

SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Product Code: NIP - Stent, Superficial Femoral Artery

Device Trade Name: S.M.A.R.T.® CONTROL® and S.M.A.R.T.® Vascular Stent Systems

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

Date(s) of Panel Recommendation: N/A

Premarket Approval Application (PMA) Number: P120002

Date of FDA Notice of Approval: November 7, 2012

II. INDICATIONS FOR USE

The Cordis S.M.A.R.T.® CONTROL®/ S.M.A.R.T.® Vascular Stent System is indicated for use to improve luminal diameter in the treatment of patients with de novo or restenotic native lesion(s) of the superficial femoral artery and/or proximal popliteal artery with total length up to 150 mm and with a reference vessel diameter ranging from 4 mm to 7 mm.

III. CONTRAINDICATIONS

- Patients with a known hypersensitivity to nickel titanium.
- Patients who cannot receive antiplatelet or anticoagulation therapy.
- Patients who are judged to have a lesion that prevents complete inflation of an angioplasty balloon or proper placement of the stent or stent delivery system.

IV. WARNINGS AND PRECAUTIONS

The Warnings and Precautions can be found in the Instructions for Use for the Cordis S.M.A.R.T.® CONTROL® and S.M.A.R.T.® Vascular Stent Systems

V. DEVICE DESCRIPTION

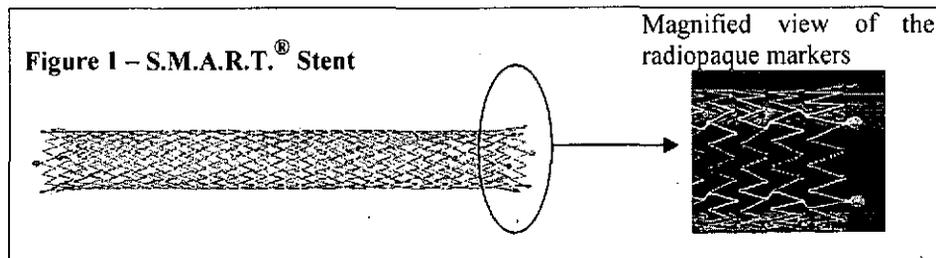
The S.M.A.R.T.[®] CONTROL[®] and S.M.A.R.T.[®] Vascular Stent Systems consist of a self-expanding stent made of Nitinol (nickel-titanium alloy) material that is pre-mounted on an over-the-wire delivery system. The stents contain tantalum markers at each end.

The S.M.A.R.T.[®] CONTROL[®] and S.M.A.R.T.[®] stents are provided in multiple lengths and diameters. **Table 1** lists the available stent diameters and lengths for the S.M.A.R.T.[®] CONTROL[®] and S.M.A.R.T.[®] Vascular Stent Systems.

L Ø	S.M.A.R.T. [®] CONTROL [®] Stent System (Handle)						S.M.A.R.T. [®] Stent System (Pin/Pull)	
	20 mm	30 mm	40 mm	60 mm	80 mm	100 mm	120 mm	150 mm
6mm	x	x	x	x	x	x	x	x
7mm	x	x	x	x	x	x	x	x
8mm	x	x	x	x	x	x	x	x

Ø = Diameter L=Length

The S.M.A.R.T.[®] CONTROL[®] and S.M.A.R.T.[®] Vascular Stents are designed to open to a pre-programmed diameter at body temperature. **Figure 1** provides an illustration of the stent.

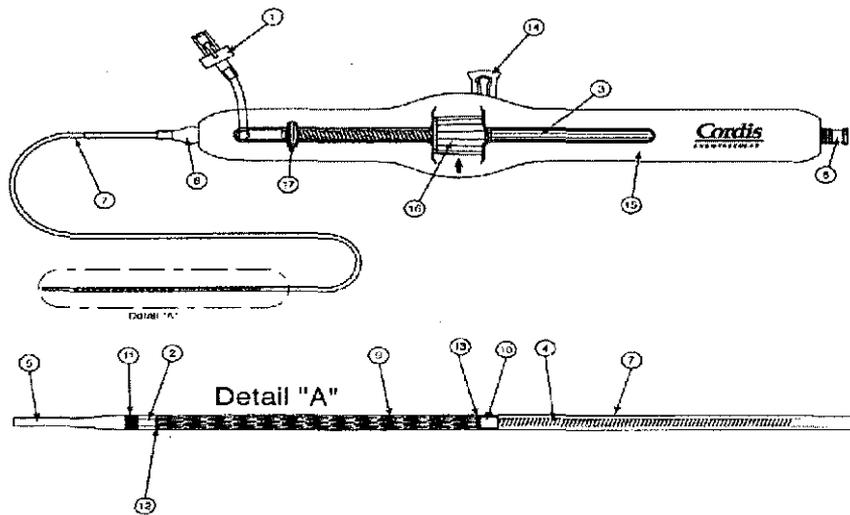


There are two delivery system configurations, S.M.A.R.T.[®] CONTROL[®] and S.M.A.R.T.[®], which are illustrated in **Figures 2 and 3**, respectively. The stent is contained within the outer sheath of the delivery system. Once the distal end of the delivery system reaches the treatment site, the outer sheath of the delivery system is retracted to expose the stent and start its self-expansion. For the S.M.A.R.T.[®] CONTROL[®] Stent System, sheath retraction is achieved by grasping the handle in a fixed position with the tuning dial held between the thumb and index fingers, and rotating the tuning dial in a clockwise direction until the distal end of the stent is visibly apposed to the vessel wall. For the S.M.A.R.T.[®] Stent System, sheath retraction is achieved by grasping the inner shaft in a fixed position and moving the outer sheath proximally relative to the inner shaft.

The stents for the S.M.A.R.T.[®] CONTROL[®] system are available in diameters of 6, 7, and 8 mm and in lengths of 20, 30, 40, 60, 80, and 100 mm. The stents for the S.M.A.R.T.[®] system are also available in diameters of 6, 7, and 8 mm and in lengths of 120 and 150 mm. The S.M.A.R.T.[®] CONTROL[®] delivery system uses a handle controlled mechanism to

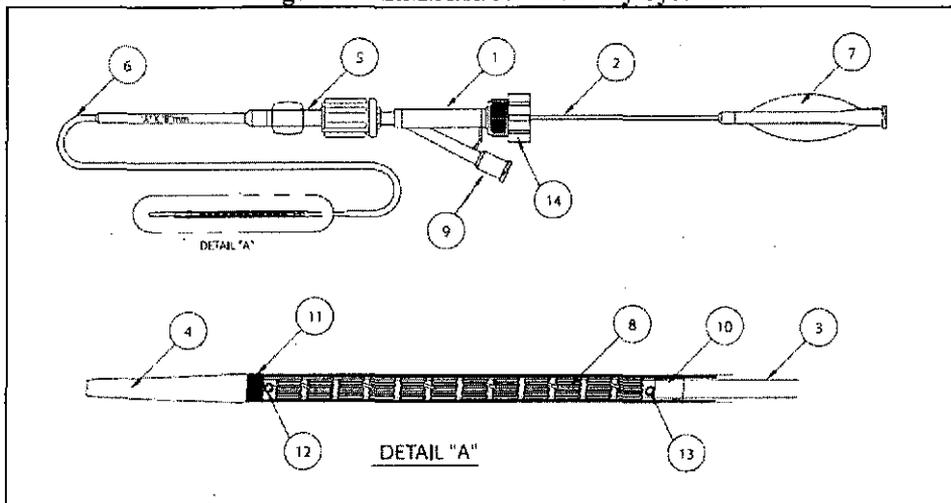
deploy the stent. This delivery system is available in lengths of 80 and 120 cm. The S.M.A.R.T.[®] delivery system uses a “pin/pull” mechanism. This delivery system has a length of 120 cm. Both delivery systems are compatible with 6F sheath introducers and with 0.035 guidewires.

Figure 2 - S.M.A.R.T.® CONTROL® Delivery 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 | | |

Figure 3 – S.M.A.R.T.® Delivery System



- | | | | |
|---|----------------------------------|----|---|
| 1 | Tuohy Borst valve | 8 | S.M.A.R.T. Stent |
| 2 | Inner shaft: metallic tube | 9 | Y connection on the Tuohy Borst valve |
| 3 | Inner shaft: Polymeric tube | 10 | Inner shaft stent stop |
| 4 | Catheter tip (Distal wire lumen) | 11 | Distal Radiopaque marker |
| 5 | Luer hub (outer sheath) | 12 | Distal stent marker |
| 6 | Outer sheath | 13 | Proximal stent marker |
| 7 | Luer hub (proximal wire lumen) | 14 | Proximal valve of the Tuohy Borst valve |

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the treatment of atherosclerotic disease of the superficial femoral and proximal popliteal arteries. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

These alternative practices and procedures include:

- Non invasive lifestyle modifications (e.g., exercise, weight control, cessation of smoking);
- Drug therapy;
- Minimally invasive endovascular procedures (e.g., balloon angioplasty, stent placement, stent graft placement and atherectomy); or
- Surgical intervention (e.g., by-pass)

VII. MARKETING HISTORY

The S.M.A.R.T.[®] CONTROL[®] and S.M.A.R.T.[®] Vascular stent systems, developed and manufactured by Cordis, were previously cleared/approved by FDA for palliation of malignant neoplasms in the biliary tree in 1998, for the treatment of stenotic lesions in iliac arteries in 2003, and have been commercially available in the United States since then.

The stent systems for SFA indication are identical to the systems cleared/approved for use in the biliary tree and iliac arteries. These products are also being marketed for vascular indications in a large number of countries outside the United States.

