IntraCoilÒ Self-Expanding Peripheral Stent

SUMMARY OF SAFETY AND EFFECTIVENESS DATA

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1. General Information

Device Generic Name: Vascular Stent

Device Trade Name: IntraCoil® Self-expanding Peripheral Stent

Applicant's Name and Address: Sulzer IntraTherapeutics Inc.
651 Campus Drive
St. Paul, MN 55113

PMA Number: P000033

Date of Notice of Approval to the Applicant:

GMP/QSR Inspection: January 10, 2001

2. Indications for Use

The IntraCoil® Self-expanding Peripheral Stent is indicated for improving peripheral luminal diameter in patients with symptomatic atherosclerotic disease due to stenotic lesions (length ≤ 15 cm) or occlusive lesions (length ≤ 12 cm) in femoropopliteal arteries, to the bifurcation of the tibial artery, with a reference vessel diameter of 3.0 to 7.8 mm.

3. Device Description

The IntraCoil® Self-expanding Peripheral Stent consists of

- a 40 mm long nitinol coil stent with evenly placed coils in the open configuration, and
- an over-the-wire delivery catheter with radiopaque proximal and distal marker bands that aid in placement of the stent.

The stent is wound onto the distal end of the delivery catheter and secured at both ends to release wires. Retraction of white and black knobs located on the handle of the delivery catheter releases the respective proximal and distal ends of the stent. The IntraCoil® Self-expanding Peripheral Stent is available in the following diameters: 4, 5, 6, 7 and 8 mm. See Table 1 for specifications and stent/vessel sizing.

Table 1. IntraCoilÒ Self-expanding Peripheral Stent Specifications

Model	Working Length	Model	Working Length	Stent Length	Stent Diameter	Vessel Diameter
VT440	63 cm	VT440135	135 cm	40 mm	4 mm	3-4 mm
VT540	63 cm	VT540135	135 cm	40 mm	5 mm	4-5 mm
VT640	63 cm	VT640135	135 cm	40 mm	6 mm	5-6 mm
VT740	63 cm	VT740135	135 cm	40 mm	7 mm	6-6.8 mm
VT840	63 cm	VT840135	135 cm	40 mm	8 mm	6.9-7.8 mm

4. Contraindications

The IntraCoil® Self-expanding Peripheral Stent is contraindicated for use in patients who have a lesion that cannot be crossed with a wire and/or balloon catheter.

5. Warnings and Precautions

See WARNINGS AND PRECAUTIONS in the final labeling (Instructions for Use).

6. Adverse Events

6.1 Observed Adverse Events

A total of 357 patients were enrolled in a multi-center U.S. clinical trial as summarized in Table 2. Randomized patients from the U.S. Trial form the basis of the observed adverse events in Table 3 at nine months.

Table 2. Patient Enrollment in Clinical Studies

	IntraCoilÒ Stent	PTA	Patient Totals
U.S. Trial			
Roll-in patients	91	--	91
Randomized patients	135	131	266
PATIENT TOTALS	**226**	**131**	**357**

A total of eighteen deaths occurred in the U.S. randomized trial (five stent patients, thirteen percutaneous transluminal angioplasty (PTA) patients). The five stent patients died after discharge, the first at 52 days from multiple system failure, the second at 693 days from colon cancer, the third at 738 days from unknown cause, the fourth at 757 days from lung cancer and the fifth at 789 days from cardiac death. Of the thirteen PTA deaths, one occurred in-hospital (due to renal failure and pulmonary edema), and twelve after discharge (at 34, 37, 252, 390, 505, 652, 690, 699, 762, 839, 840 and 962 days post-procedure). Causes of death for the late cases were, respectively, renal failure, septicemia, cardiac arrest, cardiogenic shock with severe CAD, lung cancer, respiratory failure, cardiac death, cardiac death, unknown, complications from extraction bile duct stone, stroke and cardiac death.

There were nine deaths in the Roll-in group; at 49, 84, 324, 581, 607, 645, 875, 883 and 1026 days post-procedure. Causes of death were, respectively, congestive heart failure, hepatic failure, multi-system failure, colon cancer, unknown, stroke, complications from MS, ischemic cardiomyopathy and respiratory failure.

