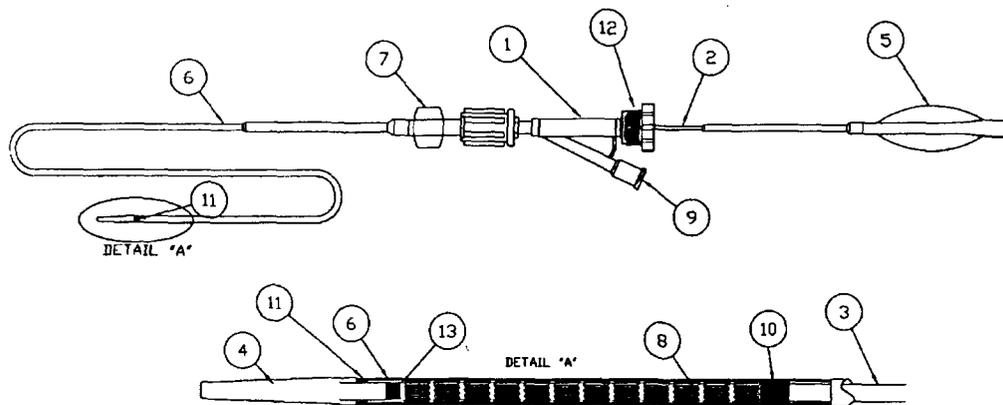


Figure 1: S.M.A.R.T.™ Nitinol Stent System

- | | |
|----------------------------|---|
| 1. Touhy Borst valve | 8. S.M.A.R.T. Stent |
| 2. Stainless steel tube | 9. Y connection on the Touhy Borst valve |
| 3. Polymeric shaft | 10. Proximal Radiopaque marker |
| 4. Catheter tip | 11. Distal Radiopaque marker |
| 5. Luer hub (Proximal) | 12. Proximal Valve on the Touhy Borst valve |
| 6. Outer sheath | 13. Distal inner shaft stent marker |
| 7. Luer hub (Outer sheath) | |

B. SMART Control stent system

The SMART Control stent system includes a self-expanding stent (SMART Control stent) made of Nitinol (nickel-titanium alloy) material and a 6 French (2.0 mm) sheathed delivery system. The stent is cut from a solid nitinol tube into a fine mesh (“Z” configuration) design. The stent expands to its unconstrained diameter when released from the deployment catheter into the iliac 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 1-2 mm smaller in diameter than the unconstrained diameter of the stent. The stent is equipped with 12 tantalum markers, 6 at each end, to increase the visibility of the stent under fluoroscopic imaging. The SMART Control stent system is designed to be delivered through an appropriately sized catheter sheath introducer.

The stent will be available in the sizes indicated in the following table (Table 2) listing catalog numbers for the 80 cm and 120 cm lengths of the stent delivery system (SDS):

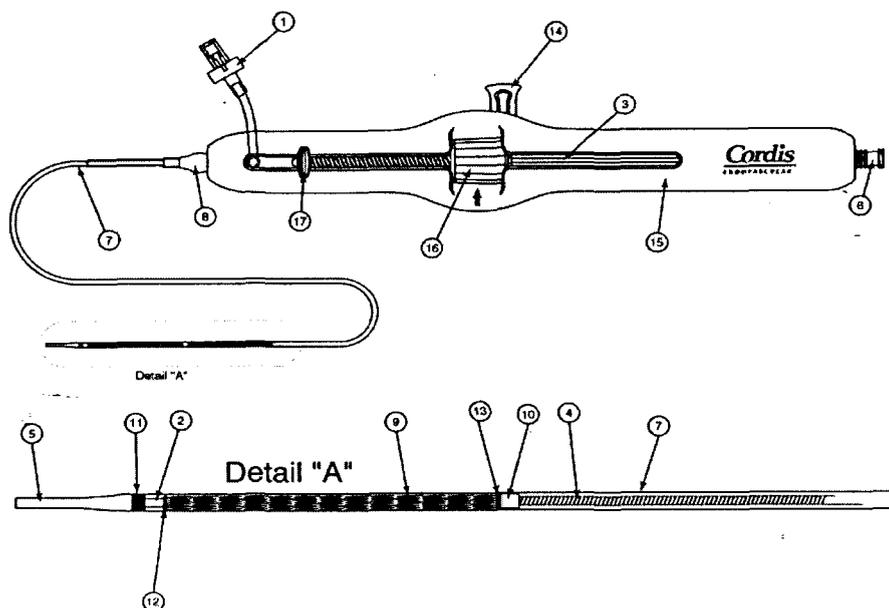
Table 2. Catalog Numbers for Cordis SMART Control stent system

| 80 cm SDS | | Stent Length (mm) | | | | | |
|---------------------|----|-------------------|----------|----------|----------|----------|----------|
| | | 20 | 30 | 40 | 60 | 80 | 100 |
| Stent Diameter (mm) | 6 | C06020SL | C06030SL | C06040SL | C06060SL | C06080SL | C06100SL |
| | 7 | C07020SL | C07030SL | C07040SL | C07060SL | C07080SL | C07100SL |
| | 8 | C08020SL | C08030SL | C08040SL | C08060SL | C08080SL | C08100SL |
| | 9 | C09020SL | C09030SL | C09040SL | C09060SL | | |
| | 10 | C10020SL | C10030SL | C10040SL | C10060SL | | |

| 120 cm SDS | | Stent Length (mm) | | | | | |
|---------------------|----|-------------------|----------|----------|----------|----------|----------|
| | | 20 | 30 | 40 | 60 | 80 | 100 |
| Stent Diameter (mm) | 6 | C06020ML | C06030ML | C06040ML | C06060ML | C06080ML | C06100ML |
| | 7 | C07020ML | C07030ML | C07040ML | C07060ML | C07080ML | C07100ML |
| | 8 | C08020ML | C08030ML | C08040ML | C08060ML | C08080ML | C08100ML |
| | 9 | C09020ML | C09030ML | C09040ML | C09060ML | | |
| | 10 | C10020ML | C10030ML | C10040ML | C10060ML | | |

The delivery system of the SMART Control stent system comprises of inner shaft and a 6 French outer sheath, which are locked together with a hemovalve. The delivery system has a nominal working length of either 80 cm or 120 cm, and is designed to be used with an appropriately sized catheter sheath introducer. The inner shaft is comprised proximally of a stainless steel tube and distally of a stainless steel coil covered with a polymeric jacket. The inner shaft terminates distally in a catheter tip and originates proximally in a luer hub designed to accept up to a 0.035” (0.89mm) guidewire. The outer sheath has a radiopaque marker on its distal end; prior to stent deployment, this marker is “overshadowed” by the brighter distal (leading edge) marker on the stent. The self-expanding stent is constrained within the space between the inner shaft and the outer sheath. For stent deployment, a locking pin is removed from the proximal deployment handle, which is designed to allow one-handed operation for stent delivery. Stent movement during sheath retraction is restricted by a stent stop connected to the inner shaft.