Since 2000, Cordis has executed 5 recalls on the SMART[®] stent family of products. In 2000, Cordis executed a recall on 2 lots of product which were packaged in the incorrect carton. The issue was caused by human error and it was addressed via retraining personnel. In 2003, a recall was executed for deployment difficulties on SMART[®] CONTROL[®] vascular codes marketed outside the United States; the deployment difficulty was attributed to design and it was addressed via a minor design change. The third recall took place in 2008, when ten lots of one catalog number were recalled due to a manufacturing error which resulted in the use of a prior version of wire lumen material. The error was caused by a transcription error between the documentation system and the manufacturing information system. A Corrective Action and Preventive Action (CAPA) file was opened and the issue was fully resolved. In February 2012, Cordis initiated a recall of the SMART[®] CONTROL[®] product due to observations of small channels in the seal of the package detected during product testing. The defect was attributed to lack of adhesive transfer due to inconsistent execution of the process. A Corrective and Preventive Action (CAPA) file was opened to address the finding and product distribution was restored. On April 9, 2012, Cordis initiated a limited recall on 32 lots of SMART[®] Cordis Nitinol Stent Transhepatic Biliary System and SMART[®] CONTROL[®] Nitinol Stent Transhepatic

Biliary System for potential sterility breach due to holes in the Tyvek package. The root cause was identified and corrected, and product distribution was restored.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the device.

- Abrupt closure
- Access failure
- Allergic / anaphylactoid reaction to anticoagulant and/or antithrombotic therapy or contrast medium
- Allergic reaction to nitinol
- Amputation
- Anemia
- Aneurysm
- Angina / coronary ischemia / myocardial infarction
- Arrhythmia
- Arterial occlusion / thrombus
- Arterial restenosis
- Arterial spasm
- Arterial stenosis, or dissection
- Arteriosclerosis
- Arteriovenous fistula
- Blue toe syndrome
- Bradycardia
- Worsened claudication or rest pain
- Death
- Disseminated intravascular coagulation
- Edema, peripheral
- Embolism
- Emergent repeat hospital intervention
- Encephalopathy (new or worse)
- Fever
- Fistulization
- Gangrene
- Gastrointestinal bleed from anticoagulation/antiplatelet medication
- Hematoma/hemorrhage
- Hypotension / hypertension
- Infection/ abscess at insertion site
- Ischemia requiring intervention (bypass or amputation of toe, foot, or leg)
- Multi-organ failure
- Muscle hemorrhage
- Pain
- Pseudoaneurysm
- Renal failure
- Respiratory arrest
- Septicemia / bacterimia (sepsis)
- Stent embolization
- Stent migration

- Stent occlusion
- Tissue necrosis
- Trauma to adjacent structures
- Stroke /TIA (hemorrhagic/embolic)
- Vascular injury, including perforation, rupture and dissection
- Venospasm
- Venous occlusion / thrombosis, puncture site (restenosis or recurrent stricture)

For the specific adverse events that occurred in the clinical studies, please see Tables 11-12 in Section X below.

IX. SUMMARY OF PRECLINICAL STUDIES

A. *IN VITRO*/BENCH TESTING

In vitro bench testing to support the safety and effectiveness of the S.M.A.R.T.[®] CONTROL[®] and S.M.A.R.T.[®] stent systems was consistent with FDA Guidance, Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems, April 18, 2010. The relevant *in vitro* tests outlined in the guidance document and included in support of the SMART[®] devices are summarized in Table 2. Unless otherwise specified, all test units were sterilized using a validated Ethylene Oxide sterilization process.

Table 2: Summary of Bench Testing of the S.M.A.R.T.[®] CONTROL[®] and S.M.A.R.T.[®] Stent Systems

Test	Purpose	Acceptance Criteria	Results
Material Characterization			
Material Composition (Stent)	To verify that the stent materials conform to the chemical composition requirements of ASTM F2063 (nitinol) and ASTM F560 (tantalum)	The stent materials, nitinol and tantalum, must meet ASTM F2063 and ASTM F560 specifications respectively	Pass
Material Composition (Delivery Systems)	The composition of the materials used to manufacture the SMART CONTROL and SMART delivery systems meet required material specifications	All materials and components must meet specifications	Pass
Corrosion Resistance	To evaluate the susceptibility of the stent material to corrosion, including pitting and fretting for overlapped stents and galvanic corrosion for overlapped stents of dissimilar materials.	Fretting Corrosion per ASTM F2129	Pass
		Pitting corrosion comparable to an approved stent	Pass
		Galvanic corrosion was assessed for characterization	No localized corrosion at the interface between dissimilar metals

**Table 2: Summary of Bench Testing of the S.M.A.R.T.[®] CONTROL[®] and S.M.A.R.T.[®] Stent Systems
(Cont.)**

Test	Purpose	Acceptance Criteria	Results
Stent Dimensional and Functional Attributes			
Diameter & Length Verification	To evaluate the stent dimensions post-deployment	Stent dimensions should meet labeled specifications	The acceptance criteria were met
Percent Surface Area	To determine the stent surface area that contacts the vessel	Report surface area calculations based on product drawings	The percent surface area ranges from 16% to 25%
Foreshortening	To report the decrease in length of the stent between the catheter-loaded condition and the deployed diameter	Characterization study	The average foreshortening values were < 5%
Stent Integrity	To report any defects on the deployed stent	No stent damage (cracks, broken struts, gouges or dents) or permanent set	The acceptance criteria were met
Radial Stiffness and Radial Strength (Radial Resistive Force and Chronic Outward Force)	To determine the radial stiffness of the stent at the expanded state and the passive forces imparted on the vessel wall by the stent	Radial Resistive Force ≥ 0.90 N/cm Chronic Outward Force ≤ 0.75 N/cm	The acceptance criteria were met
Mechanical Properties	To specify mechanical properties of the stent material pre and post-processing.	Raw materials must meet incoming acceptance specifications. Post processing study was for characterization purposes	Mechanical properties of the raw materials met specifications
Stress/Strain and Fatigue Analysis	Determine Fatigue Safety Factors under physiologically relevant pulsatile loading conditions Determine mean strains and strain amplitudes under single-mode non-radial deformations including : a) Axial compression b) Bending c) Torsion Determine mean strains and strain amplitudes under various multi-axial non radial deformations	Fatigue Safety Factors > 1.0 Characterization study Characterization study	The acceptance criterion was met Strain amplitudes determined to be below fatigue limit for published single-mode deformation conditions established from biomechanics Validated fracture predictions via FEA with bench-top fatigue tests under multi-axial deformation conditions

Table 2: Summary of Bench Testing of the S.M.A.R.T.® CONTROL® and S.M.A.R.T.® Stent Systems (Cont.)

Test	Purpose	Acceptance Criteria	Results
Accelerated Durability Testing	<p>Evaluate stent structural durability under physiologically relevant pulsatile loading conditions</p> <p>Evaluate stent structural durability under single-mode non-radial deformations including:</p> <ul style="list-style-type: none"> • Axial compression • Bending • Torsion <p>Evaluate stent structural durability under various multi-axial non radial deformations.</p>	<p>No strut fracture after 400 million cycles</p> <p>Characterization study</p> <p>Characterization study</p>	<p>The acceptance criterion was met</p> <p>No stent fractures were observed for published single-mode deformation conditions established from biomechanics</p> <p>Fatigue to fracture study completed for secondary deformation modes superimposed on a primary deformation mode</p>
MRI Safety & Compatibility	To assess the safety of conducting MRI testing after stent implantation	Characterization study	The implanted single and overlapped stents were determined to be "MR Conditional"
Radiopacity	To evaluate the radiopacity of the stent	Visibility under fluoroscopy compared to commercially available stent	The stents were determined to have visibility under X-Ray and fluoroscopic imaging, that is comparable to other commercial stents
Crush Resistance	To demonstrate the ability of the stent to recover its desired size and shape after application and removal of external loads, deformations, or both	Following an acute crush event and load release, the stent diameter must meet diametrical specification	The acceptance criterion was met
Kink Resistance	To determine the smallest radius of curvature that the deployed stent can withstand without kinking	No permanent deformation of the stent or distortion of the geometric pattern should be visible after this test	The acceptance criterion was met

**Table 2: Summary of Bench Testing of the S.M.A.R.T.[®] CONTROL[®] and S.M.A.R.T.[®] Stent Systems
(Cont.)**

Test	Purpose	Acceptance Criteria	Results
Delivery System Dimensional and Functional Attributes			
Dimensional Verification	To verify the key dimensional specifications of the delivery system	Must meet the labeled dimensions	The acceptance criteria were met
Delivery, Deployment, and Retraction	To demonstrate that the delivery catheter can safely and reliably deliver the stent to the intended location without adversely affect the stent by the delivery catheter during deployment and withdrawal	The stents must be able to be delivered to the target zone with no anomalies or stent damage upon deployment and delivery system withdrawal	The acceptance criteria were met
Deployment Accuracy	To evaluate the accuracy of deployment relative to a target location	Characterization study	Average deployment accuracy was within 1 mm of the pre-established target
Catheter Bond Strength	To test the bond strength of the delivery system	Various acceptance criteria for outer sheath bonds, and support member and tip	The acceptance criteria were met
Tip Pull Test	To determine the tensile force that will separate the distal tip from the catheter		
Flexibility & Kink Test	To verify that the stent delivery system will not kink at a worst case bend radius that is appropriate for the intended anatomy	The SDS must not kink when bent around a radius of curvature of 0.325"	The acceptance criterion was met
Torque Strength	To evaluate the torque strength of the stent delivery system when the distal tip is not free to rotate	The SDS must withstand a minimum of five rotations before exhibiting failure	The acceptance criterion was met
Coating Integrity/ Particulate Evaluation	To measure the total number of particulates and size of the particulates generated during the simulated stent delivery and deployment	Characterization study	Limits were well below the guidelines of USP <788> for small volume injections

B. STERILIZATION

The S.M.A.R.T.[®] CONTROL[®] and S.M.A.R.T.[®] Stent Systems are sterilized in compliance with ANSI/AAMI/ISO 11135-1:2007 and EN556-1. Routine testing of biological indicators is performed to confirm that the sterilization process is effective in eradicating viable microorganisms. Results from sterilization studies demonstrate that the S.M.A.R.T.[®] CONTROL[®] and S.M.A.R.T.[®] stent systems will maintain a Sterility Assurance Level (SAL) of 10⁻⁶.

