Summary of Safety and Effectiveness Data
WALLSTENT® Venous Endoprosthesis
with Unistep™ Plus Delivery System

1. General Information

Device Generic Name: Intravascular Stent

Device Trade Name: WALLSTENT® Venous Endoprosthesis with Unistep™ Plus Delivery System

Applicant's Name and Address: Boston Scientific Scimed Inc.
One Scimed Place
Maple Grove MN 55311-1566

PMA Number: P980033

Date of Notice of Approval to the Applicant: Novermber 16, 2001

2. Indications for Use

The Wallstent® Venous Endoprosthesis is indicated for improving central venous diameter following unsuccessful angioplasty in patients on chronic hemodialysis with stenosis of the venous outflow tract. Unsuccessful angioplasty is defined as:

- residual stenosis $\geq$ 30 percent for a vein $\leq$ 10 mm in diameter or $\geq$ 50 percent for a vein > 10 mm in diameter;
- a tear which interrupts the integrity of the intima or lumen;
- abrupt lesion site occlusion or refractory spasm.

The vessels that can be treated with the Wallstent® Venous Endoprosthesis are the innominate and subclavian veins ranging from 8 mm to 15 mm in diameter.

3. Device Description

The Wallstent® Venous Endoprosthesis is comprised of two components: the implantable metallic stent and the Unistep™ Plus Delivery System.

- The stent is composed of biomedical superalloy wire with a radiopaque core braided in a tubular mesh configuration.

- The delivery system is composed of co-axial tubes which allow reconstrainment as indicated by the limit marker and has radiopaque marker bands which aid in accurate placement of the stent.

The Wallstent® Venous Endoprostheses is available in the following diameters: 10, 12, 14, 16 mm. See Table 1 for stent sizing information.

Stent diameter selected should be approximately 1 mm to 2 mm larger than the vessel diameter desired. Deployed lengths reflect expansion to desired vessel diameter. Constricting the stent to a smaller diameter will cause a longer deployed length, depending on the degree of constriction. On average, a 0.5 mm change in diameter yields a 10-15 percent change in length. Once the desired vessel diameter is reached, no additional reduction in stent length should occur.

Table 1: Stent Sizing Specifications

WALLSTENT® Venous Endoprosthesis Vessel Diameter and Approximate Implanted Stent Length						
	Fully Opened Stent Diameter / Length		WALLSTENT® Venous Endoprosthesis When Implanted in Specified Vessel Diameter			
Order Number	Diam. (mm)	Length (mm)	Vessel Diam. (mm)	Stent Length (mm)	Vessel Diam. (mm)	Length (mm)
71-132	10	20	8	33	9	27
71-134	10	42	8	54	9	48
71-136	10	68	8	77	9	69
71-138	10	94	8	115	9	103
40210	12	20	10	31	11	26
40211	12	40	10	51	11	47
40212	12	60	10	73	11	66
40213	12	90	10	110	11	100
40310	14	20	12	33	13	27
40311	14	40	12	50	13	46
40312	14	60	12	72	13	65
40313	14	90	12	107	13	98
40330	16	20	14	28	15	23
40331	16	40	14	49	15	45
40332	16	60	14	70	15	64
40333	16	90	14	105	15	97

MRI Safe: The Wallstent® Venous Endoprosthesis has shown no deflection or torque in the area of maximum spatial gradient (450 gauss centimeter) of a 1.5 tesla MRI system under conditions that produced a Specific Absorption Rate (SAR) of 1.3 W/kg. Imaging artifacts affect the region of interest at the location of the device (artifact ratio 1.2 to 6.7), while areas away from the device appear unaffected by their presence.

4. Contraindications

The Wallstent® Venous Endoprosthesis is contraindicated for use in:
Patients with bleeding disorders unresponsive to vitamin K or blood product therapy.

5. Warnings and Precautions

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

6. Adverse Events

6.1 Observed Adverse Events

A total of 42 patients were enrolled in the multi-center study of Wallstent Venous Endoprosthesis for central lesions. This study was conducted at 12 investigational sites.

Patients from the Wallstent® Venous Endoprosthesis study form the basis of the observed events described in Table 2.