Figure 2: S.M.A.R.T.™ Control™ Nitinol Stent System



- | | |
|-------------------------------------|------------------------------|
| 1. Flushing valve | 10. Inner shaft stent stop |
| 2. Inner shaft: polymeric tube | 11. Distal radiopaque marker |
| 3. Inner shaft: metallic tube | 12. Distal stent markers |
| 4. Inner shaft: metallic coil | 13. Proximal stent markers |
| 5. Catheter tip (Distal wire lumen) | 14. Locking pin |
| 6. Luer hub (Proximal wire lumen) | 15. Handle |
| 7. Outer sheath | 16. Tuning dial |
| 8. Luer hub (Outer Sheath) | 17. Deployment lever |
| 9. S.M.A.R.T. Stent | |

VI. Alternative Practices and Procedures

Alternative procedures to treat atherosclerotic disease of the iliac arteries include percutaneous transluminal angioplasty (PTA), surgical procedures, and other stents for which there is an approved PMA.

VII. Marketing History

The SMART stent system and the SMART Control stent system have been marketed for peripheral vascular use in the following countries: Argentina, Belgium, Benelux, Chile, Columbia, Costa Rica, El Salvador, France, Germany, Hong Kong, India, Italy, Korea, Malaysia, Mexico, Nicaragua, Pakistan, Panama, Paraguay, Philippines, Peru, Portugal, Singapore, Spain, Thailand, and United Kingdom. The SMART stent system and SMART Control stent system have not been withdrawn from marketing for any reason relating to the safety or effectiveness of the device.

VIII. Adverse Effects of the Device on Health

A. Observed Adverse Events

A total of 203 patients were enrolled in the CRISP-US study, a multicenter, randomized, concurrently controlled study comparing the SMART stent system to the Schneider WALLSTENT® Iliac Endoprosthesis. Patients with a suboptimal percutaneous transluminal angioplasty (PTA) result during the treatment of a *de novo* or restenotic lesion in the common and/or external iliac artery(ies) were randomized to either the SMART stent (N=102) or the WALLSTENT® (N=101).

Table 3 below summarizes major adverse events reported in both treatment groups to 9 months. Two patients in the SMART stent treatment group died within the first 30 days. One patient developed acute renal insufficiency and died in the hospital 4 days after the procedure. A second patient was discharged from the hospital but returned to the emergency room 2 days after the procedure; the patient's condition deteriorated and the patient died 3 days after the procedure of unknown causes. Both deaths were believed to be procedure-related. Other major adverse events reported in the SMART stent treatment group included amputation of the target limb (n=1), target vessel revascularization (n=2), and stent thrombosis (n=1). Other major adverse events reported in the WALLSTENT® treatment group included target vessel revascularization (n=4) and stent thrombosis (n=1).

There were seven additional deaths that were not related to the device or the procedure, two in the SMART stent treatment group and five in the WALLSTENT® treatment group. The two deaths in the SMART stent treatment group were non-cardiac: one patient died at 229 days of complications secondary to congestive heart failure, and one patient died at 246 days of a lymphoproliferative disorder. Three of the deaths in the WALLSTENT® treatment group were cardiac: one patient died at 92 days following an MI, one patient died at 302 days due to cardiac arrest, and one patient died at 465 days due to coronary atherosclerosis. The remaining two deaths in the WALLSTENT® treatment group were non-cardiac: one patient died at 253 days following surgery for bladder cancer, and one patient died at 306 days from lung cancer.

(Note: The CRISP-US study, together with preclinical data showing the design equivalence of the SMART and SMART Control stent systems, was used to provide reasonable assurance of the safety and effectiveness of the SMART Control stent system.)

Table 3. Major Adverse Events In-Hospital and Out-of-Hospital (to 9 months)