Table 3. Adverse Events during the First 9 Months
%[± 95% Exact Confidence Intervals] (Number) All randomized U.S. patients (n=266)

Adverse Event	IntraCoilÒ Stent (n=135)	PTA (n=131)	Difference [95% CI]
ANY MACE Event	16.3% [10.8%, 23.4%] (22)	16.0% [10.2%, 23.1%] (21)	0.3% [-8.0%, 9.3%]
Early (in-hospital)	0.7% [0%, 3.7%] (1)	2.3% [0.6%, 6.3%] (3)	-1.6% [-6.0%, 2.1%]
Out–of-hospital	15.6% [10.0%, 22.8%] (21)	13.7% [8.4%, 20.7%] (18)	1.8% [-7.0%, 10.5%]
Death Total	0.7% [0%, 3.7%] (1)	3.1% [1.1%, 7.2%] (4)	-2.3% [-7.0%, 1.4%]
Early (in-hospital)	0% [0%, 2.6%] (0)	0.8% [0%, 3.8%] (1)	-0.8% [-4.6%, 2.1%]
Out–of-hospital	0.7% [0%, 3.7%] (1)	2.3% [0.6%, 6.3%] (3)	-1.6% [-6.0%, 2.1%]
Q-wave MI Total	0% [0%, 2.6%] (0)	0% [0%, 2.7%] (0)	0.0% [-3.1%, 3.0%]
Early (in-hospital)	0% [0%, 2.6%] (0)	0% [0%, 2.7%] (0)	0.0% [-3.1%, 3.0%]
Out–of-hospital	0% [0%, 2.6%] (0)	0% [0%, 2.7%] (0)	0.0% [-3.1%, 3.0%]
Non-Q-wave MI Total	2.2% [0.6%, 6.2%] (3)	0% [0%, 2.7%] (0)	2.2% [-0.7%, 6.7%]
Early (in-hospital)	0% [0%, 2.6%] (0)	0% [0%, 2.7%] (0)	0.0% [-3.1%, 3.0%]
Out–of-hospital	2.2% [0.6%, 6.2%] (3)	0% [0%, 2.7%] (0)	2.2% [-0.7%, 6.7%]
Amputation Total	0% [0%, 2.6%] (0)	0.8% [0%, 3.8%] (1)	-0.8% [-4.6%, 2.1%]
Early (in-hospital)	0% [0%, 2.6%] (0)	0.8% [0%, 3.8%] (1)	-0.8% [-4.6%, 2.1%]
Out–of-hospital	0% [0%, 2.6%] (0)	0% [0%, 2.7%] (0)	0.0% [-3.1%, 3.0%]
Abrupt Closure Total	0% [0%, 2.6%] (0)	2.3% [0.6%, 6.3%] (3)	-2.3% [-6.9%, 0.6%]
Early (in-hospital)	0% [0%, 2.6%] (0)	2.3% [0.6%, 6.3%] (3)	-2.3% [-6.9%, 0.6%]
Out–of-hospital	0% [0%, 2.6%] (0)	0% [0%, 2.7%] (0)	0.0% [-3.1%, 3.0%]
Subacute Closure Total	0.7% [0%, 3.7%] (1)	2.3% [0.6%, 6.3%] (3)	-1.6% [-6.0%, 2.1%]
Early (in-hospital)	0.7% [0%, 3.7%] (1)	1.5% [0.3%, 5.4%] (2)	-0.8% [-4.8%, 3.0%]
Out–of-hospital	0% [0%, 2.6%] (0)	0.8% [0%, 3.8%] (1)	-0.8% [-4.6%, 2.1%]
Distal Embolization Total	0% [0%, 2.6%] (0)	0.8% [0%, 3.8%] (1)	-0.8% [-4.6%, 2.1%]
Major Bleeding Complications	0.7% [0%, 3.7%] (1)	0.8% [0%, 3.8%] (1)	-0.02% [-3.9%, 3.6%]
Major Vascular Complications	3.7% [1.5%, 8.1%] (5)	4.6% [2.0%, 9.6%] (6)	-0.9% [-6.7%, 4.6%]
Renal Failure	0% [0%, 2.6%] (0)	2.3% [0.6%, 6.3%] (3)	-2.3% [-6.9%, 0.6%]

ANY MACE Event includes death, peri-procedure Q Wave MI, target lesion revascularization (TLR)

Early (in-hospital) refers to events during the hospitalization for the initial trial treatment. In cases where a patient experienced both an in-hospital event and an out-of-hospital event, they are counted once in each group, but only once in the event total. Hence, the sum of the in-hospital and the out-of-hospital event rate may not equal the total event rate.

Amputation: any requirement for amputation transmetatarsal or higher that was unanticipated before the procedure.

Abrupt Closure: slow or reduced flow due to mechanical dissection (of grade E or higher), thrombus, or severe microvascular spasm that resulted in additional unplanned stent use or surgery.

Subacute Closure: target lesion site occlusion within 30 days of the procedure.

Distal Embolization: migration of a filling defect or thrombus to a distal vessel.

Renal Failure: decrement in renal function related to the index procedure requiring temporary or chronic dialysis; or repeat hospitalization for worsening renal function attributable to the index procedure.

6.2 Potential Adverse Events

Adverse events (in alphabetical order) that may be associated with the use of vascular stents in peripheral vessels (in addition to those listed in Table 3) include:

- AV Fistula Formation
- Dissection
- Drug reactions to antiplatelet agents/ contrast medium
- Hematoma
- Hypotension/hypertension
- Infection and/or pain at the access site
- Pseudoaneurysm, femoral
- Restenosis of stented segment
- Spasm
- Stent embolization
- Stroke/cerebrovascular accident
- Vessel perforation or rupture

6.3 Observed Device Malfunctions

Five stent delivery failures were attributed to release wire breakage (2) and failure of stent to deploy (3). In the two wire breakage cases the release wire was successfully manipulated to deploy the stent. In the three non-deployment cases, two devices were removed unused. In the third case the physician released the distal stent end, after which the proximal end fully deployed.