C. PACKAGING AND SHELF LIFE

Packaging qualification testing was performed on the S.M.A.R.T.[®] CONTROL[®] and S.M.A.R.T.[®] Stent Systems which are packaged in a preformed tray, sealed in packaging

pouch and placed in a folding carton. A shelf life of 2 years has been established for the S.M.A.R.T.[®] CONTROL[®] and S.M.A.R.T.[®] Stent Systems based on product and package shelf life testing.

D. *IN VIVO* ANIMAL STUDIES

The S.M.A.R.T.[®] CONTROL[®]/S.M.A.R.T.[®] Stent was subjected to a series of sub-chronic and chronic animal studies. The preclinical animal studies primarily focused on the inflammatory response, procedural techniques and the overall safety of the S.M.A.R.T.[®] Stent devices *in vivo* in both canine and porcine models. The results of the animal studies demonstrated that the stents produce minimal injury, inflammation, and neointimal hyperplasia following implantation in canine and porcine iliac arteries. **Table 3** summarizes the results of the GLP studies conducted on devices representative of the final device design.

Table 3: Summary of GLP Studies Conducted with the SMART[®] Stent

Study Design	Summary of Results
Chronic (up to 180 Day) Study in Canine Iliac Arteries	Sirolimus-eluting and bare metal SMART [®] stents were implanted bilaterally in the iliac canine arteries of 60 animals and followed up for 3, 30, 90 and 180 days. All stents were successfully and accurately delivered and deployed with acceptable performance characteristics. Animals remained hemodynamically stable during delivery and deployment. None of the implants stents elicited acute or chronic thrombosis. All implanted stents had good luminal patency and no significant mural injury or inflammation.
Sub-Chronic (30 Day) Study in Canine Iliac Arteries	Subacute studies (30 days) were performed with Sirolimus-eluting and bare metal SMART [®] stents implanted in the iliac arteries of 25 animals. At 30 days, all stents showed similar low injury scores and no evidence of stenosis in the non-stented portion of the vessel. Animals remained hemodynamically stable during delivery and deployment. All stents were patent when they were explanted.
Chronic (up to 180 Day) Study in Porcine Iliac Arteries	Long-term stent implantation studies were performed using Sirolimus-eluting and bare metal SMART [®] stents, implanted in the iliac arteries of 64 animals. Results from this study showed low inflammation and injury scores for all treatment groups throughout the study. A patent lumen was maintained immediately after deployment and through 30, 90 and 180 days.
Overlapped Stents Chronic (up to 180 Day) Study in Porcine Iliac Arteries using	Overlapping stent pairs were implanted bilaterally in the iliac arteries of 24 animals. All stents were successfully deployed without complication. Neointimal area and percent stenosis were greater in the overlapped region than in the non-overlapped regions at all time points, and increased from 30-days to 90-days, but then decreased slightly at 180 days. Injury and inflammation scores also increased from 30 days to 90 days, but then decreased at 180 days. There was no evidence of hemorrhage, perforation or vessel dilation in any of the animals.

E. BIOCOMPATIBILITY

Biocompatibility testing was conducted on the S.M.A.R.T.[®] CONTROL[®] and S.M.A.R.T.[®] Stent Systems in accordance with applicable Good Laboratory Practices (21 CFR 58) and ISO 10993-1:2003 *Biological Evaluation of medical Devices*. All testing was conducted on sterilized product. For biocompatibility testing, the stent was classified as an implant device in permanent contact (> 30 days) with blood. The stent delivery systems (SDS) were classified as external communicating devices, in limited contact (<24 hours) with circulating blood. **Table 4** summarizes the biocompatibility testing conducted on devices representative of the final design.

Table 4: Biocompatibility Testing Summary on SMART[®] Stents

	SMART [®] Stent	Delivery Systems		Results
		SMART [®] CONTR OL [®]	SMART [®]	
Cytotoxicity – ISO MEM Elution	√	√	√	Pass; Non-toxic
Sensitization – Guinea Pig Maximization	√	√	√	Pass; Non-Sensitizing
Irritation / Intracutaneous Reactivity	√	√	√	Pass; Non-irritating
Acute Systemic Toxicity	√	√	√	Pass; No evidence of systemic Toxicity
Materials Mediated Rabbit Pyrogenicity	√	√	√	Pass; Non-pyrogenic
Bacterial Mutagenicity – Ames Assay	√	√	√	Pass; Non-mutagenic
<i>In Vitro</i> Chromosome Aberration	√	√	√	Pass; Non-clastogenic
<i>In Vitro</i> Mouse Lymphoma Assay	√	√	√	Pass; Non-mutagenic
<i>In Vitro</i> Hemolysis ASTM Direct & Extract	√	√	√	Pass; Non-hemolytic
Partial Thomboplastin Time (PTT)	√	√	√	Pass; Non-activator of the intrinsic coagulation pathway.
Platelet and Leukocyte Count	√	√	√	Pass; No significant difference in the platelet and leucocyte counts.
Complement Activation (SC3a & SC5b-9 Assay)	√	√	√	Pass; Non-activating
<i>In Vivo</i> Thrombogenicity	√	N/A	N/A	Pass. Non-thrombogenic
26 Week Rabbit Intramuscular Implant with Chronic Data	√	N/A	N/A	Pass; Non-irritant, no evidence of systemic/ chronic toxicity Acceptable tissue response in canine coronary arteries
Physicochemical Tests	√	√	√	Pass; Met the USP acceptance criteria.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of the safety and effectiveness of the S.M.A.R.T.[®] CONTROL[®] and S.M.A.R.T.[®] Vascular Stent Systems for improving luminal diameter in the treatment of de novo or restenotic lesion(s) up to 150mm in length in the native superficial femoral artery and/or proximal popliteal arteries with reference vessel diameters ranging from 4-7mm, in the US under IDE G060033. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

The applicant conducted a study titled S.M.A.R.T.[™] Nitinol Self-Expandable Stent in the Treatment of Obstructive Superficial Femoral Artery Disease (STROLL). STROLL was a prospective, multi-center, non-randomized, unblinded, single arm study comparing percutaneous transluminal angioplasty (PTA) and primary stenting with the S.M.A.R.T.[®] Nitinol Stent System to performance goals of PTA alone in the treatment of atherosclerotic lesions of the native superficial femoral artery (SFA) or the superficial femoral and proximal popliteal arteries. The safety and performance goals were based on an aggregate of published trial data as described by VIVA physicians Inc. (VPI). STROLL was conducted at 39 US investigational sites. A total of 250 subjects were enrolled. Eligible subjects either had stenotic, restenotic (non-stented) or occluded lesions. The reference vessel diameter of the treated subjects was to be 4.0 – 6.0 mm and the lesion length from 4-15 cm. Subjects with Rutherford/Becker Clinical Categories of 2-4 were included in the study. Subject follow-up occurred at 30 days, 6 months, and 12 months, and will continue with annual follow-up for up to 3 years.

Patients were treated between August 14, 2008 and March 15, 2010. The database for this PMA reflected data collected through June 18, 2012 and included 250 patients. There were 39 investigational sites.

The primary study endpoints were as follows:

- The primary safety endpoint was major adverse event rate at 30 days, defined as freedom from all causes of death, index limb amputation and clinically driven Target Lesion Revascularization (TLR) through 30 days post-procedure.
- The primary effectiveness endpoint at 12 months was defined as primary Duplex ultrasound (DUS) stent patency rate, and no further clinically driven target vessel revascularization (TVR) performed in the interim. Primary DUS stent patency rate was defined as binary restenosis (>50% diameter stenosis) with a peak systolic velocity ratio (PSVR) > 2.0, as measured by Duplex ultrasound.

For the 30-day safety endpoint, the Agresti-Coull method was used to compare the observed 30-day safety rate against the VIVA performance goal of 88%, using a one-

sided significance level of 0.025. For the primary effectiveness endpoint, the Agresti-Coull method was used to compare the observed primary effectiveness against the VIVA performance goal of 66%, using a one-sided significance level of 0.025. The results were evaluated using the Intent-to-Treat (ITT) population. The ITT population was designed to include all screened patients who met eligibility criteria, had the guidewire positioned across the target lesion(s) and located intraluminally within the distal vessel (regardless whether the patient received the S.M.A.R.T.[®] Stent or not).

The STROLL study was monitored by a Clinical Research Organization (CRO). Independent core laboratories reviewed and analyzed key study variables. An independent Data Safety Monitoring Board (DSMB) was used to review study data on an ongoing basis and identify any potential safety trends. Final adjudication of major adverse events was conducted by an independent Clinical Events Committee (CEC).

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the STROLL study was limited to patients who met the following inclusion criteria:

- The subject was 30 years of age, or older.
- For women of child bearing potential, a pregnancy test done within 7 days prior to the study procedure and negative test results to be eligible.
- Symptomatic leg ischemia by Rutherford/Becker Classification categories 2- 4 (mild to severe claudication) with a resting or exercise ABI < 0.8.
- A single superficial femoral artery lesion with > 50% stenosis or total occlusion.
- Stenotic lesion or occluded length within the same vessel (one long or multiple serial lesions) ranging from 4.0-15.0 cm by visual estimate. The stenosis had to be treatable with no more than two stents, minimizing the stent overlap whose combined length should not exceed 170 mm.
- Reference vessel diameter ranging from 4.0 to 6.0 mm, by visual assessment.
- All lesions located at least three centimeters proximal to the superior edge of the patella.
- There must have been a patent infrapopliteal and popliteal artery, i.e. at least one vessel runoff with at least one of three vessels patent (< 50% stenosis) to the ankle or foot.
- The guidewire must have been across the target lesion(s) and located intraluminally within the distal vessel.
- Poor aortoiliac or common femoral "inflow" (i.e. angiographically defined > 50% stenosis of the iliac or common femoral artery) that would be deemed inadequate to support a femoropopliteal bypass graft was successfully treated prior to treatment of the target lesion. After treatment of the inflow lesion, if the peak to peak pressure gradient across the inflow lesion was < 20 mmHg and the peak to peak pressure gradient across the SFA target lesion was > 20 mmHg, then the patient could be included in the study.
- A patient with bilateral obstructive SFA disease was eligible for enrollment into the study.
- A patient must have been eligible for standard surgical repair, if necessary.