| Description of Event | SMART (N=102) | WALLSTENT (N=101) | All Randomized (N=203) | Relative Risk [95% C.I.] | P-Value |
|--|------------------|----------------------|------------------------------|-----------------------------|---------|
| In-Hospital Complications | | | | | |
| MAIE | 1.0% (1/102) | 0.0% (0/101) | 0.5% (1/203) | NA | 1.000 |
| Death | 1.0% (1/102) | 0.0% (0/101) | 0.5% (1/203) | NA | 1.000 |
| MI (in-hospital) | 0.0% (0/102) | 0.0% (0/101) | 0.0% (0/203) | NA | -- |
| Amputation of the target limb | 0.0% (0/102) | 0.0% (0/101) | 0.0% (0/203) | NA | -- |
| Target vessel revascularization | 0.0% (0/102) | 0.0% (0/101) | 0.0% (0/203) | NA | -- |
| Stent thrombosis | 0.0% (0/102) | 0.0% (0/101) | 0.0% (0/203) | NA | -- |
| Major bleeding complications | 0.0% (0/102) | 0.0% (0/101) | 0.0% (0/203) | NA | -- |
| Major vascular complications | 0.0% (0/102) | 0.0% (0/101) | 0.0% (0/203) | NA | -- |
| CVA/TIA | 0.0% (0/102) | 0.0% (0/101) | 0.0% (0/203) | NA | -- |
| Out-of-Hospital Complications (to 9 months) | | | | | |
| MAIE | 3.9% (4/102) | 4.0% (4/101) | 3.9% (8/203) | 1.0 [0.3, 3.9] | 1.000 |
| Death (30 days) | 1.0% (1/102) | 0.0% (0/101) | 0.5% (1/203) | NA | 1.000 |
| Amputation of the target limb | 1.0% (1/102) | 0.0% (0/101) | 0.5% (1/203) | NA | 1.000 |
| Target vessel revascularization | 2.0% (2/102) | 4.0% (4/101) | 3.0% (6/203) | 2.0 [0.4, 10.8] | 0.445 |
| Stent thrombosis | 1.0% (1/102) | 1.0% (1/101) | 1.0% (2/203) | 1.0 [0.1, 15.9] | 1.000 |
| Major bleeding complications | 0.0% (0/102) | 0.0% (0/101) | 0.0% (0/203) | NA | -- |
| Major vascular complications | 0.0% (0/102) | 0.0% (0/101) | 0.0% (0/203) | NA | -- |
| CVA/TIA | 0.0% (0/102) | 0.0% (0/101) | 0.0% (0/203) | NA | -- |
| Cumulative Complications (to 9 months) | | | | | |
| MAIE | 4.9% (5/102) | 4.0% (4/101) | 4.4% (9/203) | 0.8 [0.2, 3.0] | 1.000 |
| Death (30 days) | 2.0% (2/102) | 0.0% (0/101) | 1.0% (2/203) | NA | 0.498 |
| MI (in-hospital) | 0.0% (0/102) | 0.0% (0/101) | 0.0% (0/203) | NA | -- |
| Amputation of the target limb | 1.0% (1/102) | 0.0% (0/101) | 0.5% (1/203) | NA | 1.000 |
| Target vessel revascularization | 2.0% (2/102) | 4.0% (4/101) | 3.0% (6/203) | 2.0 [0.4, 10.8] | 0.445 |
| Stent thrombosis | 1.0% (1/102) | 1.0% (1/101) | 1.0% (2/203) | 1.0 [0.1, 15.9] | 1.000 |
| Major bleeding complications | 0.0% (0/102) | 0.0% (0/101) | 0.0% (0/203) | NA | -- |
| Major vascular complications | 0.0% (0/102) | 0.0% (0/101) | 0.0% (0/203) | NA | -- |
| CVA/TIA | 0.0% (0/102) | 0.0% (0/101) | 0.0% (0/203) | NA | -- |

A subject was counted at most once for multiple occurrences of an adverse event.

All variables were judged by Clinical Events Committee (CEC).

MAIE (Major Adverse Ischemic Event) was defined as death within 30 days, in-hospital myocardial infarction, amputation of the target limb, or target vessel revascularization.

Relative risk = Risk of event in WALLSTENT group as compared to SMART stent; SE=sqrt[(1-p₁)/n₁₁+(1-p₂)/n₂₁] CI=RR*exp(±1.96SE)

B. Potential Adverse Events

Adverse events (in alphabetical order) that may be associated with implantation of a stent in iliac arteries (in addition to those listed in Table 3) include:

- Allergic/anaphylactoid reaction
- Aneurysm
- Angina/coronary ischemia
- Arterial occlusion/thrombus, near the puncture site
- Arterial occlusion/thrombus, remote from puncture site
- Arterial occlusion / restenosis of the treated vessel
- Arteriovenous fistula
- Arrhythmia
- Death related to procedure
- Death unrelated to procedure
- Embolization, arterial
- Embolization, stent

- Fever
- Hematoma bleed, remote site
- Hematoma bleed at needle, device path: nonvascular procedure
- Hematoma bleed, puncture site: vascular procedure
- Hypotension/hypertension
- Intimal injury/dissection
- Ischemia/infarction of tissue/organ
- Local infection
- Malposition (failure to deliver the stent to the intended site)
- Migration
- Pulmonary embolism
- Pseudoaneurysm
- Renal failure
- Septicemia/bacterimia
- Stroke
- Vasospasm
- Venous occlusion/thrombosis, remote from puncture site
- Venous occlusion/thrombosis, near the puncture site

C. Observed Device Malfunctions

There were no delivery failures or device malfunctions observed with the SMART stent system. There were four failures to deploy at the intended location observed with the Schneider WALLSTENT® Iliac Endoprosthesis. In two cases, the stent was removed and a non-study stent was placed. In the other two cases, an additional WALLSTENT® was placed.

VIII. Summary of Non-Clinical Laboratory Studies

A. Biocompatibility

Biocompatibility of the materials used on SMART stent system and the SMART Control stent system were performed in accordance with International Standard ISO 10993-1, "Biological Evaluation of Medical Devices Part 1: Evaluation and Testing" and the FDA's blue book memorandum dated May 1, 1995. Testing was conducted in accordance with GLPs. The following biocompatibility tests were performed, on materials processed through all of the manufacturing steps, including sterilization: cytotoxicity (MEM elution), sensitization, irritation/intracutaneous toxicity (USP), acute systemic toxicity, sub-chronic toxicity, genotoxicity (bacterial reverse mutation), hemocompatibility (hemolysis and, for some materials, PTT, platelet and leucocyte count), pyrogenicity, and chronic cytotoxicity. All materials were found to be non-toxic. In addition, the sponsor provided the results of a 26-week intramuscular implant test conducted on the stent wire. The purpose of this study was to evaluate the local and long-term toxic effects of the device in direct contact with living muscular tissue. The results of testing in 5 rabbits found no significant histopathologic differences between the test and control material in each animal.

Tests of the tantalum ribbon used in the micro-markers of the SMART Control stent included cytotoxicity (agar diffusion method), sensitization (saline only), intracutaneous injection, acute systemic toxicity, bacterial reverse mutation (saline only, with and without metabolic activation), hemolysis, *in vitro* hemocompatibility, Lee and White coagulation test, and pyrogenicity; all tests gave non toxic results.

B. Bench Testing and calculations

Magnetic Resonance Imaging (MRI) Compatibility

Literature review was performed to determine MRI compatibility of the Nitinol stent of the SMART stent system and the SMART Control stent system. The evidence provided in these articles indicates that the Nitinol stent is MRI safe with minimal artifacts.