7. Alternative Practices or Procedures

Alternative procedures include percutaneous transluminal angioplasty (PTA), medication (e.g. thrombolysis), atherectomy and bypass graft surgery.

8. Market History

The IntraCoil® Self-expanding Peripheral Stent (formerly called "VascuCoil") was first sold commercially in 1993 by InStent, Inc. The device is currently marketed for vascular use in several major markets including the European Union (CE Mark 1998), Australia (since 1995), and Canada (since 1999). The device has been available in the USA since 1999 for use in the treatment of bronchial strictures produced by malignant neoplasms, or in benign strictures after all alternative therapies have been exhausted. The IntraCoil® Self-expanding Peripheral Stent has not been withdrawn from marketing for any reason relating to the safety and effectiveness of the device.

9 Summary of NonClinical Studies

9.1 Biocompatibility

Biocompatibility testing of the stent and the delivery system meets the requirements of the FDA-modified matrix of International Standard ISO-10093, "Biological Evaluation of Medical Devices Part 1: Evaluation and Testing." The following tests were conducted: cytotoxicity, sensitization, irritation, systemic toxicity, implantation, hemolysis, mutagenicity, and pyrogenicity. The results of all biocompatibility tests were acceptable.

9.2 Bench Testing

Stent Material Specification and Conformance Testing

Stent Material Composition Conformance

Chemical analysis of the stent wire was conducted on two samples to verify conformance with the material specification of: Ni 55.9%±0.5%, Ti 44% (ref.), C < 0.05%, O^2 < 0.05%, and Trace Elements < 0.50%. The chemical analysis confirmed that the stent wire met the material specifications.

Stent Wire Mechanical Properties Conformance

Mechanical analysis of the stent wire was conducted on four wire samples to verify conformance to the following specifications: minimum ultimate tensile strength (203 ksi), elongation (15%), Austenite start temperature ($-15^oC \pm 5^0$ C), and minimum loading (87, 000 psi) and unloading stresses (50, 750 ksi). The mechanical analysis confirmed that the stent wire met all of the material specifications, and verified the accuracy of the material specification certification received from from the supplier.

Corrosion Resistance

Ten IntraCoil stents were subjected to corrosion testing using a methodology incorporating serum proteins in an electrochemical corrosion test. The corrosion testing used a commercially available medical device as a control for a comparative analysis. The control device is also manufactured from nitinol material and is intended as a permanent implant. The comparative analysis found that the corrosion resistance of the stent samples was comparable or better than the control device.

Stent Integrity Testing

Stent Covered Area Percentage

The percentage of vessel covered by the implanted IntraCoil stent was calculated by determining the interior vessel surface area and the surface area of the expanded stent. The percentage of vessel covered by the stent was 10.2%, 10.1%, 13.3%, 13.3%, and 9.5% for the 4.0, 5.0, 6.0, 7.0 and 8.0 mm stents, respectively. The percentage of vessel area covered by the IntraCoil stent is similar to the percentage of vessel coverage by other stents approved for the vascular system.

Stent Uniformity

To determine the minimum vessel diameter in which a stent can be implanted without collapsed or leaning coils, 93 samples representing all stent diameters and lengths were deployed in tubing with inner diameters: 0.2, 0.5, 1.0, and 1.5 mm smaller than the nominal diameter of the stent. Visual inspection of the deployed stents found that the minimum diameter for implanting a stent without collapsed or leaning coils was one mm smaller than the nominal stent diameter.

Stent Dimensional Length Change

To characterize the percent of stent shortening from the constrained stent length to the deployed and fully open stent length, the stent length was calculated using the coil pitch, length and diameter of each stent diameter size. The deployed stent length was also measured in tubing with inner diameters 0.2 to 0.5 mm smaller than the nominal stent diameter. The mathematical calculations determined that the length of the constrained stent shortens by 38% to 46% when the stent is deployed and fully expanded. The measured stent lengths supported the mathematically calculated stent lengths and met the product specification for a fully open stent.

Radial Strength

To characterize the external force necessary to collapse the fully deployed stent, five samples of each diameter were mounted in a V-block and compressed until the stent collapsed. The stent was considered collapsed when the coils were no longer perpendicular. The average force required to collapse the stents ranged from 7.8 lbs. for the largest diameter to 16.8 lbs. for the smallest diameter. The results of the Radial Strength testing were considered acceptable.