- A patient who required a coronary intervention, should have had it performed at least 7 days prior to the treatment of the target lesion.
- Patient or authorized representative provided written informed consent and written HIPAA authorization prior to initiation of study procedures.
- Patient was willing to comply with the specified follow-up evaluation schedule.

Patients were not permitted to enroll in the STROLL study if they met any of the following exclusion criteria:

- The patient showed evidence of thrombophlebitis, uremia, or deep venous thrombus, within 30 days prior to the index procedure.
- The patient was receiving dialysis or immunosuppressant therapy.
- Thrombolysis of the target vessel within 72 hours prior to the index procedure where complete resolution of the thrombus was not achieved.
- The patient had a stroke within 90 days prior to the index procedure.
- The patient had femoral, iliac or aortic aneurysm or aneurysm in the SFA or popliteal artery within 5 years prior to the index procedure.
- The patient required stent placement via a popliteal approach or required stent placement across or within 0.5 cm of the SFA / PFA bifurcation.
- The patient had procedures which were pre-determined to require stent-in-stent placement to obtain patency, such as severe calcification which is resistant to stenting, or for in-stent restenosis.
- The patient had significant vessel tortuosity or other parameters prohibiting access to the lesion or 90° tortuosity which would prevent delivery of the stent device.
- The patient had a previously deployed stent within the SFA of the target limb.
- The patient had known allergies to the following: aspirin, clopidogrel bisulfate (Plavix®) or ticlopidine (Ticlid®), heparin, nitinol (nickel titanium), contrast agent that could not have been medically managed.
- The patient had presence of thrombus prior to crossing the lesion
- The patient had serum creatinine level > 2.5 mg/dl at time of screening visit.
- The patient had known or suspected active infection at the time of the procedure.
- The patient had bleeding diathesis.
- The patient had presence of an aortic, iliac or femoral artificial graft
- The patient had a life expectancy less than one year, or any other factors preventing clinical follow up.
- The patient required the use of cryoplasty, laser, or atherectomy devices on the target vessel at the time of index procedure.
- The patient had in-stent restenotic lesions at the time of procedures or had a restenotic lesion that had previously been treated by atherectomy, laser, or cryoplasty within 90 days prior to the index procedure.
- The patient was unwilling or unable to comply with procedures specified in the protocol or had difficulty or inability to return for follow-up visits as specified by the protocol.

- The patient was known to be pregnant, incarcerated, mentally incompetent, and/or an alcohol or drug abuser.
- The patient was currently participating in any another investigational drug or medical device study that had not completed primary endpoint(s) evaluation or which clinically interfered with the endpoints from this study or future participation in such studies prior to the completion of this study.
- The patient had major surgical or interventional procedures unrelated to this study within 30 days prior to this study or planned surgical or interventional procedures within 30 days of entry into this study. Interventional procedures performed to the ipsilateral iliac artery to provide access were allowed.
- The patient had tissue loss due to ischemic disease (Rutherford/Becker category 5 or 6).

2. Follow-up Schedule

All patients were scheduled to return for follow-up examinations at 30 days, 6 months, 1, 2 and 3 years post-procedure. Table 5 provides a summary of the study requirements at each stage of the study.

Table 5: Follow Up Schedule

Event	Baseline/Treatment			Follow-up				
	Screen	Index Procedure	Prior to Discharge or within 7 days post-procedure	30 Day (+/- 7 days)	180 Days (+/- 15 days)	360 Days (+/- 30 days)	720 Days (+/- 45 days)	1080 Days (+/- 60 days)
Informed Consent	X							
Inclusion/Exclusion Criteria ^a	X							
Vascular Examination	X ^d			X	X	X	X	X
Demographics & Medical History	X							
Physical Examination ¹	X							
Screening laboratory tests including lipid profile and serum creatinine	X			X ²				
CBC with differential and platelet count ³	X							
Concomitant Anti-platelet Medication ⁴	X		X	X	X	X	X	X
Rutherford/Becker Classification	X		X	X	X	X	X	X
ABI (Resting or Exercise)	X ^b			X	X	X	X	X
Angiography (QA)		X						
Procedural Data		X						
Duplex Ultrasound			X ⁷	X ⁷	X	X	X	X
X-Ray of stented region ⁶					X	X	X	X
Peripheral Artery Questionnaire, Walking Impairment Questionnaire SF-12, EQ-5D	X			X	X	X	X	X
Adverse Event Monitoring		X	X	X	X	X	X	X

¹ Must be completed within seven (7) days prior to the day of the index procedure

² Only serum creatinine will be checked at 30 days

³ If WBC is within normal limits (WNL), differential is not required.

⁴ Plavix® or Ticlid® is recommended for at least one month post procedure; ASA recommended for all patients indefinitely. If Ticlid® is used, the product label should be followed for appropriate patient follow-up

⁵ Patients known to be pregnant should be excluded from study participation – for women of child bearing potential, a pregnancy test must be completed within 7 days of index procedure

⁶ In the event of a stent fracture, X-rays will be conducted every 6 months

⁷ To be done prior to hospital discharge OR on or before the 30 day visit

⁸ Less than or equal to 30 days prior to index procedure

3. Clinical Endpoints

The primary safety endpoint was freedom from all causes of death, index limb amputation and clinically driven TLR through 30 days post-procedure.

Secondary safety endpoints included:

- Major adverse event (MAE) defined as death, limb ischemia/amputation of target limb, TLR; significant embolic events, defined as causing end-organ damage, (e.g. lower extremity ulceration or gangrene) at 6 months and 1, 2, and 3 year follow-up
- Stent fracture rate assessed by x-ray evaluation at 6 months and 1, 2, and 3 year follow-up

The primary effectiveness endpoint was primary patency at the 1 year follow-up time point, and was defined as no significant reduction of flow detectable by Duplex ultrasound (DUS) through the index lesion and no further clinically driven target vessel revascularization (TVR). Significant reduction of flow was determined as binary restenosis, defined as the diameter stenosis > 50% with a peak systolic velocity ratio (PSVR) > 2.0 as measured by DUS.

Secondary effectiveness endpoints included:

- Device success, defined as achievement of a final residual diameter stenosis of <50% (by QA), using the assigned treatment only
- Limb ischemia by Rutherford/Becker Classification at 6 months and 1, 2, and 3 year follow-up
- Ankle-Brachial Index (ABI) at 1 month, 6 months and 1, 2, and 3 year follow-up
- Patency of the target vessel defined as no significant reduction of flow detectable by Duplex ultrasound, and no further clinically driven target vessel revascularization performed in the interim. Significant reduction of flow was determined as binary restenosis, defined as the diameter stenosis > 50% with a peak systolic velocity ratio > 2.0 as measured by DUS at 6 months and 2 and 3 year follow-up

Patient-reported, health-related quality of life (HRQOL) outcomes on physical limitations, physical and social function, symptoms and general HRQOL were also measured and evaluated in the STROLL study using validated instruments such as the Walking Impairment Questionnaire (WIQ).

With regard to success/failure criteria, the STROLL study was designed to compare the primary clinical endpoints to a pre-established performance goal of 88% for safety and 66% for effectiveness.

B. Accountability of PMA Cohort

A total of 250 patients signed the informed consent and were enrolled in the STROLL study. These patients comprise the ITT population. **Table 6** summarizes the study compliance for all follow-up time points. **Tables 7, 8, and 9** show detailed patient accountability for the 30-day, 12-month, and 24 month visits, respectively. Tables 6-9 reflect study compliance data obtained on September 24, 2012.

Table 6: Summary of Subject Compliance

Time	Compliance
Procedure	250/250 (100%)
Discharge	250/250 (100%)
30 Days	242/250 (96.8%)
6 Months	219/250 (87.6%)
1 Year	219/250 (87.6%)
2 Year	203/250 (81.2%)
3 Year	85/250 (34%)

¹3-Year follow-up was ongoing at the time of data export.

Table 7: 30-Day Follow-Up Compliance

30-day Follow-Up	N=250
Available	242/250 (96.8%)
Unavailable	8/250 (3.2%)
Died	0/250 (0.0%)
Lost-to-Follow-Up	0/250 (0.0%)
Missed Visit	6/250 (2.4%)
Withdrew	2/250 (0.8%)

Two (2) patients withdrew consent prior to their 30 day visit, resulting in a total of 248 patients with sufficient data for evaluation of the 30-day primary safety endpoint.

Table 8: 12-Month Follow-Up Compliance

12-month Follow-Up	N=250
Available	219/250 (87.6%)
Unavailable	31/250 (12.4%)
Died	5/250 (2.0%)
Lost-to-Follow-Up	0/250 (0.0%)
Missed Visit	16/250 (6.4%)
Withdrew	10/250 (4.0%)

By the 12-month visit, a total of 5 patients died and 10 withdrew consent, for a total of 235 eligible patients in the 12-month population (see Figure 4). A total of 236 patients had sufficient follow-up data to be included in the evaluation of the 12-month clinical safety endpoints. This includes patients who died prior to the 12-month visit or who had adequate follow-up through 330 days, the start of the 12-month visit window.

Only those patients for whom an evaluable Duplex Ultrasound Assessment was obtained at 12 months follow-up or who had a Target Vessel Revascularization (TVR) performed within 360 days post-index procedure were included in the assessment of the primary effectiveness endpoint for the pivotal STROLL study.