Stent Length vs. Diameter

Empirical calculations were used to document changes in length as a function of stent diameter ("foreshortening"). Calculations were made for a range of stent diameters, because the stents are placed in vessels with reference diameters smaller than the nominal stent diameter. As summarized below, the results demonstrate that there is less stent foreshortening with the SMART Control stent.

| <u>SMART stent:</u> | | <u>SMART Control stent:</u> | |
|--------------------------|-----------------------|-----------------------------|-----------------------|
| <u>Expanded Diameter</u> | <u>Foreshortening</u> | <u>Expanded Diameter</u> | <u>Foreshortening</u> |
| 4.0 mm | 0.60% | 6.0 mm | 1.05% |
| 5.0 mm | 1.33% | 7.0 mm | 1.82% |
| 6.0 mm | 2.34% | 8.0 mm | 2.80% |
| 7.0 mm | 3.66% | 9.0 mm | 4.01% |
| 8.0 mm | 5.29% | 10.0 mm | 5.46% |
| 9.0 mm | 7.24% | | |
| 10.0 mm | 9.55% | | |

Verification measurements were performed on a quantity of ten SMART stents of 10 mm diameter. Analysis of the measured stent values produced a mean foreshortening of 9.48%, which compares with the empirically predicted value of 9.55%.

Percent Open Area

Empirical calculations were used to calculate the percentage of area not in contact with the vessel wall. The percent open area increases slightly with increasing stent diameter. Values for the SMART stent ranged from 78.7% (6 mm diameter) to 86.2% (10 mm diameter). Values for the SMART Control stent ranged from 78.8% to 86.9%.

Other Bench Testing

Information on bench testing of the SMART stent system and the SMART Control stent system is summarized in Table 4 below. In all cases, results demonstrated compliance with the established specifications, with appropriate safety factors. Any observed failures during product performance testing (e.g., individual samples that produced inspection observations or values not meeting specification) were satisfactorily addressed by the sponsor.

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Table 4. Preclinical testing summary for SMART stent system and SMART Control stent system

| System tested | Preclinical Test | Purpose / Acceptance Criteria | Sizes (mm) | No. of Samples Tested |
|----------------------------|---|---|---------------------------------------|----------------------------|
| SMART stent system | Visual Inspection | To ensure that no product defects are present | 6x20 7x20 8x40 9x40 10x80 | 20 11 20 10 20 |
| SMART Control stent system | Visual Inspection | To ensure that the following anomalies are not present: Contamination, gross damage to the tray or carton, rips, tears, open seals, channels, punctures of inner/outer pouches | 6x20 6x80 8x100 10x60 | 15 15 15 15 |
| SMART stent system | Stent Delivery System Dimensional Inspection | Useable Length= 80.0 cm +3/-1cm Useable length = 120.0 cm +3/-1 cm Proximal end OD = .089± .002" Distal end OD = .089± .002" | 6x20 8x40 9x40 10x80 | 20 20 10 20 |
| SMART Control stent system | Stent Delivery System Dimensional Inspection | Useable length = 120.0 cm +3/-1 cm 80.0 cm +3/-1 cm Proximal end OD = .079" +.002/- .001" Distal end OD = .079" +.002/- .001" | 6x20 6x80 8x100 10x60 | 15 15 15 15 |
| SMART stent system | Stent Delivery Preparation | Confirmation of fluid flow: <ul style="list-style-type: none"> from distal guidewire lumen from distal tip of outer sheath and ease of guidewire movement | 6x20 7x20 8x40 9x40 10x80 | 20 11 20 10 20 |
| SMART Control stent system | Stent Delivery Preparation | Confirmation of fluid flow: <ul style="list-style-type: none"> from distal guidewire lumen from distal tip of outer sheath and ease of guidewire movement | 6x20 6x80 8x100 10x60 | 15 15 15 15 |
| SMART stent system | Stent Deployment Force | The deployment force shall be ≤ 8.0 lbs. | 6x20 7x20 8x40 9x40 10x80 | 20 10 20 10 20 |
| SMART Control stent system | Stent Deployment Force | The deployment force shall be ≤ 5.0 lbs. | 6x20 6x80 8x100 10x60 | 15 15 15 15 |
| SMART stent system | Deployed stent uniformity and expanded stent outer diameter measurement | Uniformity measurement: The (X-Y) diameter measurement must not be greater than 1.25 mm at any location Expanded stent OD: Mean OS (X&Y) measurements (proximal/distal) will have the following specifications: Nominal (+0.75 mm, -0.50 mm) | 6x20 7x20 8x40 9x40 10x80 | 20 10 10 10 10 |
| SMART Control stent system | Deployed stent uniformity and expanded stent outer diameter measurement | Uniformity measurement: The (X-Y) diameter measurement must not be greater than 1.25 mm at any location Expanded stent OD: Mean OS (X&Y) measurements (proximal/distal) will have the following specifications: Nominal (+0.75 mm, -0.50 mm) | 6x20 6x80 8x100 10x60 | 15 15 15 15 |

Table 4. Preclinical testing summary for SMART stent system and SMART Control stent system (cont.)