Fatigue

Twenty-five stents (5 of each diameter) were subjected to cyclical 120° flexing at body temperature for an equivalent of 10-years. Scanning electron microscopic examination of the flexed stents showed no evidence of fatigue cracking or permanent deformation. A finite element stress analyses performed on the largest diameter stent indicated a satisfactory safety factor was present and fatigue failure of the stent was unlikely.

Magnetic Resonance Imaging (MRI) Compatibility

A literature review was performed to assess compatibility of the IntraCoil stent with MRI. The IntraCoil Stent is manufactured from nitinol (nickel-titanium alloy) wire. *In vivo* and clinical studies found that implanted nitinol devices did not dislodge, and caused minimal or no artifacts on the MRI evaluation.

Stent and Delivery System Testing

Delivery Catheter Tensile Strength

To determine the strength of the delivery catheter shaft and the delivery catheter to proximal handle bond, tensile strength testing was performed on 25 catheters (5 for each stent diameter). Testing was also performed to determine the tensile strength of the release wire ball weld on the proximal and distal release wires (10 samples each). The test results found that the strength of the catheter shaft, the catheter to handle bond and the proximal and distal release wire ball weld, all exceeded the product specification of 5 lbs.

Contralateral Tracking of the IntraCoil stent system

To verify that the delivery catheter with mounted IntraCoil® can pass through the bend encountered in the contralateral approach, 58 of the smallest and largest stents were mounted on the longest delivery catheter and tracked over a 0.35 inch diameter guide wire through a contralateral anatomical model. All stent/delivery systems tracked successfully over the guide wire and through the angles of the contralateral model.

Stent Retention

To verify that the force necessary to cause premature release of the stent is greater than the maximal forces expected during clinical use, the distal tip to proximal luer connector of 25 delivery catheters with mounted stents (5 of each stent diameter) were tensile tested. The results showed that for all samples, the tensile force necessary to prematurely release the stent was > 8 lbs for the 6, 7 and 8 mm models, and > 6.5 lbs for the 4 and 5 mm models. The product specifications were met.

Stent Release Force

Fifteen stent systems were tested to determine the force necessary to release the stent when the delivery catheter is placed in a straight and a U-shaped configuration. The testing found that for either configuration of the delivery catheter, the force necessary to release the stent was < 2.5 lbs. The product specification was met.

Stent Release Wire Performance

To validate the performance of the stent release wires, testing was conducted on a total of 69 samples ranging from the smallest to the largest stent diameter. The testing was conducted to assess the potential for protrusion of the stent release wires from the distal tip of the delivery catheter during insertion or placement of the stent system in a worst-case tortuous position. Stent release wires withstood > 5 lbs, a force 2.5 times that of the maximum insertion force. In addition, placement of the stent system in the tortuous position did not lead to premature release of the stent.

9.3 Sterility Packaging and Shelf Life Testing

Sterility

The IntraCoil® Self-expanding Peripheral Stent is sterilized using a validated EtO process. The validated process was based on ISO 11135:1994, Sterilization of health care products – EtO sterilization. Validation results demonstrated the sterilization process achieved a sterility assurance level of 10^{-6}.

Packaging and Shelf-life Tests
To support a five-year shelf-life labeling claim, product and packaging stability testing was conducted on four stent/delivery catheter systems (two each of the smallest and largest stent diameter) that were accelerated aged for an equivalent of 5 years. Product stability testing included visual inspection of the product, verification of the product profile, guide wire compatibility and release wire position, stent release force, deployed stent dimensions, and the tensile strength of the catheter to handle bond and the release wires. Packaging stability testing included a visual inspection and peel strength testing of the package, and the maintenance of the sterile barrier through sterility testing of the product. The results of the product and packaging stability testing showed that the accelerated aged product and packaging remained within the test specifications.

Shipping tests in accordance with the ASTM D4169-94 Standard Practice for Performance Testing of Shipping Containers and Systems were also conducted on packaged samples. The results of the testing found that the packaging protected the product from damage and maintained product functionality during shipping

Based on the results of the product and packaging stability testing, an expiration date of five years has been established.

9.4 Animal Testing
A porcine study was conducted to evaluate the early (1 month) and late (3 and 6 months) response to implantation of the IntraCoil® stent and to evaluate the performance of the delivery system. Seventeen IntraCoil stents were implanted in the iliac/femoral location of 7 animals. A total of 6 implanted stents in two animals sacrificed at 1-month showed patent stents with endothelial cells covering the lumen surface. Advential hemorrhage, inflammation and fibrosis were noted in areas with high-grade mural injury. Long term implant, as evaluated in one animal with 2 stents sacrificed at 3-months and four animals with a total of 11 implanted stents sacrificed at 6-months showed patent stents and an endothelized lumenal surface with less hemorrhage and inflammation than was observed at one month.

The performance of the stent/delivery catheter system was evaluated for the following characteristics: preparation of the delivery catheter, ease of loading the system on the guide wire and through the sheath, pushability and trackability of the system through the sheath and radiopacity of the system under flouroscopy. The stent/delivery catheter system received scores ranging from acceptable to excellent for these characteristics.