Five (5) patients enrolled in the Wallstent® Venous Study died during the trial. None of these deaths occurred in the first 6 months following the Wallstent procedure and none were considered device related. The cause of death was reported as follows: (1) hyperkalemia 475 days post procedure; (2 and 3) cardiac arrest at 343 and 631 days post procedure; (4) septicemia with peripheral vascular disease and gangrene 902 days post procedure; (5) stomach cancer 276 days post procedure.

Table 2 Safety Results, Wallstent Venous Central Patients (N=42)		
Adverse Event	Result	95% C.I.
General Events		
Death	11.9% (5/42)	[4.0%, 25.6%]
Surgical Revision	4.8% (2/42)	[0.6%, 16.2%]
Access abandoned from central lesion	40.5% (17/42)	[25.6%, 56.7%]
Access abandoned from peripheral graft	21.4% (9/42)	[10.3%, 36.8%]
Non-Stent-Related Events		
Graft Occlusion/Restenosis	45.2% (19/42)	[29.8%, 61.3%]
Pseudoanuerysm	16.7% (7/42)	[7.0%, 31.4%]
Infection	14.3% (6/42)	[5.4%, 28.5%]
Hematoma	4.8% (2/42)	[0.6%, 16.2%]
Stent-Related Events		
Stent Restenosis	76.2% (32/42)	[60.5%, 87.9%]
Stent Thrombosis	50.0% (21/42)	[34.2%, 65.8%]
Migration	2.4% (1/42)	[0.1%, 12.6%]
Edema	40.5% (17/42)	[25.6%, 56.7%]

Results are percent (count/sample size) of all patients experiencing the event, and reflect each patient's entire study experience regardless of length of follow-up.

Mean $\pm$ SD (sample size) (min, max) length of follow-up in days; 350.5$\pm$299.4 (42) (4.0.1434). Confidence intervals are based on exact limits.

Note: Surgical revision refers to those events where the graft was revised, but not abandoned. Patients reporting edema are a subset of patients with stent restenosis/thrombosis.

Additional clinical safety data was retrospectively obtained on 12 patients enrolled in a physician's registry study of the Wallstent Venous Endoprosthesis for the treatment of stenotic or occluded subclavian veins of patients undergoing hemodialysis. Four deaths were reported among these 12 patients. The reported cause and time of occurrence for these deaths is: sepsis at 16 days post-procedure, aspiration pneumonia at 32 days post-procedure, myocardial infarction/subdural hematoma at 81 days post-procedure, and hypotension at 240 days post procedure.

Adverse events related to either the stent or the stent implant procedure included stent thrombosis (5), stent restenosis (8), stent migration (3), and an allergic reaction to contrast media (1). The three stent migrations in this physician single-center study and the one stent migration in the multi-center Wallstent Venous central lesion study were attributed to incorrect sizing of the stent and/or dislodgment with the guide catheter. All of the stent migration cases were treated with a

percutaneous procedure and none resulted in abandonment of the access site.

6.2 Potential Adverse Events

Potential adverse events associated with use of the WALLSTENT® Venous Endoprosthesis may include the usual adverse events reported for conventional percutaneous transluminal angioplasty such as: hemorrhage, infection, contrast media reactions, dissection, distal emboli, graft rupture, graft/vein thrombosis or occlusion, perforation of the vein, suture disruption of the anastomosis, thromboembolism or transient spasm.

Potential adverse events associated with the WALLSTENT® Venous Endoprosthesis are stent misplacement, stent migration, or vein perforation.

6.3 Observed Device Malfunctions

Two incidents of stent malfunction were reported in the central venous lesion study. In one incident, the delivery system failed to deploy. In the second incident, the stent did not fully expand.

7. Alternative Practices or Procedures

Alternative procedures include percutaneous transluminal angioplasty (PTA).

8. Marketing History

Boston Scientific Scimed has not marketed the Wallstent® Venous Endoprosthesis for the central vein indication.

9. Summary of Preclinical Studies

9.1 Biocompatibility

The biocompatibility of the WALLSTENT Venous Endoprosthesis and the Unistep Plus delivery catheter was evaluated in accordance with the FDA-modified matrix of International Standard ISO-10993, "Biological Evaluation of Medical Devices Part 1: Evaluation and Testing." All materials were found to be biocompatible.