| System tested | Preclinical Test | Purpose / Acceptance Criteria | Sizes (mm) | No. of Samples Tested |
|----------------------------|---|---|---------------------------------------|----------------------------|
| SMART stent system | Expanded stent length and flare | The expanded length of the stent will be: 8x40 mm – 40.5 (+ 3.5 mm, - 2.0 mm) 9x40 mm – 39.5 (+ 3.5 mm, - 2.0 mm) 10x80 mm – 77.5 (± 3.5 mm) The OD of the ends (stent flare) will be larger than the stent OD. | 6x20 7x20 8x40 9x40 10x80 | 20 10 10 10 10 |
| SMART Control stent system | Expanded stent length and flare | The expanded length of the stent will be: 6x20 mm – 23.7 (+ 2.5 mm, - 2.0 mm) 6x80 mm – 85.1 (+ 5.5 mm, - 3.0 mm) 8x100 mm – 102.5 (+ 5.5 mm, - 3.0 mm) 10x60 mm – 60.3 (+5.0 mm, - 3.0mm) The OD of the ends (stent flare) will be larger than the stent OD. | 6x20 6x80 8x100 10x60 | 15 15 15 15 |
| SMART stent system | Stent Radial Resistance Force and Chronic Outward Force | Radial resistance force: ≥ 0.90 N/cm Chronic Outward Force: ≤ 0.75 N/cm | 6x20 7x20 8x40 9x40 10x80 | 20 10 10 10 10 |
| SMART Control stent system | Stent Radial Resistance Force and Chronic Outward Force | Radial resistance force: ≥ 0.90 N/cm Chronic Outward Force: ≤ 0.75 N/cm | 6x20 6x80 8x100 10x60 | 15 15 15 15 |
| SMART stent system | Hub/Hypotube Pull Test | Test conducted to evaluate the ability of the molded hub/hypotube seal to withstand the required force of ≥ 2.2 lbs. | 8x40 9x40 10x80 | 5 5 5 |
| SMART Control stent system | Hub/Hypotube Pull Test | Test conducted to evaluate the ability of the molded hub/hypotube seal to withstand the required force of ≥ 2.2 lbs | 6x20 6x80 8x100 10x60 | 10 10 10 10 |
| SMART stent system | Inner member tip pull test | Test conducted to evaluate the ability of the inner member / tip seal to withstand the required force of 2.2 lbs | 6x20 8x40 9x40 10x80 | 10 20 10 20 |
| SMART Control stent system | Hub/Hypotube/ wire lumen (inner member)/tip pull test | Test conducted to evaluate the ability of the Inner Member Tip Seal including the Guide wire hub, wire lumen and hypotube bond to withstand the required force of ≥ 1.1 lbs. | 6x20 6x80 8x100 10x60 | 10 10 10 10 |
| SMART stent system | Hypotube/Inner member sleeve pull test | Test conducted to evaluate the ability of the Hypotube / Inner member sleeve seals to withstand the required force of ≥ 1.0 lbs. (Specification is based upon maximum force required to withdraw the Hypotube/Inner member sleeve from the body after stent deployment.) | 8x40 9x40 10x80 | 5 5 5 |
| SMART Control stent system | Hypotube/Coil/coil sleeve pull test | Test conducted to evaluate the ability of the Hypotube/Coil/Coil Sleeve Seal to withstand the required force of ≥ 0.7 lbs. (Specification is based upon maximum force required to withdraw the Hypotube/Inner member sleeve from the body after stent deployment. Due to the lower profile (6F) of the SMART Control stent system a lower withdrawal force is required.) | 6x20 6x80 8x100 10x60 | 10 10 10 10 |

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Table 4. Preclinical testing summary for SMART stent system and SMART Control stent system (cont.)

| System tested | Preclinical Test | Purpose / Acceptance Criteria | Sizes (mm) | No. of Samples Tested |
|----------------------------|--|--|--------------------------------|-----------------------|
| SMART stent system | Hub/Hypotube/Inner member/ Sleeve/ Stop Compression test | The inner member assembly must be capable of being compressed by a force of ≥ 7.0 lbs. | 6x20 8x40 9x40 10x80 | 5 10 5 10 |
| SMART Control stent system | Stop Pull Test | This test was conducted to evaluate the heat seal bond between the stop, coil and coil sleeve. The pull force shall be greater than or equal to 0.7 lbs. after being compressed to ≥ 7.0 lbs. | 6x20 6x80 8x100 10x60 | 10 10 10 10 |
| SMART stent system | Outer member /hub pull test | Test conducted to evaluate the ability of the outer member hub/ body seal to withstand the required pull force of ≥ 7.0 lbs. | 8x40 9x40 10x80 | 5 5 5 |
| SMART Control stent system | Outer member /hub pull test | Test conducted to evaluate the ability of the outer member hub/ body seal to withstand the required pull force of ≥ 5.0 lbs. (Requirement for the hub pull test for the SMART Control stent system is based on stent deployment force specification of ≤ 5.0 lbs.) | 6x20 6x80 8x100 10x60 | 10 10 10 10 |
| SMART stent system | Body/Brite tip Fuse joint pull test | Test conducted to evaluate the ability of the Outer Member body/brite tip seal to withstand the required pull force of ≥ 2.2 lbs. | 6x20 8x40 9x40 10x80 | 10 10 5 10 |
| SMART Control stent system | Brite tip/TTI fuse joint pull test | Test conducted to evaluate the ability of the Outer Member body/brite tip seal to withstand the required pull force of ≥ 2.2 lbs. | 6x20 6x80 8x100 10x60 | 10 10 10 10 |
| SMART stent system | Body elongation pull test | Test conducted to evaluate the ability of the outer member body to withstand the required force of ≥ 7.0 lbs at the 0.2" displacement point prior to elongation. | 8x40 9x40 10x80 | 5 5 5 |
| SMART Control stent system | Body elongation pull test | Test conducted to evaluate the ability of the outer member body to withstand the required force of ≥ 4.5 lbs at 5% strain | 6x20 6x80 8x100 10x60 | 10 10 10 10 |

Table 4. Preclinical testing summary for SMART stent system and SMART Control stent system (cont.)

| System tested | Preclinical Test | Purpose / Acceptance Criteria | Sizes (mm) | No. of Samples Tested |
|----------------------------|--|---|--|-----------------------|
| SMART stent system | Pulsatile Fatigue Testing – 400 million cycles | To determine wear and fatigue related failure of the stent after being subjected to 400 million cycles of pulsatile fatigue | 10x80 mm stents were tested | Eight |
| SMART Control stent system | Pulsatile Fatigue Testing – 10 million cycles and Safety Analysis Pulsatile Fatigue Justification For SMART Control | To determine wear and fatigue related failure of the stent after being subjected to 10 million cycles of pulsatile fatigue. Justification for applicability of results from 10 million cycle pulsatile fatigue test and FEA to satisfy the requirements for fatigue characterization prior to human use. | 10x60 mm stents were tested N/A | Seven N/A |
| SMART stent system | Stent Corrosion Resistance in Hank's and Bile Physiological Solutions | Breakdown Potential 503 ± 70 mV for the Palmaz Schatz Test. The calculated lifetime (based upon corrosion current density $\{I_{corr}\}$)of the SMART Stent should be at least 10 years | N/A | N/A |
| SMART Control stent system | Stent Corrosion Resistance in Hank's and Bile Physiological Solutions | Breakdown Potential 503 ± 70 mV for the Palmaz Schatz Test The calculated lifetime(Based upon I_{corr})of the SMART Control Stent should be at least 10 years | N/A | N/A |

In the pulsatile fatigue testing of the SMART stent, there were no component fractures in any stent after 400 million cycles of pulsatile fatigue. In the pulsatile fatigue testing of the SMART Control stent, there were no component fractures in any stent, nor any indication of wear or corrosion, after 10 million cycles of pulsatile fatigue. Finite Element Analysis (FEA) demonstrated that both the mean and alternating strains on the SMART Control stent were no higher than the SMART stent.