10. Summary of Clinical Studies
A total of 357 patients were treated at 23 U.S. investigational sites (Table 2). The purpose of the study was to compare the IntraCoil stent to balloon angioplasty in the superficial femoral and popliteal arteries. Physicians unfamiliar with coil stents were allowed to complete learning cases before starting in the randomized trial. These ninety-one learning cases are referred to as the Roll-in group. A total of 266 patients were enrolled in the U.S. Randomized Trial which is summarized below.

Study Endpoints: The primary endpoint was the determination of MACE at nine months. MACE was defined as a composite of death within 30 days, peri-procedural Q Wave MI, and clinically driven target lesion revascularization (TLR) within nine months. Secondary endpoints included acute angiographic success, major complication rate at 30 days and change in ankle/brachial index. An independent clinical events committee adjudicated all of the major clinical endpoints.

Patients Studied: Eligible patients were candidates for percutaneous transluminal angioplasty (PTA), with symptomatic leg ischemia, requiring treatment of the superficial femoral/popliteal vessel with an occluded lesion length ≤ 12 cm or stenotic lesion length ≤ 15 cm and located proximal to the bifurcation of the tibial artery.

Methods: Patients were prospectively randomized to treatment with the IntraCoil® stent or PTA. Patients in the PTA arm were allowed to crossover to the IntraCoil stent arm only if 1) acute results indicated abrupt closure or impending closure due to severe recoil or extensive dissection, not correctable despite repeated balloon inflations to high pressure, longer inflation, or larger balloon size (if appropriate) or 2) during follow-up there was angiographically defined restenosis or dissection that was limb threatening.

Clinical follow-up visits were conducted at six months, nine months and one year, with continuing annual follow-up for safety. To assess patency, nine-month angiographic follow-up was requested from the first 250 patients. Patients were to receive aspirin (325 mg daily) and ticlopidine HCL (250 mg/twice daily) at least one day before the procedure. They were to continue the aspirin therapy indefinitely and the ticlopidine for one month post-procedure. Anticoagulation therapy was at the discretion of the physician.

Results: The study was originally designed to enroll 500 patients, but was stopped early due to slow patient enrollment. The slow enrollment was attributed to physician's reluctance to include all eligible lesions in a randomized study with balloon angioplasty.

Baseline characteristics were similar for the two treatment groups in the randomized trial (Table 4).

Table 4. Baseline Characteristics
All randomized U.S. patients (n=266 patients, 352 lesions)

Characteristics	IntraCoilÒ Stent (n=135 patients, 177 lesions)	PTA (n=131 patients, 175 lesions)	Difference [95% CI]
Age (yrs), mean±SD (N)	66.8±10.6 (129)	68.1±10.2 (131)	-1.3[-3.8, 1.3]
Number of men	67.4% (87/129)	63.4% (83/131)	4.1% [-7.5%, 15.6%]
History of smoking	81.9% (104/127)	80.0% (104/130)	1.9% [-7.7%, 11.5%]
History of diabetes mellitus	38.0% (49/129)	37.4% (49/131)	0.6% [-11.2%, 12.4%]
History of myocardial infarction	37.2% (48/129)	29.1% (37/127)	8.1% [-3.4%, 19.6%]
Reference vessel diameter (*mm*), mean±SD (N)	4.20±0.96 (150)	4.16±1.05 (150)	0.04 [-0.19, 0.27]
Lesion length (cm), mean±SD (N)	3.56±3.00 (147)	3.26±2.96 (144)	0.29 [-0.39, 0.98]
Occlusion	22.7% (40/176)	16.8% (31/184)	5.9% [-2.3%, 14.1%]

The higher percentage of males in the U.S. Randomized Trial 65.4% (170/ 260) is representative of current treatment patterns. The number of males randomized between the IntraCoil® stent group and the PTA group was not statistically significant. Univariate analysis for gender of freedom from clinically driven TLR at 9-months demonstrated a statistically significant difference between men and women (p=0.009). Women tended to have a lower freedom from TLR rate compared to men.

This difference may be due to anatomical differences. Women tend to have smaller arteries; smaller arteries have historically demonstrated lower freedom from clinically driven TLR. A statistically significant difference was also observed in the univariate analysis for reference vessel diameter (p=0.027). Smaller reference vessel diameters tended to have a lower freedom from TLR rate.

All patients were included in the intent-to-treat efficacy analysis. No statistical difference was found for nine month MACE between the IntraCoil® stent and PTA groups. Table 5 shows the principal effectiveness and safety results for this comparison.

Additional analyses were conducted to determine if the equivalent results continued through long-term follow-up. Figures 1 and 2 show the primary endpoint, actuarial freedom from MACE, and freedom from TLR, through three years. The TLR rate based on the length of the lesion treated is shown in Figure 3. Lesion length is grouped in 3 cm categories: 0-3 cm, 3-6 cm, 6-9 cm, 9-12 cm and 12-15 cm.