Table 9: 24-Month Follow-Up Compliance

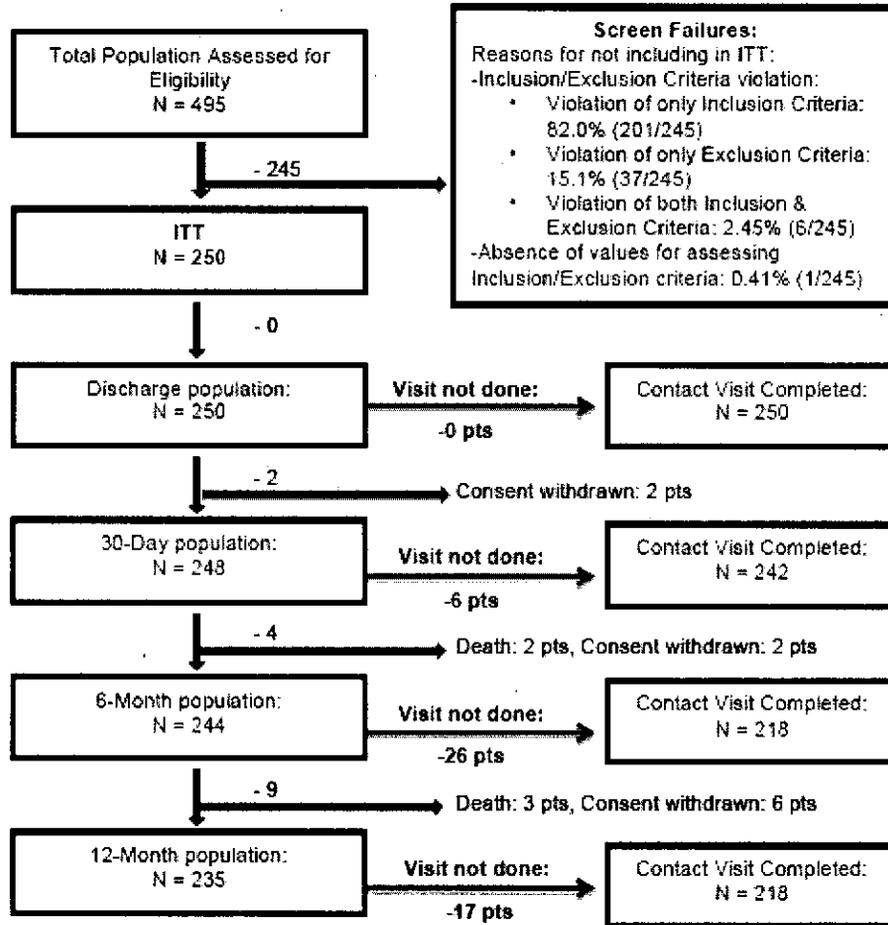
24-month Follow-Up	N=250
Available	203/250 (81.2%)
Unavailable	47/250 (18.8%)
Died	10/250 (4.0%)
Lost-to-Follow-Up	2/250 (0.8%)
Missed Visit	19/250 (7.6 %)
Withdrew	14/250 (5.6%)
Exit the study due to other reasons*	2/250 (0.8%)

*Two (2) patients were withdrawn by the Investigator due to safety concerns

By the 24-month visit, a total of 10 patients died, 14 withdrew consent, and 2 were withdrawn by the Investigator due to safety concerns for a total of 224 eligible patients in the 24-month population. A total of 225 patients had sufficient follow-up data to be included in the evaluation of the 24-month clinical safety endpoints. This includes patients who died prior to the 24-month visit or who had adequate follow-up through 675 days, the start of the 24-month visit window.

Figure 4. Patient compliance flow chart up to 12-months

Patient Compliance Flow Chart



Note:

1. Each N represents the population at the beginning of that visit.
2. The ITT population was designed to include all screened patients who met eligibility criteria and had the guidewire across the target lesion(s) and located intraluminally within the distal vessel (regardless of whether the patient received the S.M.A.R.T. Stent or not).

C. Study Population Demographics and Baseline Parameters

Baseline demographics and clinical characteristics for all patients enrolled in the STROLL study are summarized in **Table 10**. **Table 11** presents baseline lesion characteristics (assessed by the angiographic core laboratory, except as otherwise noted), including lesion location, length, and pre-procedure vessel diameter. The demographics, and baseline clinical and lesion characteristics are considered to be typical of interventional peripheral vascular studies conducted in the United States.

Table 10: Demographics and Baseline Clinical Characteristics

Patient Characteristic	SMART [®] Stent (N=250 Patients N=250 Lesions)
Age (Years), Mean +/- SD (N)	67.71±10.32 (N=250)
Gender (Male)	61.6% (154/250)
Race	
Asian	0.4% (1/250)
Black or African American	12.4% (31/250)
White or Caucasian	85.6% (214/250)
Middle Eastern	0.4% (1/250)
Hispanic	1.2% (3/250)
BMI	29.48±5.81 (250)
Risk Factors	
Diabetes	47.2% (118/250)
Hypercholesterolemia	87.4% (216/247)
Hypertension	88.8% (222/250)
History of Smoking	84.8% (212/250)
Medical History	
Allergies	47.4% (117/247)
Carotid disease (carotid artery stenosis >50%)	31.0% (67/216)
Q-wave or non-Q wave Myocardial infarction (MI)	22.5% (54/240)
Previous coronary percutaneous revascularization	39.9% (97/243)
Previous CABG	26.1% (65/249)
Previous peripheral vascular interventions	89.6% (224/250)
Previous peripheral vascular (low extremity) interventions	39.2% (98/250)
Clinical Characteristics	
Target Limb ABI ¹ , Mean +/- SD (N); Range (min, max)	0.66 ± 0.15 (247) (0.24, 1.32)
<0.4	6.1% (15/247)
0.4-0.8	84.6% (209/247)
>0.8	9.3% (23/247)
Rutherford/Becker Scale ²	
2 = Moderate claudication	45.8% (114/249)
3 = Severe claudication	51.4% (128/249)
4 = Ischemic rest pain	2.8% (7/249)

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

¹ Baseline target limb ABI was not available for three (3) patients - ABI was not recorded for one patient, not done for the second patient and was recorded as "0.00" for the third patient.

² Baseline Rutherford/Becker assessment was not performed for one patient.

Table 11: Baseline Target Lesion Characteristics

Lesion Characteristics	SMART® (N=250 Patients N=250 Lesions)
Lesion Location	
Proximal 1/3 of SFA	10.8% (27/250)
Middle 1/3 of SFA	68.0% (170/250)
Distal 1/3 of SFA	20.0% (50/250)
Lesions extending into proximal popliteal	15.6% (39/250)
Lesion length (mm), normal-to-normal, by core lab ¹	
Mean +/- SD (N)	77.31 ± 35.31 (250)
Range (min, max)	(15.73, 200.10)
Pre-procedural Reference Vessel Diameter, RVD (mm)	
Mean +/- SD (N)	4.87 ± 0.68 (250)
Range (min, max)	(2.71, 8.54)
Pre-procedural Minimum Lumen Diameter, MLD (mm)	
Mean +/- SD (N)	1.17 ± 0.82 (250)
Range (min, max)	(0.00, 3.53)
Pre-procedural Diameter Stenosis (%)	
Mean +/- SD (N)	76.05 ± 16.07 (250)
Range (min, max)	(44.10, 100.00)
Eccentric	20.4% (51/250)
Bend (≥45 degrees)	0.4% (1/250)
Thrombus	0.0% (0/249)
Calcification	
None/Mild	59.2% (141/238)
Moderate	21.4% (51/238)
Severe	19.3% (46/238)
Ulceration Present	1.6% (4/249)
Aneurysm Present	0.0% (0/249)
Total Occlusion	23.6% (59/250)

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

¹ Measured by quantitative angiography (CMS) as the distance (in millimeters) from the proximal to the distal shoulder of the lesion in the projection that demonstrates the stenosis in its most elongated segment.

The total number of subjects who withdrew from the study, were lost to follow-up, or died, regardless of the follow-up visit or visit-window status through the duration of the study are provided in **Table 12**.

Table 12: Subjects who have exited the study

Exited Study	Subjects
Died	22/250 (8.8%)
Lost-to-Follow-Up (LTFU)	3/250 (1.2%)

Exited Study	Subjects
Withdrew	23/250 (9.2%)
Other*	3/250 (1.2%)
Total	51/250 (20.4%)

*Two (2) patients were withdrawn by the Investigator due to safety concerns and one (1) patient had medical records review at the 3-year follow-up visit.

The number of patients who did not complete the 12-month follow up is listed in **Table 13**, along with the reason for the missing data.

Table 13: Reasons for Missing Data for Primary Effectiveness Endpoint

Reason	Number of Subjects
Exited study	
Death (\leq 390 days post-index procedure)	5
Withdrawal of consent*	10
Non-Diagnostic Duplex at 1-year	3
Missing 1-year Duplex Ultrasound Assessment and no interim TVR	17
TOTAL	35

*Patient 469-3 withdrew consent at 320 days post procedure but experienced a TVR at 187 days, thus this patient was included in the analysis.

D. Safety and Effectiveness Results

1. Safety Results

The primary analysis of safety was based on the 248 subjects available for the 30-day evaluation. The key safety outcomes are presented below in **Tables 14 and 15**. Adverse effects are presented in **Tables 16 and 17**.

The primary safety endpoint was freedom from all causes of death, index limb amputation, and clinically driven TLR through 30 days. Among the subjects for whom 30-day safety data were available, the rate of freedom from death, amputation and TLR was 100% with a lower 95% Agresti-Coull Confidence Interval of 98.2%. This is higher than the performance goal of 88%. Therefore, the primary safety endpoint was met. Per protocol, two (2) subjects who did not have reported adverse events or a reintervention prior to 30 days, and who did not complete the 30 day follow-up visit and were without any further follow-up information were not included in this analysis.