The results of the electrochemical measurements of both stent systems demonstrated that the lifetime of the stent is at least 10 years with a breakdown potential greater than that of the predicate stainless steel Palmaz Schatz stent.

C. Animal Testing

Two canine animal studies were conducted to evaluate the SMART stent system. The purpose of these GLP studies was to obtain information with respect to early and late patency rates, the healing response of the vessel to the device, the endothelialization process, changes in stent diameter with time, and the 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 SMART stent in the left iliac artery, and evaluations were made at 48 hours, 4 weeks, and 6 and 12 months. The results showed that 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 6 months was not present at 12 months, and simply reinforces the precaution already made about correct stent sizing.

A single porcine animal study was also conducted using the Precise™ Nitinol Stent and Delivery System, of which the SMART Control stent system is considered a line extension. (Like the SMART Control stent system, the Precise stent system has a 6F delivery catheter, but it does not have the tantalum micro-markers on the stent or the proximal handle on the catheter.) The results showed that the stent can be successfully deployed.

D. Sterility Packaging and Shelf Life Testing

Sterility

The SMART stent system and the SMART Control stent system are ethylene oxide sterilized per the requirements specified in the ANSI/AAMI/ISO standard No. 11135:1994, "Medical devices -- Validation and routine control of ethylene oxide sterilization." The validation results demonstrated that the sterilization process can achieve a sterility assurance level (SAL) of 10^{-6} , and that residual levels were within acceptable ranges in accordance with the ISO 10993-7 standard. Device and package performance were also assessed after sterilization and found to be within specification.

Shelf Life Tests

A two-year shelf life testing was performed on 30 SMART stent systems. The results of this test demonstrate that the SMART stent system complies with product specification, quality characteristics, functional, safety requirements after two years of storage.

A two year accelerated shelf life testing was performed on 75 SMART Control stent systems. The results of this test demonstrate that the SMART Control stent system complies with product specification, quality characteristics, functional and safety requirements after two years of storage.

Packaging Tests

The packaging for the SMART stent system was tested utilizing 74 samples from three different lots. The tests included: packaging visual inspection; seal strength of pouch; burst strength of pouch; packaging challenge test; catheter / device visual test requirements; and dye penetration test. The results demonstrate that all the units met the acceptance criteria.

The packaging for the SMART Control stent system was tested utilizing 328 samples from one lot. The packaging tests included: packaging visual inspection; package integrity (package challenge test); dye penetration test; and pouch peelability. The results demonstrated that all the units met the acceptance criteria.

IX. Summary of Clinical Investigations Involving Human Subjects

A multi-center, randomized study (CRISP-US) was conducted at 20 investigative sites in the United States. The purpose of the CRISP-US study was to assess the equivalent performance of the SMART stent system and the Schneider WALLSTENT® Iliac Endoprosthesis, in patients with *de novo* or restenotic lesions in the common and/or external iliac artery(ies), following suboptimal percutaneous transluminal angioplasty (PTA). A total of 203 subjects with 226 lesions were treated in the study -- 102 patients with 114 lesions were randomized to receive the SMART stent, while 101 patients with 112 lesions were randomized to receive the WALLSTENT® device.

This randomized clinical study of the SMART stent system (CRISP-US), together with the preclinical data summarized above showing the design equivalence of the SMART Control stent system, was used to provide reasonable assurance of the safety and effectiveness of the SMART Control stent system.

Study Endpoints: The primary effectiveness endpoint was the rate of restenosis via duplex ultrasound at 9 months. The primary safety endpoint was a composite of the rate of patient death within 30 days of the procedure and the rate of target vessel revascularization (TVR) within 9 months of the procedure. Secondary endpoints included the rate of acute procedural success, adverse events, and the rates of early and late clinical success based on changes in the Ankle/Brachial Index (ABI), Thigh/Brachial Index (TBI), and/or Rutherford/Becker Scale.

An independent clinical events committee adjudicated all of the major adverse events (MAEs) and deaths. All duplex and angiographic measurements were determined by independent central laboratories. Endpoints were analysed on an intent-to-treat basis.

Patients Studied: Eligible patients had either *de novo* or restenotic lesions in the common and/or external iliac artery of up to 145 mm in length with a documented suboptimal PTA result, a reference vessel diameter of 4 to 9 mm, and angiographic evidence of a patent profunda or superficial femoral artery. Baseline characteristics for the patients in the CRISP-US study are presented in Table 5.

Table 5. Baseline Demographics and Clinical Characteristics

| Patient Characteristic | SMART (N=102 Patients) | WALLSTENT (N=101 Patients) | All Randomized (N=203 Patients) | Difference [95% C.I.] | P-Value |
|---|---------------------------|-------------------------------|------------------------------------|--------------------------|---------|
| Age (years)* | | | | | |
| Mean±SD (N) | 65.8 ± 11.00 (102) | 66.6 ± 9.67 (101) | 66.2 ± 10.34 (203) | 0.8% [0.2%, 3.0%] | 0.597 |
| Number of men* | 62.7% (64/102) | 61.4% (62/101) | 62.1% (126/203) | -1.3% [-15%, 3-12.1%] | 0.817 |
| History of Peripheral Vascular Disease (PVD)* | 89.2% (91/102) | 94.1%(95/101) | 91.6% (186/203) | 4.9%[-2.7%, 12.5%] | 0.031 |
| Diabetes mellitus* | 21.6% (22/102) | 30.7% (31/101) | 26.1% (53/203) | 9.1%[-2.9%, 21.1%] | 0.164 |
| History of smoking* | 90.2% (92/102) | 92.1% (93/101) | 91.1% (185/203) | 1.9%[-5.9%, 9.7%] | 0.768 |
| Reference vessel diameter (mm)** | | | | | |
| Mean±SD (N) | 7.9 ± 1.71(118) | 7.4 ± 2.12(114) | 7.7±1.93(232) | -0.5 [-1.0, -0.0] | 0.072 |
| Minimal lumen diameter (mm)** | | | | | |
| Mean±SD (N) | 2.9 ± 1.42(118) | 2.5 ± 1.50(114) | 2.7 ± 1.47(232) | -0.4 [-0.8, -0.0] | 0.041 |
| Lesion length (mm)** | | | | | |
| Mean±SD (N) | 24.7 ± 15.60(115) | 24.5 ± 19.11(114) | 24.6 ± 17.39(229) | -0.2 [-4.7, 4.3] | 0.921 |
| Percent diameter stenosis (mm)** | | | | | |
| Mean±SD (N) | 62.6 ± 17.20(118) | 65.7 ± 15.45(114) | 64.1 ± 16.40(232) | 3.1 [-1.1, 7.3] | 0.149 |