Table 5. Principal Effectiveness and Safety Results All randomized U.S. patients (n=266)

Efficacy Measures	**IntraCoilÒ Stent (n=135 patients, 177 lesions)**	**PTA (n=131 patients, 175 lesions)**	**Difference [95% CI]**
Acute angiographic success	85.4% (152/178)	82.2% (143/174)	3.2%[-4.5%,10.9%]
Acute (30 day) procedure success	80.6% (108/134)	77.1% (101/131)	3.5%[-6.3%,13.3%]
Device success	91.8% (123/134)	89.3% (117/131)	2.5%[-4.6%,9.5%]
Change of ABI (from baseline to 9 mos.)	0.19 ± 0.20 (83)	0.08 ± 0.19 (64)	0.1 [0.04,0.16]
Range (min, max)	(-0.43, 0.56)	(-0.25, 0.52)	
9-mo follow-up in-lesion binary restenosis rate	41.2% (40/97)	33.7% (31/92)	7.5%[-6.2%,21.3%]
TLR-free at 9 months (K-M)	85.7% [79.9%, 91.5%]	83.9% [78.0%, 89.7%]	1.8%[-6.4%,10.2%]
TVR-free at 9 months (K-M)	81.1% [73.9%, 88.4%]	83.1% [76.1%, 90.2%]	-2.0%[-12.1%,8.1%]
MACE-free at 9 months (K-M)	80.5% [73.2%, 87.8%]	81.2% [73.9%, 88.4%]	-0.7%[-11.0%,9.6%]
Safety Measures			
In-Hospital MACE	0.7% (1/135)	2.3% (3/131)	-1.5%[-4.5%,1.4%]
Out-of-Hospital MACE to 9 months	15.6% (21/135)	13.7% (18/131)	1.8%[-6.7%,10.3%]
Major Complications at 30 days	1.5% (2/135)	8.4% (11/131)	-6.9%[-12.1%,-1.7%]
Major bleeding complications	0.7% (1/135)	0.8% (1/131)	0.0%[-2.1%,2.1%]
Major vascular complications	3.7% (5/135)	4.6% (6/131)	-0.9%[-5.7%,3.9%]
Amputation to 9 months	0.0% (0/135)	0.8% (1/131)	-0.8%[-2.3%,0.7%]
Abrupt closure	0.0% (0/135)	2.3% (3/131)	-2.3%[-4.9%,0.3%]
Subacute closure	0.7% (1/135)	2.3% (3/131)	-1.5%[-4.5%,1.4%]
Distal embolization	0.0% (0/135)	0.8% (1/131)	-0.8%[-2.3%,0.7%]
Renal Failure	0.0% (0/135)	2.3% (3/131)	-2.3%[-4.9%,0.3%]

Numbers are % (counts/sample size) or mean ± standard deviation. **CI** is Confidence Interval.

Acute Angiographic Success: achievement of a final residual stenosis of <50% and =20% improvement in diameter stenosis by QA.

Acute Procedural Success: achievement of a final residual diameter stenosis of <50% and =20% improvement in diameter stenosis by QA without death, stroke, Q wave MI, bleeding requiring >2 units transfusion, or any other complication which was device- or procedure- related and which required an unanticipated interention or surgical procedure within the first 30 days after treatment. If no in-stent measurements were available, in-lesion measurements were used, and if no QA was available, visual estimates were used.

Device Success: achievement of a final residual diameter stenosis of <50% by QA with successful delivery of the assigned device at least once and freedom from stent embolization, from stent migration, and from use of a device outside the assigned treatment strategy. If no in-stent measurements were available, in-lesion measurements were used, and if no QA was available, visual estimates were used.

K-M: survival estimates by Kaplan-Meier method. Standard Error estimates by Greenwood formula.

TLR: target lesion revascularization. **TVR:** target vessel revascularization. **MACE:** death, peri-procedural Q wave MI, or target lesion revascularization. **In-Hospital:** prior to hospital discharge. **Out-of-Hospital:** after hospital discharge.

Major complications at 30 days: MACE plus amputation, major bleeding complication, renal failure and abrupt closure

Amputation: any requirement for amputation transmetatarsal or higher that was unanticipated before the procedure.

Abrupt Closure: slow or reduced flow due to mechanical dissection (of grade E or higher), thrombus, or severe microvascular spasm that resulted in additional unplanned stent use or surgery.

Subacute Closure: target lesion site occlusion within 30 days of the procedure.

Distal Embolization: migration of a filling defect or thrombus to a distal vessel.

Renal Failure: decrement in renal function related to the index procedure requiring temporary or chronic dialysis; or repeat hospitalization for worsening renal function attributable to the index procedure.

Binary restenosis rate: percentage of lesions with ≥ 50% in-lesion minimal lumen diameter stenosis at follow-up angiogram.