9.2 Bench Testing

Stent Material Composition Conformance
The chemical composition of the biomedical superalloy wire conforms to the ASTM F1058 standard and the composition of the tantalum core material conforms to the ASTM F560-68 standard.

Stent Wire Mechanical Properties Conformance
The mechanical properties (tensile strength and elongation) of the stent wire were documented through tensile testing.

Corrosion Resistance
Samples of the stent wire were tested for resistance to corrosion resistance. There was no evidence of galvanic corrosion among the test samples.

Stent Percent Free Area
The percent free area, i.e., the area not in contact with the vessel wall, was calculated for all stent diameters. The results found that the stent percent free area was approximately 80 percent from fully open to nearly 50 percent constrained.

Stent Uniformity
To determine the uniformity of the stent dimensions, the outer diameter and length (constrained and unconstrained) of all stent diameters were measured. The measurements documented the uniformity of the outer diameters and the stent lengths.

Radial Force
The force exerted by the self-expanding stent as a function of its diameter was measured to determine the exerted radial tension from one stent to another over a constrained diameter range. The test results show consistent radial force between the stents.

Fatigue
Finite element stress analysis was performed on all stent sizes. The analysis included fabrication stresses and the calculation of stress as a function of diameter, ranging from fully constrained (loaded on the catheter) to unconstrained (fully deployed). The stress analysis indicated a satisfactory safety factor was present and fatigue failure of the stent was unlikely.

Stent Deformation
To determine the ability of the stent to withstand deformation from an external force, all stent diameters underwent compression testing. The stent were exposed to a uniform external force and a focal external force. All of the stents, except one, survived the compression testing without a fracture of the stent wire.

Magnetic Resonance Imaging (MRI) CompatibilityTesting
MRI compatibility testing determined the location of the maximum spatial gradient within the scanner and measured the average deflection for each stent from the displacement force and from the displacement torque. The change in temperature of the stent was measured during a pulse sequence that produced a whole body averaged specific absorption rate of 1.3W/kg. Geometric distortion was calculated under a gradient pulse echo sequence and a conventional spin echo pulse sequence. The results found that the stent was MRI safe with artifact affecting imaging at the location of the stent.

Delivery Catheter Trackability
To determine the amount of force necessary to pass a delivery catheter with mounted stent

over a guidewire, six to seven of the smallest and largest stent sizes were tested in a simulated clinical model. The results found that the tracking forces were acceptable.

Delivery Catheter Stent Deployment Force
To determine the force required to deploy and reconstrain the stent, six to seven of the smallest and largest stent sizes were tested in a simulated clinical model. All of the samples were within the test specifications.

Delivery Catheter Bond Strength
To demonstrate the strength of the bonded joints and their ability to resist failure, bond strength testing was performed on 26-78 units per 10 different bond sites. The results of each of the bond strength tests exceeded the test specification.

9.3 **Sterility and Packaging Testing**

Sterility
The Wallstent Venous Endoprosthesis is sterilized by a validated ethylene oxide sterilization process. The validated protocol was based on the ANSI/AAMI/ISO 1135-1994 "Medical Devices-Validation and Routine Control of Ethylene Oxide Sterilization". The validation results demonstrated that the sterilization process can achieve a sterility assurance level of 10^{-6}.

Shipping and Shelf Life Tests
Sterilized, packaged devices were subjected to accelerated aging and simulated transportation testing. Results of a visual examination, peel and burst strength testing, burst strength testing, and performance testing support a claim for a 2-year shelf life.

10. Summary of Clinical Studies

A total of 42 patients at 12 investigational sites within the United States were enrolled in a prospective, multi-center, non-randomized study with a historical percutaneous transluminal angioplasty (PTA) control cohort to investigate the safety and efficacy of the Wallstent Venous Endoprosthesis for improving central venous luminal diamter following unsuccessful angioplasty in patients on chronic hemodialysis.

Primary Endpoint: The primary endpoint for the Wallstent Venous trial was *circuit secondary patency* at 6 months. Circuit Secondary Patency is defined as the proportion of patients, over time, that have an occluded vessel that is successfully opened. Failure of circuit secondary patency occurs at the time the dialysis site is abandoned due to the inability to treat the stenosis, or occlusion of either the central lesion under consideration or any other peripheral or *de novo* central lesion.