Table 14: Primary Safety Endpoint

1-Month (30-Day) Primary Safety Endpoint	S.M.A.R.T. [®] (N=250 Patients N=250 Lesions)	95% Confidence Interval*	Performance Goal	Objective Met
Absence of 30-Day Major Complications	100.0% (248/248)	[98.2%, 100.0%]	88.0%	Yes

For each parameter in the safety measures, the denominator is the number of enrolled subjects who had sufficient follow up (at least 23 days for 1 month visit) plus any subjects who had an event prior to the milestone visit.

*Agresti-Coull method was used to calculate the 95% CI of the point estimate for the endpoint primary safety endpoint.

Additional safety endpoints are discussed below.

The one year MAE rate was 14.4% (34/236) and is presented in **Table 15**.

Table 15: Major Adverse Event Rate at 1 Year

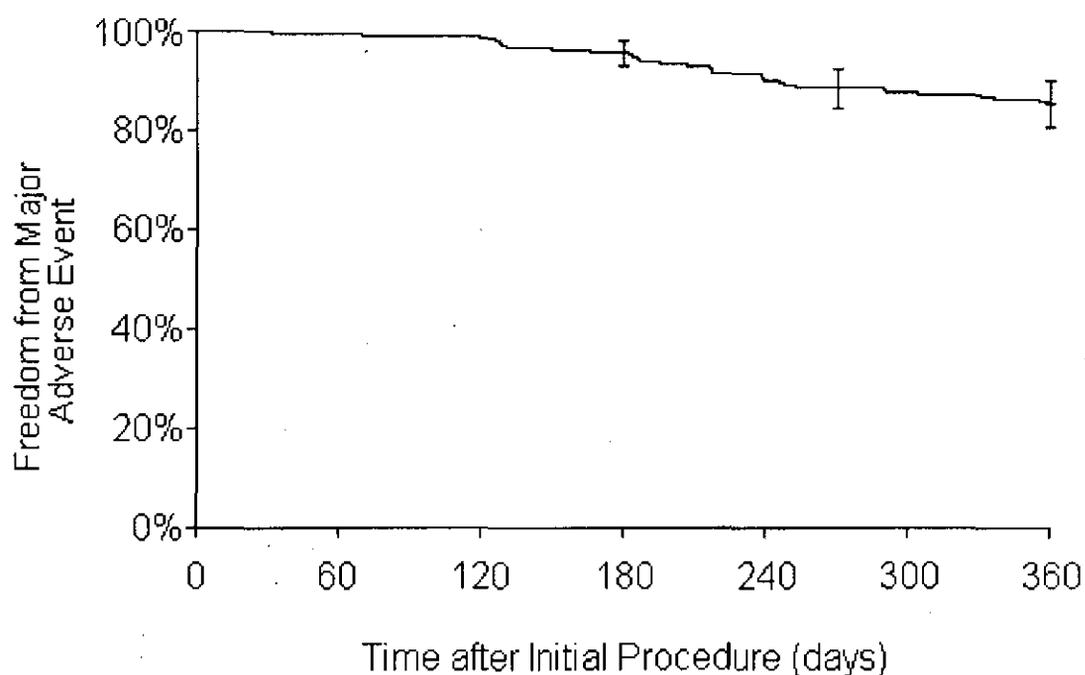
1 Year MAE	N=236
Subjects with MAE at 1-Year	14.4% (34/236)
Death	2.1% (5/236)
Limb ischemia or amputation of the target limb	0.4% (1/236)
TLR through 12 months	13.6% (32/236)
Significant embolic events (e.g., causing ulceration or gangrene)	0.0% (0/236)

For each parameter in the safety measures, the denominator is the number of enrolled subjects who had sufficient follow-up (at least 330 days for the 12 month visit) plus any subjects who had an event prior to the milestone visit).

Figure 5 below is a Kaplan-Meier plot showing freedom from Major Adverse Event to 360 days:

Figure 5. Freedom from Major Adverse Event to 360 Days

Major Adverse Event	0	7	30	180	270	360
# Entered	250	250	249	245	232	210
# Censored	0	1	4	3	5	36
# Incomplete	0	0	0	0	0	0
# At Risk	250	250	247	244	230	192
# Events	0	0	0	10	17	7
# Events/Month	--	0.0	0.0	2.0	5.7	2.3
% Survived	100.00%	100.00%	100.00%	95.89%	88.79%	85.68%
SE	0.00%	0.00%	0.00%	1.28%	2.05%	2.51%



Adverse effects that occurred in the PMA clinical study:

There have been twenty-two (22) subject deaths reported in this study. All deaths have been classified by the Clinical Events Committee (CEC) as unrelated to the S.M.A.R.T.[®] stent.

Table 16 provides a summary of the adverse events documented in the study. The data are presented as the total number of events as well as the percentage of subjects experiencing an AE at 30 days and at 1 year.

Table 16: Summary of Adverse Events

System Organ Class	Events ≤ 30 Days ¹		Events ≤ 1 Year ²	
	Number of Events	Number of Patients (N=248 Patients)	Number of Events	Number of Patients (N=236 Patients)
Any AE	35	10.1% (25/248)	113	31.8% (75/236)
Blood and lymphatic system disorders	2	0.8% (2/248)	2	0.8% (2/236)
Anaemia	2	0.8% (2/248)	2	0.8% (2/236)
Cardiac disorders	1	0.4% (1/248)	3	1.3% (3/236)
Acute myocardial infarction	0	0.0% (0/248)	1	0.4% (1/236)
Arrhythmia	0	0.0% (0/248)	1	0.4% (1/236)
Bradycardia	1	0.4% (1/248)	1	0.4% (1/236)
Gastrointestinal disorders	1	0.4% (1/248)	1	0.4% (1/236)
Upper gastrointestinal haemorrhage	1	0.4% (1/248)	1	0.4% (1/236)

System Organ Class	Events ≤ 30 Days ¹		Events ≤ 1 Year ²	
	Number of Events	Number of Patients (N=248 Patients)	Number of Events	Number of Patients (N=236 Patients)
General disorders and administration site conditions	2	0.8% (2/248)	3	1.3% (3/236)
Oedema peripheral	1	0.4% (1/248)	1	0.4% (1/236)
Pain	0	0.0% (0/248)	1	0.4% (1/236)
Pyrexia	1	0.4% (1/248)	1	0.4% (1/236)
Infections and infestations	0	0.0% (0/248)	2	0.8% (2/236)
Gangrene	0	0.0% (0/248)	1	0.4% (1/236)
Sepsis	0	0.0% (0/248)	1	0.4% (1/236)
Injury, poisoning and procedural complications	12	4.8% (12/248)	55	19.9% (47/236)
Arterial restenosis	0	0.0% (0/248)	1	0.4% (1/236)
Catheter site haematoma	5	2.0% (5/248)	5	2.1% (5/236)
Catheter site haemorrhage	4	1.6% (4/248)	4	1.7% (4/236)
Device failure	1	0.4% (1/248)	2	0.8% (2/236)
In-stent arterial restenosis	1	0.4% (1/248)	39	15.3% (36/236)
Stent occlusion	0	0.0% (0/248)	3	1.3% (3/236)
Vessel perforation	1	0.4% (1/248)	1	0.4% (1/236)
Musculoskeletal and connective tissue disorders	7	2.8% (7/248)	10	4.2% (10/236)
Muscle haemorrhage	1	0.4% (1/248)	1	0.4% (1/236)
Pain in extremity	6	2.4% (6/248)	9	3.8% (9/236)
Neoplasms benign, malignant and unspecified (incl. cysts and polyps)	0	0.0% (0/248)	1	0.4% (1/236)
Lung neoplasm malignant	0	0.0% (0/248)	1	0.4% (1/236)
Renal and urinary disorders	2	0.8% (2/248)	2	0.8% (2/236)
Renal failure acute	2	0.8% (2/248)	2	0.8% (2/236)
Vascular disorders	8	3.2% (8/248)	34	11.0% (26/236)
Arterial thrombosis limb	0	0.0% (0/248)	1	0.4% (1/236)
Arteriosclerosis	0	0.0% (0/248)	1	0.4% (1/236)
Femoral arterial stenosis	0	0.0% (0/248)	1	0.4% (1/236)
Femoral artery dissection	4	1.6% (4/248)	4	1.7% (4/236)
Femoral artery occlusion	0	0.0% (0/248)	2	0.8% (2/236)
Hypotension	1	0.4% (1/248)	1	0.4% (1/236)
Intermittent claudication	1	0.4% (1/248)	16	5.9% (14/236)
Peripheral arterial occlusive disease	0	0.0% (0/248)	1	0.4% (1/236)
Peripheral ischaemia	0	0.0% (0/248)	5	1.3% (3/236)
Vascular pseudoaneurysm	2	0.8% (2/248)	2	0.8% (2/236)

¹ Denominator for events at ≤ 30 days includes subjects who died or who had adequate follow-up for 30-day visit (through 23 days).

² Denominator for events at ≤ 1 year includes subjects who died or who had adequate follow-up for 1-year visit (through 330 days).

As indicated in **Table 17** below, three patients (3/202, 1.49%) experienced a Type I stent fracture by 6 months. Only one of these three patients experienced major adverse events (MAEs) - clinically driven target lesion and target vessel revascularizations - before 12 months. However, angiographic imaging for this patient confirmed that the restenosis was in a different location than the stent fracture. A fourth patient experienced a Type I stent fracture between 6 and 12 months, resulting in a cumulative stent fracture rate of 2.03% (4/197) by 12 months. This fourth patient did not experience an MAE. An additional Type 1 fracture was identified in a fifth patient at three year follow-up. This fifth patient did not experience an MAE.