FIGURE 1. SURVIVAL FREE FROM MACE (TO 1080 DAYS)
Event-Free Survival ± 1.5SE; All Randomized Patients Treated With Survival Information

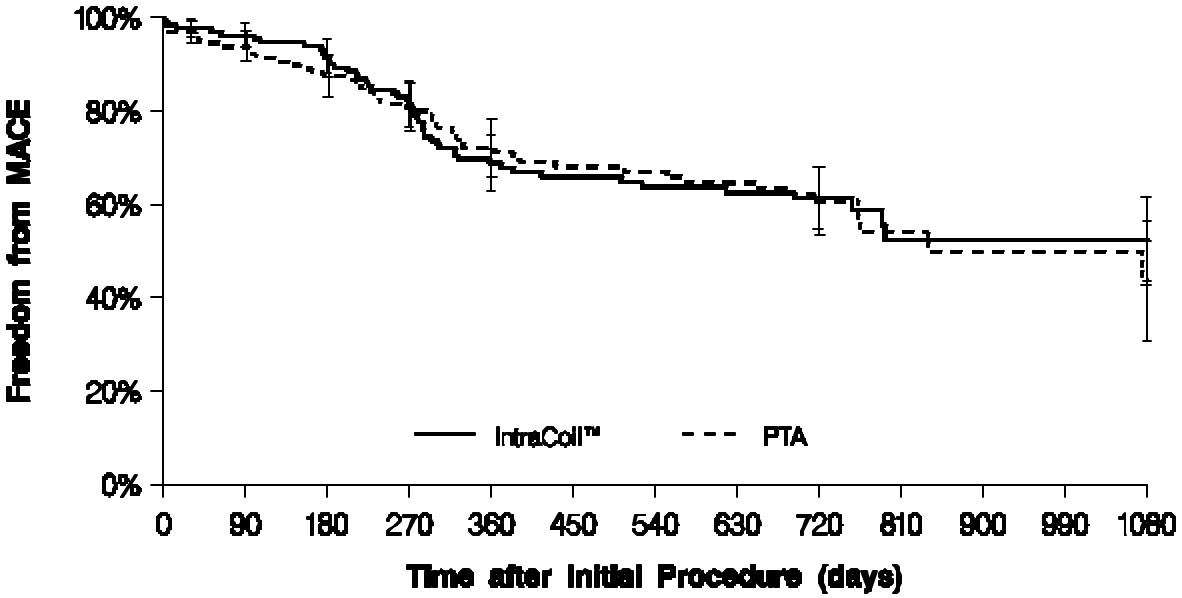


FIGURE 2. SURVIVAL FREE FROM TARGET LESION REVASCULARIZATION (TO 1080 DAYS)
Event-Free Survival ± 1.5SE; All Randomized Lesions Treated With Survival Information

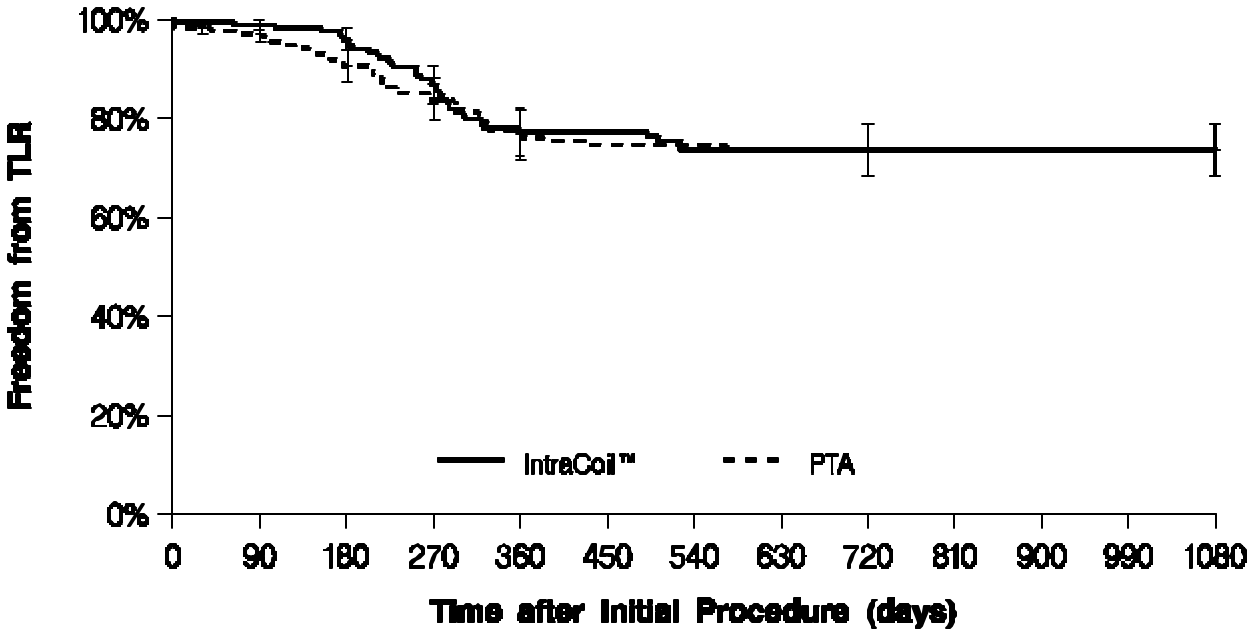
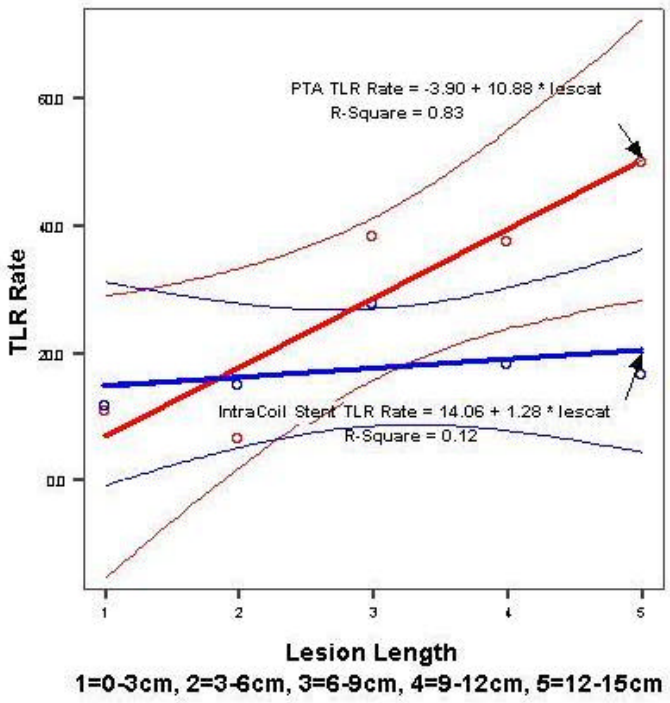