Other endpoints evaluated include:

Stent Primary Patency, defined as the proportion of patients, over time, that have had uninterrupted (intervention-free) patency since the initial procedure. Primary patency ends at the first

occurrence of one of the following: initial re-intervention for the purpose of treating patency of the central lesion; anatomical failure (50% or greater stenosis) of the central lesion; or when the dialysis site is abandoned due to the inability to treat the original central lesion. If percent stenosis of the central lesion is undetermined, the occurrence of arm/face edema indicates the end of primary patency.

Stent Secondary Patency, defined as the time to failure of the access site due to stenosis or occlusion of the stented central lesion. Anatomical failure (>50% stenosis) of the central lesion which is not successfully reopened is also considered failure of stent secondary patency. Patients failing circuit secondary patency due to other peripheral lesions, problems at the access site (e.g. pseudoaneurysm, infection), or a *de novo* central lesion that does not involve the stent margin, do not fail stent secondary patency. These patients are censored from analysis at the date of the last follow-up documenting patency of the stent.

Patency rates were estimated by means of Kaplan-Meier Survival Analysis.

Patient Elgibility: Patients were eligible for the study if they were on chronic hemodialysis and had a central venous stenosis which was treatable with PTA. If the PTA failed to reduce the stenosis to less than 50% in patients with a vein >10 mm in diameter, or 30% in a vein $\leq$10mm in diameter, the patient received a WALLSTENT® Venous Endoprosthesis. If the PTA was successful, but the stenosis recurred within 4 months, the patient received a WALLSTENT® Venous Endoprosthesis.

Study Methods: Clinical follow-up was obtained at 1 week, 2 months, 6 months, and every 6 months thereafter until study conclusion, or the graft site was abandoned. Baseline quantitative angiography was performed pre-procedure, following balloon angioplasty, following device deployment, and at the 2-month and 6-month visit. The stent primary patency, stent secondary patency, and circuit secondary patency were analyzed.

Results: Among the 42 patients enrolled in the study, lesions involved the innominate vein in 14, subclavian vein in 23, and both subclavian and innominate veins in 5 patients. The mean lesion length was 25.8mm (±18.8, range = 2.0-81.6mm). Multiple stents were implanted in 5 patients (11.9%). A total of 28.6% of the patients (12/42) had occluded (100% stenoses) veins at the time of the study enrollment.

Initial intraoperative success, as measured by the reduction in stenosis to $\leq$30%, or angiographic demonstration of an increase in venous outflow, was achieved in 100% of patients. Analysis of the clinical data demonstrated a 74.3% circuit secondary patency rate at six months for the WALLSTENT® study group, compared to a 50% secondary patency rate for the historical control of percutaneous transluminal angioplasty (PTA), resulting in a highly significant statistical difference ($p<0.0003$). The WALLSTENT® Venous Endoprosthesis was found to provide superior efficacy in the central venous patient cohort when compared to the historical control (PTA).

Baseline demographic and lesion characteristics were individually regressed on time to loss of circuit secondary patency to assess possible predictors of clinical outcome (univariate analysis). Presence of an occluded lesion pre-procedure was significantly associated with circuit secondary patency

(p=0.022). The same variables were analyzed using stepwise selection to identify a multivariate predictor model. Presence of a totally occluded lesion pre-procedure was the only variable associated with time to loss of circuit secondary patency (p=0.0072). Implantation of multiple stents approached significance in the multivariate model (p=0.062).
Principal Efficacy and Safety results are summarized in Table 3.

Table 3. Principal Efficacy and Safety Results, BSC Patients (N=42)