Table 17: Stent Fractures (Cumulative Assessment)

Stent Fracture	1-month	6-month	12-month
Type I	N/A	1.49% (3/202)	2.03% (4/197)
Type II	N/A	0.0% (0/202)	0.0% (0/197)
Type III	N/A	0.0% (0/202)	0.0% (0/197)
Type IV	N/A	0.0% (0/202)	0.0% (0/197)
Type V	N/A	0.0% (0/202)	0.0% (0/197)
Any Stent Fracture	N/A	1.49% (3/202)	2.03% (4/197)
Type I Single Strut fracture Type II Multiple single Strut fracture Type III Complete transverse linear separation without stent displacement Type IV Complete transverse linear fracture with stent displacement Type V Spiral dissection of stent			

2. Effectiveness Results

The analysis of primary effectiveness was based on 215 evaluable patients at the 12-month time point, as shown in **Table 18** below.

The primary effectiveness of the S.M.A.R.T.[®] stent system was compared to the predetermined VIVA Objective Performance Goal (OPG) of 66% primary patency, using a Peak Systolic Velocity (PSV) ratio ≤ 2.0 and no further clinically driven Target Vessel Revascularization (TVR). The mean primary patency rate as a measure of primary effectiveness at 12 months was 66.5%, with a lower two-sided 95% CI of 60.0%. The lower confidence interval was not greater than the performance goal of 66%, so the effectiveness endpoint was not met.

In further consideration of the overall device performance as well as to allow the application of a more modern study design, a secondary analysis of the data was also performed. The secondary analysis applied the modified VIVA criteria which uses a higher PSV ratio and also uses TLR in place of TVR. Using these modified criteria of a PSV ratio < 2.5 and no further clinically driven TLR, the mean primary

patency rate as a measure of primary effectiveness at 12 months was 71.2% with a lower 95% CI of 64.8%.

Key effectiveness outcomes are presented in **Table 18 through Table 24** and **Figure 6** below.

Table 18: Summary of Primary Effectiveness Endpoint Data

	S.M.A.R.T.[®] (N=250 Patients N=250 Lesions)	95% Confidence Interval³	Performance Goal	Objective Met
Primary Endpoint				
12-Month Primary Effectiveness¹ (protocol-defined)	66.5% (143/215)	[60.0%,72.5%]	66%	No
Primary DUS Stent Patency ² (PSV ratio ≤ 2.0)	77.0% (144/187)	[70.3%,82.8%]	n/a	
Absence of Clinically Driven TVR	86.1% (199/231)	[81.0%,90.3%]	n/a	
12-Month Primary Effectiveness¹ (modified VIVA criteria)	71.2%(153/215)	[64.8%,76.8%]	66%	No
Primary DUS Stent Patency ² (PSV ratio < 2.5)	81.1% (154/190)	[74.7%,86.4%]	n/a	
Absence of Clinically Driven TLR	87.4% (202/231)	[82.5%,91.4%]	n/a	
¹ 12-month primary effectiveness, a composite endpoint, is based on 215 available patients in the modified ITT population. There were 35 patients who were not included in the analysis of 12-month primary effectiveness: <ul style="list-style-type: none"> • 5 patients died • 30 patients did not complete 12-month follow-up (withdrew consent, no Duplex ultrasound assessment at 12 month) The number of available patients for this endpoint is the sum of the number of patients who had ultrasound within the 12 month window and the number of patients whose TLR/TVR was evaluable but who had no ultrasound by 12 months (i.e. patients had revascularization within 360 days or had sufficient follow-up for revascularization evaluation by 330 days). There were four (4) patients who overlap and met both criteria.				
² Primary DUS stent non-patency is binary restenosis defined as diameter stenosis > 50% with a specific peak systolic velocity ratio as measured by Duplex ultrasound.				
³ Agresti-Coull method was used to calculate the 95% CI of the point estimate for the primary effectiveness endpoint, exact (binomial) method was used to calculate the 95% CI of the point estimate for other endpoints.				

The primary stent patency rate was also analyzed using the Kaplan Meier method. The analysis cohort consisted of all enrolled subjects. In analysis conducted using the protocol-defined primary effectiveness endpoint, the freedom from loss of primary patency (PSVR < 2.0 and no clinically driven TVR within the stented segment) at 12 months was 79.5%. Using the modified VIVA criteria for defining 12 month primary patency (PSVR < 2.5 and no clinically driven TLR), the freedom from loss of primary patency was 81.7%

Figure 6 below is a Kaplan-Meier plot showing freedom from Clinically-Driven Target Lesion Revascularization to 360 days. The analysis cohort consisted of all enrolled subjects.

Figure 6. Freedom from Clinically-Driven Target Lesion Revascularization to 360 Days

Clinically Driven TLR	0	7	30	180	270	360
# Entered	250	250	249	245	232	210
# Censored	0	1	4	3	5	36
# Incomplete	0	0	0	2	2	1
# At Risk	250	250	247	243	229	192
# Events	0	0	0	8	15	6
# Events/Month	--	0.0	0.0	1.6	5.0	2.0
% Survived	100.00%	100.00%	100.00%	96.69%	90.35%	87.60%
SE	0.00%	0.00%	0.00%	1.16%	1.94%	2.39%

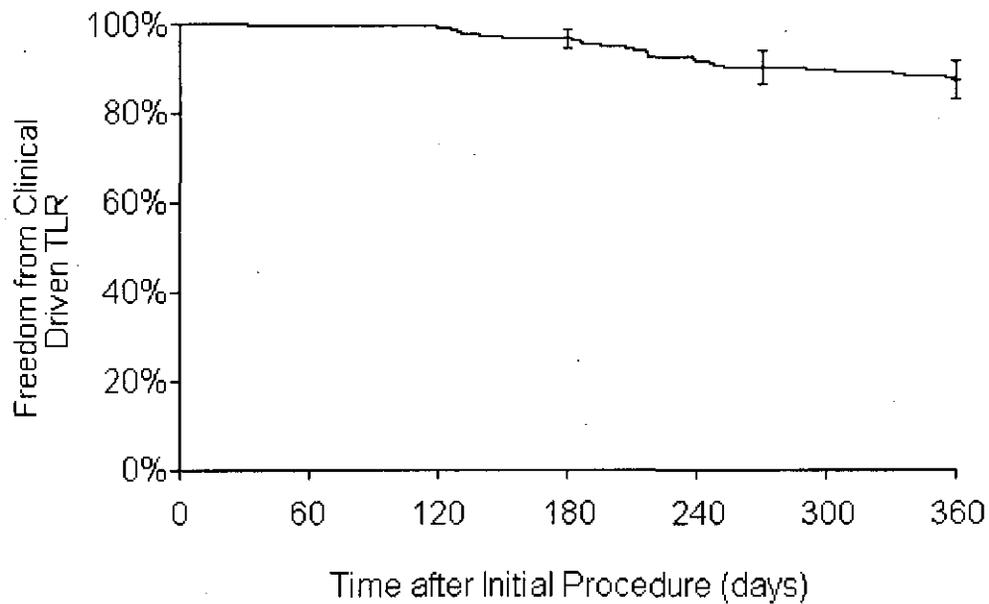


Table 19 presents a lesion length tercile analysis based on STROLL outcomes and analyzed using a PSV ratio threshold of 2.0 and clinically-driven TVR as well as using modified VIVA criteria using a higher PSV ratio (2.5) and no further clinically driven TLR.

Table 19: Primary Effectiveness as a Function of Lesion Length

	Lower (N= 83 Patients N= 83 Lesions)	Mid (N= 84 Patients N= 84 Lesions)	Upper (N= 83 Patients N= 83 Lesions)
Pre-Procedure Lesion Length(mm)			
Mean±SD (N)	39.4±9.9 (83)	74.0±12.0 (84)	118.5±19.1 (83)
Median	42.0	74.3	115.5
Range (min,max)	(15.7,55.0)	(55.5,93.3)	(94.1,200.1)
Primary Endpoint			
12-Month Primary Effectiveness¹ (protocol-defined)	75.0% (51/68)	72.6% (53/73)	52.7% (39/74)
Primary DUS Stent Patency ² (PSV ratio ≤ 2.0)	81.0% (51/63)	82.8% (53/64)	66.7% (40/60)
Absence of Clinically Driven TVR	92.1% (70/76)	88.6% (70/79)	77.6% (59/76)
12-Month Primary Effectiveness¹ (modified VIVA criteria)	79.4% (54/68)	78.1% (57/73)	56.8% (42/74)
Primary DUS Stent Patency ² (PSV ratio < 2.5)	84.4% (54/64)	87.7% (57/65)	70.5% (43/61)
Absence of Clinically Driven TLR	93.4% (71/76)	89.9% (71/79)	78.9% (60/76)

¹ "Available cases" for primary effectiveness includes in the denominator all the patients that had evaluable ultrasound assessment performed between 271 days to 540 days, and all patients who either had revascularization within 360 days, or who had sufficient follow-up for revascularization evaluation (330 days).

² Primary DUS stent non-patency is binary restenosis defined as diameter stenosis > 50% with a specific peak systolic velocity ratio as measured by Duplex ultrasound.

Table 19a presents an analysis based on the same STROLL outcomes as presented in Table 19 but in two different groups: patients with lesion length ≤ 150 mm and patients with lesion length > 150 mm.

Table 19a: Primary Effectiveness as a function of Lesion Length (≤ 150 mm and > 150 mm)

	Subjects with Lesion Length ≤ 150 mm (N= 247 Subjects) (N= 247 Lesions)	Subjects with Lesion Length > 150 mm (N= 3 Subjects) (N= 3 Lesions)
Pre-Procedure Lesion Length(mm)		
Mean \pm SD (N)	76.02 \pm 33.46 (247)	183.56 \pm 20.60 (3)
Median	72.96	190.10
Range (min,max)	(15.73,149.22)	(160.49,200.10)
Primary Endpoint		
12-Month Primary Effectiveness¹ (protocol-defined)	66.5% (141/212)	66.7% (2/3)
Primary DUS Stent Patency ² (PSV ratio ≤ 2.0)	76.8% (142/185)	100.0% (2/2)
Absence of Clinically Driven TVR	86.4% (197/228)	66.7% (2/3)
12-Month Primary Effectiveness¹ (modified VIVA criteria)	71.2% (151/212)	66.7% (2/3)
Primary DUS Stent Patency ² (PSV ratio < 2.5)	80.9% (152/188)	100.0% (2/2)
Absence of Clinically Driven TLR	87.7% (200/228)	66.7% (2/3)
¹ "Available cases" for primary effectiveness includes in the denominator all the patients that had evaluable ultrasound assessment performed between 271 days to 540 days, and all patients who either had revascularization within 360 days, or who had sufficient follow-up for revascularization evaluation (330 days).		
² Primary DUS stent non-patency is binary restenosis defined as diameter stenosis $> 50\%$ with a specific peak systolic velocity ratio as measured by Duplex ultrasound.		