*Variables are counted by patient

**Variables are counted by lesion

Methods: Patients eligible for the study underwent a PTA and were randomized following an angiographically documented suboptimal result defined by the presence of an unfavorable lesion morphology such as: a) a documented inadequate angiographic and/or hemodynamic result as defined by a 30% or greater residual stenosis resultant to PTA, lesion recoil or intimal flaps and/or b) flow limiting dissections post PTA longer than the initial lesion length, and/or c) a 5 mm Hg, or greater mean transtenotic pressure gradient post PTA. Lesions treated could be single, multiple, and/or bilateral. Baseline quantitative angiography was performed pre-procedure, post-PTA, and post-procedure in all patients. Duplex Ultrasound was performed prior to discharge. Duplex Ultrasound was utilized in all patients to make an initial determination of restenosis at the 9-month follow-up. If restenosis was observed, or if the Duplex Ultrasound was non-diagnostic, a confirmatory angiogram was performed to document the amount of restenosis present. Computer assisted quantitative angiographic analysis (QA) and Duplex Ultrasound were performed at central laboratories.

Results: Visit compliance at 9 months was 88.2% (90/102) vs. 81.2% (82/101) in the SMART stent vs. WALLSTENT® groups, respectively; of the surviving patients, compliance to duplex/angiographic follow-up was 84.7% (83/98) and 78.8% (78/99) patients, respectively.

There were no statistically significant differences between the test and control stent groups in either the primary safety endpoint or the primary effectiveness endpoint. Both the SMART stent and WALLSTENT groups had comparably low rates of death within 30 days (2.0% vs. 0.0%), TVR (2.0% vs. 4.0%), and restenosis (3.5% vs. 2.7%), respectively. Acute procedural success was achieved in 98.2% of patients receiving the S.M.A.R.T™ Nitinol Stent compared to 87.5% in the WALLSTENT® group, which is a statistically significant difference of 10.7% (95% CI = -17% to -4.1%). Primary patency was maintained in 95% of all patients at 9 months. Only one patient experienced a major adverse ischemic event in the hospital; at 9 months, the occurrence was 4.9% vs. 4.0% in the SMART stent and WALLSTENT groups, respectively. The principal effectiveness and safety results are presented in Table 6. The freedom from major adverse ischemic events Kaplan-Meier curve is presented in Figure 3.

Gender bias

A higher percentage of males (62%) than females (38%) were included in the trial; however, this is reflective of the distribution of the disease in the population, and there was no evidence of gender bias. Evaluation of 9-month restenosis by gender showed no significant difference between groups of either gender, although incidents of restenosis occurred more frequently in males in the WALLSTENT® group (4 to 0, male to female). Acute procedural success was more likely to occur in males in the SMART stent group, which had 100% success compared with 81.5% in the WALLSTENT® group, a significant difference of 18.5% (95% CI=-28%, -9.1%). There were no significant differences between females in either treatment group in acute procedural success, or in the early or late clinic success rates for either gender. The occurrence of major adverse events was comparable between treatment groups for both males and females. A larger percentage of females experienced events than did males overall, although the total number of events was too small to make this difference statistically significant.

Table 6. Principal Effectiveness and Safety Results - All Patients Treated (N=203)

| Effectiveness Measure | SMART (N=102) | WALLSTENT (N=101) | Difference [95% CI] | P-Value |
|-------------------------------------|------------------|----------------------|------------------------|---------|
| Composite Endpoint* | 6.9% (7/102) | 5.9% (6/101) | -1.0% [-7.7%, 5.7%] | 1.000 |
| 9-month restenosis rate** | 3.5% (4/114) | 2.7% (3/112) | -0.8% [-5.3%, 3.7%] | 1.000 |
| Death within 30 days* | 2.0% (2/102) | 0.0% (0/101) | -2.0% [-4.7%, 0.7%] | 0.498 |
| TV-revascularization at 9 months* | 2.0% (2/102) | 4.0% (4/101) | 2.0% [-2.7%, 6.7%] | 0.445 |
| Effectiveness Measures | | | | |
| Acute procedural success** | 98.2% (112/114) | 87.5% (98/112) | -11% [-17%, -4.1%] | 0.002 |
| Early clinical success** | 81.6% (93/114) | 75.9% (85/112) | -5.7% [-16%, 4.9%] | 0.331 |
| Late clinical success** | 64.9 (74/114) | 66.1 (74/112) | 1.2% [-11%, 13.6%] | 0.889 |
| Primary patency to 9 months | 94.7% (108/114) | 94.6% (106/112) | -0.1% [-6.0%, 5.8%] | 1.000 |
| Revascularization within 9 months** | 0.0% (0/114) | 2.7% (3/112) | 2.7% [-0.3%, 5.7%] | 0.120 |
| Bypass within 9 months** | 1.8% (2/114) | 0.9%(1/112) | -0.9% [-3.9%, 2.1%] | 1.000 |
| Safety Measures | | | | |
| In-hospital MAIEs* | 1.0% (1/102) | 0.0% (0/101) | -1.0% [-2.9%, 0.9%] | 1.000 |
| Out-of-hospital MAIEs to 9 months* | 3.9% (4/102) | 4.0% (4/101) | -0.04% [-5.4%, 5.3%] | 1.000 |
| Cumulative MAIEs to 9 months* | 4.9% (5/102) | 4.0% (4/101) | -0.9% [-6.6%, 4.8%] | 1.000 |
| Stent thrombosis* | 1.0% (1/102) | 1.0% (1/101) | 0.0% [-2.7%, 2.7%] | 1.000 |
| Major bleeding complications* | 0.0% (0/102) | 0.0% (0/101) | 0.0% [0.0%, 0.0%] | -- |
| Major vascular complications* | 0.0% (0/102) | 0.0% (0/101) | 0.0% [0.0%, 0.0%] | -- |
| CVA/TIA* | 0.0% (0/102) | 0.0% (0/101) | 0.0% [0.0%, 0.0%] | -- |

*Variables are counted by patient.