Efficacy Measures	**Result**	**95% C.I.**
Device Success	100.0% (42/42)	[91.6%,100.0%]
Initial Intraoperative Success:		
Criterion 1: ≤30% Residual Stenosis	64.3% (27/42)	[48.0%,78.4%]
Criterion 2: Increased Venous Flow	90.5% (38/42)	[77.4%,97.3%]
Met Either Criterion	100.0% (42/42)	[91.6%,100.0%]
Acute Procedure Success	64.3% (27/42)	[48.0%,78.4%]
Initial Clinical Success	95.8% (23/24)	[78.9%,99.9%]
Pre-PTA RVD (mm)	12.6±3.7 (42) (3.0,20.1)	[11.5,13.7]
Post-Stent MLD (mm)	8.8±2.8 (39) (3.7,20.2)	[7.9,9.7]
Post-Stent %DS	24.1±18.4 (42) (0.0,63.0)	[18.5,29.6]
6-Month RVD (mm)	10.4±3.3 (25) (4.0,18.3)	[9.1,11.7]
6-Month MLD (mm)	3.0±2.7 (26) (0.0,11.0)	[1.9,4.0]
6-Month %DS	67.9±29.1 (26) (9.0,100.0)	[56.7,79.1]
Patency		
6-Month Stent Primary Patency (K-M)	24.4%	[9.8%,39.0%]
6-Month Stent Secondary Patency (K-M)	82.5%	[69.7%,95.2%]
6-Month Circuit Secondary Patency (K-M)	74.3%	[60.6%,88.1%]
Stent Restenosis	76.2% (32/42)	[60.5%,87.9%]
Arm-Face Edema	40.5% (17/42)	[25.6%,56.7%]
Safety Measures	**Result**	**95% C.I.**
Major In-Hospital Event	0.0% (0/42)	[0.0%,8.4%]
Out-of-Hospital (Stent-Related) Event		
Stent Thrombosis	50.0% (21/42)	[34.2%,65.8%]
Migration	2.4% (1/42)	[0.1%,12.6%]
Death	11.9% (5/42)	[4.0%,25.6%]

Results are mean ± SD (sample size) (min, max) for continuous variables, and percent (count/sample size) for binary variables.
Confidence intervals for binomial proportions are based on exact limits.
Patency rates are Kaplan-Meier estimates at 180 days; confidence intervals based on Greenwood standard errors.
RVD = Reference Vessel Diameter
MLD = Minimum Lumen Diameter
%DS = percent diameter stenosis which refers to "within lesion" measurement technique
Device Success = Stent(s) deployed completely.

Initial Intraoperative Success, Criterion 2 = angiographic demonstration of an increase in venous outflow (visualization of less collateral flow, more rapid rate of contrast media clearing or less reflux flow post-procedure).

Acute Procedure Success = ≤30% residual stenosis and absence of major in-hospital event.

Initial Clinical Success = <20% recirculation fraction one week post-procedure. (Note: incomplete number of assessments (N=24) reflects a change in clinical practice during the course of the study in which many institutions stopped using recirculation fractions to monitor patients.)

Stent Restenosis = within stent %DS of 50% or greater, or in the absence of angiography presence of arm-face edema.

Stent Thrombosis = total thrombotic stent occlusion documented by angiography. (Note: Stent Thrombosis is a subset of stent restenosis).

Additional clinical efficacy data was also retrospectively obtained on 12 patients enrolled in physician's registry study of the Wallstent Venous Endoprosthesis for the treatment of stenotic or occluded subclavian veins of patients undergoing hemodialysis. The enrollment criteria for this study were similar to the multicenter Wallstent Venous central lesion study. A Kaplan-Meier Survival analysis estimated the six-month circuit secondary patency, stent primary patency, and stent secondary patency rates at 68.6%, 33.8%, and 75%, respectively, for this patient cohort.

11. Conclusions Drawn from Studies

The preclinical studies indicate that the Wallstent Venous Endoprosthesis with Unistep Plus Delivery Catheter meets or exceeds safety, reliability and performance specifications. The results of the clinical study indicate that the data show that the Wallstent Venous Endoprosthesis with Unistep Plus Delivery System is reasonably safe and effective for the treatment of patients on chronic hemodialysis following unsuccessful angioplasty of the innominate and subclavian veins, when used in accordance with the directions for use.

12. Panel Recommendations

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

13. FDA Decision

The FDA issued an approval order on November 16, 2001. .

A condition of the sale of the device was further characterization of long-term safety and effectiveness of the Wallstent Venous Endoprosthesis through clinical follow-up of the study patients out to one-year post-procedure.

14. Approval Specifications

Directions for Use: See the labeling.

Hazards to Health from User of the Device: See INDICATIONS, CONTRAINDICATIONS,WARNINGS AND PRECAUTIONS, AND ADVERSE EVENTS in the final draft labeling (Information for Use).
Post-approval Requirements and Restrictions: See Approval Order