Figure 3. 9 Month TLR Rate By Lesion Length



Lesion Length (cm)	IntraCoil Stent	PTA
0-3	11.9% (7/59)	11.0% (8/73)
3-6	15.0% (6/40)	6.7% (2/30)
6-9	27.7% (8/30)	38.5% (10/26)
9-12	18.2% (2/11)	37.5% (3/8)
12-15	16.7% (1/6)	50% (2/4)

11. Conclusions Drawn from Studies

The preclinical studies indicate that the stent system meets or exceeds safety, and performance specifications.

Multicenter clinical data show that the IntraCoil® Stent is comparable to the control treatment (PTA) in the treatment of symptomatic atherosclerotic disease in the femoropoplital arteries.

The preclinical testing information and the results of the randomized clinical trial provide valid scientific evidence and reasonable assurance that the IntraCoil® Stent is safe and effective when used in accordance with its labeling.

12 Panel Recommendation

The IntraCoil Peripheral Self-expanding Stent was presented to the Circulatory System Devices Panel (Panel) on April 23, 2001. However, the indication presented to the Panel was for use following abrupt closure or a suboptimal PTA procedure, rather than the primary stenting indication evaluated in the clinical study. The abrupt closure or suboptimal PTA indication was proposed for the following reasons: Due to slow enrollment, the clinical study was stopped with approximately half of the originally proposed study sample size. Analysis of the clinical data found that the majority of the treated lesions were short; 61.5% (179/291) lesions were 3cm or less. In addition,

the analysis showed no significant differences in safety and effectiveness between stenting and PTA at the 9-month follow-up.

The Panel recommended not approvable of the abrupt or suboptimal PTA indication based primarily on the retrospective nature of the analysis, which was performed on a subgroup of the stented patients, and lack of long-term safety and effectiveness data.

13 FDA Decision

In June 2001, FDA issued a letter that concurred with the Panel's recommendation of April 23, 2001, and requested clinical data on patients implanted with an IntraCoil® stent following a suboptimal PTA procedure, and long-term follow-up on implanted patients. In a subsequent amendment to the PMA, the sponsor submitted additional two and three-year follow-up on patients (randomized and roll-in) entered into the study, and requested approval for the original indication of primary treatment of symptomatic atherosclerotic disease in the femoropopliteal arteries.

Based on the additional long-term clinical data and consultation with a Panel member from the April 23, 2001 meeting, FDA determined that there was adequate information present to demonstrate reasonable assurance of safety and effectiveness to approve the IntraCoil® stent for the primary treatment of symptomatic atherosclerotic disease in the femoropopliteal arteries.

The FDA issued an approval order on

In addition to the General Conditions of Approval, all patients implanted with an IntraCoil stent (randomized and roll-in) are to be followed out to 3 years after the implant procedure.

The applicant's manufacturing facility was inspected and was found to be in compliance with the Quality System Regulation (Part 820).

14 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.