** Variables are counted by lesion.

Numbers are % (counts/sample size) or Mean±SD

Relative risk=risk of event in WALLSTENT group as compared to SMART stent; SE= $SE=\sqrt{[(1-p_1)/n_{11}+(1-p_2)/n_{21}]}$
 CI=RR*exp(±1.96SE)

Difference=WALLSTENT-SMART; SE= $SE=\sqrt{p_1*q_1/n_1+p_2*q_2/n_2}$ CI=Diff±1.96*SE

Primary Endpoint = A composite of 1) nine month restenosis rate via duplex ultrasound of the CFA and 2) the presence of any adverse clinical outcome defined as a) peri-procedural (30-day) death or b) repeat revascularization of the target vessel at the 9-month follow-up visit.

Acute Procedural Success = Vessels with 30% residual stenosis immediately after stent placement. Mean transtenotic pressure gradient < 5mmHg and no occurrence of a procedure related adverse event within the Lab. This is determined at both clinical site and the core lab.

Early Clinical Success = Vessels with Rutherford/Becker Classification >=1 at the latest follow-up between baseline and 30-day post-treatment follow-up.

Late Clinical Success = Maintenance of achieved improvement in the appropriate segmental limb pressure index (ABI and TBI) which if not normalized (>.90) must have increased by at least 0.10 over the initial preoperative level and not have deteriorated by more than 0.15 from the maximum early post-procedure level.

MAIE = Major adverse ischemic events = Death to 30 days, in-hospital MI, TVR, or amputation

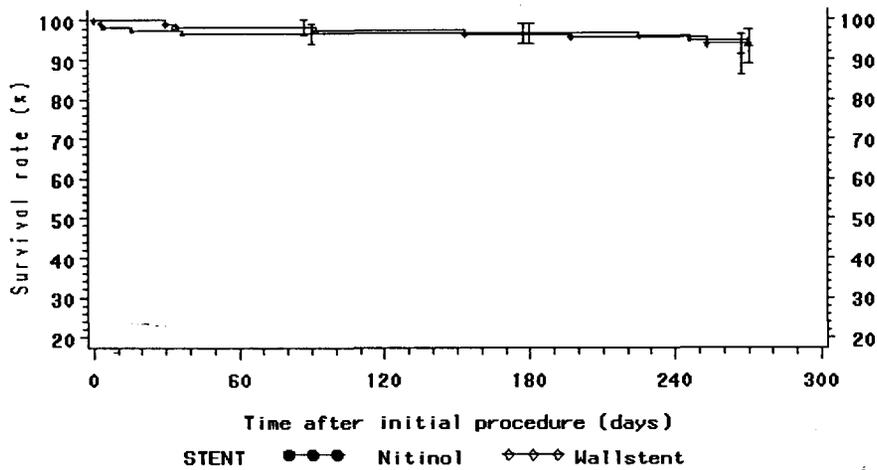
Primary patency = continuous flow without revascularization, determined as any patient who did not die, and did not have a revascularization, amputation, or bypass within the first 9 months. Presented as proportion of patients with primary patency.

Revascularization = continuous flow assisted by revascularization within the first 9 months, excluding bypass ("Primary assisted patency")

Bypass = reestablishment of flow to distal arteries following bypass of the target vessel ("Secondary patency")

Note: 9-month patency endpoints unavailable for lesions in patients not surviving to 9 months (SMART=4, WALLSTENT=2)

Figure 3. Freedom from Major Adverse Ischemic Events - All Patients Treated (N=203)



SMART

| Category | 90 Days | 180 Days | 270 Days |
|----------------|---------|----------|----------|
| # Entered | 102 | 98 | 98 |
| # Censored | 0 | 0 | 96 |
| # At Risk | 102 | 98 | 50 |
| # Events | 4 | 0 | 2 |
| # Events/Month | 1.333 | 0 | 0.6667 |
| % Survived | 96.1 | 96.1 | 92.2 |
| SE % | 1.9 | 1.9 | 3.2 |

WALLSTENT

| Category | 90 Days | 180 Days | 270 Days |
|----------------|---------|----------|----------|
| # Entered | 101 | 99 | 97 |
| # Censored | 0 | 0 | 95 |
| # At Risk | 101 | 99 | 49 |
| # Events | 2 | 2 | 2 |
| # Events/Month | 0.667 | 0.6667 | 0.6667 |
| % Survived | 98.0 | 96.0 | 92.2 |
| SE % | 1.4 | 1.9 | 3.3 |

X. Conclusions Drawn from the Studies

The pre-clinical studies indicate that the SMART stent and the SMART Control stent meet or exceed safety and performance specifications.

Multicenter clinical data found that the rates of major adverse events were similar in the test group of patients treated with the Cordis SMART stent and the control patients treated with the WALLSTENT. There were no significant safety issues with either stent. Early and late effectiveness measures were similar in the test group and the control group, except that the SMART stent had a rate of acute procedural success that was a statistically significant improvement over the WALLSTENT.

Prior indications for use of stents currently being considered for market approval for use in the iliac artery have been limited to provisional stenting. Because of the high success with iliac stenting, stenting of iliac artery stenoses or occlusions has become the usual clinical practice regardless of whether the initial PTA was suboptimal. The literature suggests that stenting after suboptimal PTA represents the worst case for testing of a new stent. Given the acceptable results from this study, it was concluded that the Cordis stent should be indicated for primary stenting.

The results of the pre-clinical studies and the clinical investigation provide valid scientific evidence and reasonable assurance that the SMART stent system and the SMART Control stent system are safe and effective for their intended use.

XI. Panel Recommendation

In accordance with provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory Systems Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XII. CDRH Decision

FDA issued an approval order on August 12, 2003.

Based on FDA inspections of the applicant's manufacturing facilities, those facilities were found to be in compliance with the device Quality System Regulation (QSR, Part 820) regulations.

XIII. 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 and Restrictions: See approval order.