Secondary Effectiveness Endpoints

Acute success was one of the secondary endpoints for the STROLL study. Acute success is comprised of 3 components, as indicated in **Table 20** below.

Table 20: Acute Procedural Success

	S.M.A.R.T. [®] (N=250 Patients N=250 Lesions)	95% Confidence Interval
Lesion Success	100.0% (250/250)	[98.5%, 100%]
Device Success	93.2% (232/249)	[89.3%, 96.0%]
Procedure Success	100.0% (250/250)	[98.5%, 100%]

Technical (lesion) success is defined as the attainment of <50% residual stenosis by Quantitative Angiography (QA) using any percutaneous method.

Device success is defined as achievement of a final residual diameter stenosis of <50% (by QA), using the assigned treatment only.

Procedural success is defined as achievement of a final diameter stenosis of <50% (by QA) using any percutaneous method, without the occurrence of death, index limb amputation or repeat revascularization of the target lesion during the hospital stay.

Table 21 below provides a summary of results of the ABI assessment from pre-procedure through 12 months.

Table 21: Summary of ABI Data

Measures	Pre-Procedure	1 Month	6 Month	12 Month
ABI(Resting or Exercise)				
<0.4	6.1% (15/247)	0.0% (0/236)	0.5% (1/214)	0.5% (1/211)
0.4-0.8	84.6% (209/247)	10.2% (24/236)	17.3% (37/214)	18.5% (39/211)
>0.8	9.3% (23/247)	89.8% (212/236)	82.2% (176/214)	81.0% (171/211)
Absolute Value				
Mean±SD (N)	0.66±0.15 (247)	0.98±0.14 (236)	0.94±0.15 (214)	0.93±0.18 (211)
Median	0.67	0.98	0.96	0.95
Range (min,max)	(0.24,1.32)	(0.52,1.38)	(0.35,1.36)	(0.11,1.90)

Table 22 below provides a summary of results of the Rutherford/Becker Classification from pre-procedure through 12 months:

Table 22: Summary of Rutherford/Becker Classification Data

Rutherford/Becker Category	Pre-Procedure	Discharge	1 Month	6 Month	12 Month
0	0.0% (0/249)	44.6% (104/233)	64.6% (157/243)	63.3% (136/215)	58.4% (125/214)
1	0.0% (0/249)	13.3% (31/233)	16.0% (39/243)	20.9% (45/215)	18.2% (39/214)
2	45.8% (114/249)	21.5% (50/233)	15.6% (38/243)	10.2% (22/215)	15.0% (32/214)
3	51.4% (128/249)	19.3% (45/233)	3.3% (8/243)	5.1% (11/215)	7.5% (16/214)
4	2.8% (7/249)	1.3% (3/233)	0.4% (1/243)	0.5% (1/215)	0.5% (1/214)
5	0.0% (0/249)	0.0% (0/233)	0.0% (0/243)	0.0% (0/215)	0.5% (1/214)
6	0.0% (0/249)	0.0% (0/233)	0.0% (0/243)	0.0% (0/215)	0.0% (0/214)
Absolute Value					
Mean±SD (N)	2.57±0.55 (249)	1.19±1.23 (233)	0.59±0.90 (243)	0.59±0.90 (215)	0.75±1.04 (214)
Median	3.00	1.00	0.00	0.00	0.00
Range (min,max)	(2.00,4.00)	(0.00,4.00)	(0.00,4.00)	(0.00,4.00)	(0.00,5.00)
Index Limb Ischemia (3,4,5,6)	54.2% (135/249)	20.6% (48/233)	3.7% (9/243)	5.6% (12/215)	8.4% (18/214)
Change from Baseline					
Mean±SD (N)	N/A	-1.38±1.17 (233)	-1.99±1.01 (242)	-1.99±1.04 (214)	-1.83±1.15 (213)
Median	N/A	-2.00	-2.00	-2.00	-2.00
Range (min,max)	N/A	(-4.00,0.00)	(-4.00,1.00)	(-4.00,1.00)	(-4.00,2.00)

3. Subgroup Analyses

a. **Applicability to Pediatric Populations**

Peripheral artery disease is not typically found in pediatric populations with the exception of rare cases of homozygous lipid disorders. Accordingly, the safety and effectiveness of the SMART[®] CONTROL[®] and SMART[®] Vascular Stent Systems were not studied in the STROLL trial.

b. **STROLL study results by gender**

A gender analysis by patient demographics, medical history, risk factors and angiographic and morphologic lesion characteristics was conducted. There were 96 females (38.4%) and 154 males (61.6%) in the STROLL Study. The 12-month primary effectiveness rates were 57.0% (45/79) in females and 72.1% (98/136) in males, which is comparable to those seen in other studies involving PAD.

Based on this information, the apparent difference observed in primary effectiveness is most likely due to confounding differences in baseline patient and lesion characteristics impacting clinical outcomes including the primary endpoint. For example, women were older than men (female: 69.83±11.59 y vs. male:

66.39±9.23 y, difference statistically significant), had more frequently a history of cerebral ischemic attacks (TIA: female: 13.8% vs male: 4.6%, difference statistically significant), and had more often a history of kidney disease (female: 10.5% vs male: 3.3%, difference statistically significant). Further, women had smaller arteries than men at baseline with a smaller reference vessel diameter (female: 4.59±0.49mm vs male: 5.05±0.72mm, difference statistically significant), and a smaller in-stent MLD post procedure (female: 4.59±0.50mm vs male: 5.07±0.72mm, difference statistically significant).

XI. PANEL MEETING RECOMMENDATION

In accordance with the 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. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Safety Conclusions

The rate of the primary safety endpoint for the STROLL Study - freedom from all causes of death, index limb amputation, and clinically driven TLR through 30 days - was 100% with a lower 95% Agresti-Coull Confidence Interval of 98.2%. As this is higher than the VIVA performance goal of 88%, the study met its primary safety endpoint.

B. Effectiveness Conclusions

The primary effectiveness of the S.M.A.R.T.[®] stent system was compared to the predetermined VIVA performance goal using a PSV ratio ≤ 2.0 and no further clinically driven TVR. The mean rate of primary effectiveness at 12 months was 66.5%, with a lower 2-sided 95% CI of 60.0% which did not meet the VIVA performance goal of 66%.

In further consideration of the overall device performance as well as to allow the application of a more modern study design, a secondary analysis of the data was also performed. The secondary analysis applied the modified VIVA criteria which uses a higher PSV ratio and also uses TLR in place of TVR. Using these modified criteria of a PSV ratio < 2.5 and no further clinically driven TLR, the mean primary patency rate as a measure of primary effectiveness at 12 months was 71.2% with a lower 95% CI of 64.8%, which also did not meet the 66% VIVA performance goal. In addition the preliminary chronic data at 2 and 3 years included with the PMA submission continued to show evidence of acceptable device effectiveness.

C. Benefit-Risk Conclusions

The probable benefits of the device are also based on data collected in a clinical study conducted to support PMA approval as described above. The probable benefit of the S.M.A.R. T.® Control® /S.M.A.R. T.® Vascular Stent System of improving the patient symptoms and quality of life outweigh the probable risks associated with use of the device.

Additional factors to be considered in determining probable risks and benefits for S.M.A.R.T.® stent system included:

- Patient follow-up was satisfactory and with limited missing data. Follow-up for the PMA was 12 months, with some patients out to 24 months but follow-up will continue for 3 years to evaluate the longer term device performance, such as the duration of the benefit and long term adverse event rates.
- The pivotal study was a multi-center study conducted in the United States. The results obtained should not differ from the post-market performance. Additional long term data will be obtained.
- Most patients with the disease have symptoms only, but some patients may have more extensive disease involvement. The device treats the hemodynamic consequences of the disease to improve perfusion and function. The disease is chronic and affects the mobility of the patient and the quality of life. It is treatable but not curable.
- There are alternative treatments available, but this treatment is highly valued by patients and preferred to the alternatives because it improves their quality of life with lesser need for repeat procedures compared to a performance goal based upon angioplasty results without stenting.
- Patient risk is minimized by limiting use to operators who have the necessary training to use the device safely and effectively and by adherence to recommended periprocedural medication regimens.

In conclusion, given the available information above, the data support that the probable benefits outweigh the probable risks for using the device for improving luminal diameter for the treatment of de novo or restenotic symptomatic lesions in native vascular disease of the above-the-knee femoropopliteal arteries having reference vessel diameter from 4 mm to 7 mm and total lesion lengths up to 150 mm.

D. Overall Conclusions

Overall, the results from non-clinical and clinical evaluations provide reasonable assurance that the device is safe and effective. While the pre-specified effectiveness endpoint was not met, the study results are similar to the results for other US marketed

stents intended for use in patients with SFA and proximal popliteal artery lesions. Therefore, it is reasonable to conclude that the benefits of use of the device for the target population outweigh the risk of illness or injury when used as indicated in accordance with the labeling and Instructions for Use (IFU).

XIII. CDRH DECISION

CDRH issued an approval order on November 7, 2012. The final conditions of approval cited in the approval order are described below.

The applicant's manufacturing facility was inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XIV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

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

Post-approval Requirements and Restrictions: See approval order.