SUMMARY OF SAFETY AND EFFECTIVENESS DATA

Summary of Safety and Effectiveness

Summary of Safety and Effectiveness Data

I. General Information

Device Generic Name:	BeStent™ 2
Device Trade Name(s):	Medtronic AVE BeStent™ 2 with Discrete Technology™ Over-The-Wire (OTW) Coronary Stent Delivery System **and** Medtronic AVE BeStent™ 2 with Discrete Technology™ Rapid Exchange (RX) Coronary Stent Delivery System
Applicant's Name and Address:	AVE Ireland Limited (a division of Medtronic AVE Inc.) Parkmore Business Park West, Galway, Ireland
Date of Panel Recommendation:	None
Premarket Approval Application (PMA) Number:	P000022
Date of Good Manufacturing Practice Inspection:	FDA most recently inspected the AVE Ireland Limited facility on May 10-14, 1999 and the Medtronic AVE, Inc. facility (Santa Rosa) on January 13, 1999.
Date of notice of Approval to Applicant:	October 16, 2000

II. Indications For Use

Medtronic AVE BeStent™ 2 with Discrete Technology™ Over-The-Wire Coronary Stent Delivery System

The Medtronic AVE BeStent™ 2 with Discrete Technology™ Over-The-Wire Coronary Stent Delivery System (hereinafter called the BeStent™ 2 OTW) is indicated for improving coronary luminal diameter in patients with symptomatic ischemic heart disease due to discrete *de novo* lesions (length ≤ 30 mm) in native coronary arteries with reference vessel diameters ranging from 3.0 mm to 4.0 mm.

Medtronic AVE BeStent™ 2 with Discrete Technology™ Rapid Exchange Coronary Stent Delivery System

The Medtronic AVE BeStent™ 2 with Discrete Technology™ Rapid Exchange Coronary Stent Delivery System (hereinafter called the BeStent™ 2 RX) is indicated for improving coronary luminal diameter in patients with symptomatic ischemic heart disease due to discrete *de novo* lesions (length ≤ 30 mm) in native coronary arteries with reference vessel diameters ranging from 3.0 mm to 4.0 mm.

III. Contraindications

The contraindications can be found in the BeStent™ 2 labeling.

BeStent™ 2 OTW

The BeStent™ 2 OTW is contraindicated for use in:

- Patients in whom antiplatelet and/or anticoagulation therapy is contraindicated.
- Patients who are judged to have a lesion that prevents complete inflation of an angioplasty balloon.

BeStent™ 2 RX

The BeStent™ 2 RX is contraindicated for use in:

- Patients in whom antiplatelet and/or anticoagulation therapy is contraindicated.
- Patients who are judged to have a lesion that prevents complete inflation of an angioplasty balloon.

IV. Warnings and Precautions

The warnings and precautions can be found in the BeStent™ 2 labeling.

V. Device Description

The BeStent™ 2 stent is a balloon expandable coronary stent made from implant grade 316L (grade 2) stainless steel. The stent is cut from stainless steel tubing using a laser to produce a serpentine lattice structure. A single gold marker is embedded in each end of the stent to increase radiopacity. The BeStent™ 2 stent design consists of a series of corrugated ring elements which provide the primary structural support for the device. These corrugated ring elements are joined together by a series of longitudinal members. The corrugated ring elements and longitudinal members intersect in a rotating junction. The number of peaks per corrugated ring element is dependent on vessel diameter (5 for 3.0mm diameter and 6 for 3.5/4.0mm diameters). The laser cut stent is processed through a number of worksteps including cleaning, annealing/diffusion, electropolishing and inspection before being compressed and mounted onto the balloon portion of the catheter delivery system.

The BeStent™ 2 stent is provided on two delivery systems, an Over-the-Wire (OTW) delivery system and a Rapid Exchange (RX) delivery system. Both systems have a "discrete" length balloon mounted on the distal end of the catheter. The BeStent™ 2 RX catheter is a rapid exchange catheter that will allow for perfusion at an average rate of 2cc/min at nominal inflation pressure.

Both the OTW and the RX configurations are offered in diameters of 3.0mm, 3.5mm and 4.0mm and in lengths of 9mm, 12mm, 15mm, 18mm, 24mm and 30mm.

VI. Alternative Practices and Procedures

Alternative practices specific to the treatment of coronary atherosclerotic disease are:

- Balloon angioplasty (either conventional or with auto perfusion balloon)
- Drug therapy (e.g., thrombolytic agents, antiplatelet agents, and anticoagulant agents)
- Atherectomy
- Coronary Artery Bypass Graft Surgery (CABG)
- Stenting

VII. Marketing History

The BeStent™ 2 OTW and RX devices which are the subject of this original PMA submission have not been released for commercial distribution in any market.

VIII. Potential Adverse Effects of the Device on Health

The potential adverse effects of using the BeStent™ 2 OTW and RX devices (as with any other type of intravascular stent) include, but are not limited to, the following (in order of severity):

- Death
- Emergency Coronary Artery Bypass Graft Surgery (CABG)
- Stroke/Cerebrovascular Accidents
- Stent thrombosis or occlusion
- Total occlusion of coronary artery
- Acute myocardial infarction
- Restenosis of stented segments
- Perforation
- Arrhythmias (ventricular fibrillation, ventricular tachycardia, other)
- Dissection
- Emboli, distal (air, tissue or thrombotic emboli)
- Stent embolization
- Hemorrhage requiring transfusion
- Pseudoaneurysm, femoral
- Spasm
- Myocardial ischemia
- Infection and pain at the insertion site
- Drug reaction to antiplatelet agents/contrast medium
- Hypotension/Hypertension

IX. Summary of Pre-clinical Studies

1. Biocompatibility

The BeStent™ 2 OTW and RX systems have been determined to be biocompatible.

All biocompatibility testing was conducted on finished, sterile devices performed by North American Science Associates, Inc. (NAmSA). The testing was conducted in compliance with applicable requirements in the Good Laboratory Practice (GLP) regulations 21 CFR Part 58, the "Guidance for the Submission of Research and Marketing Applications for Interventional Cardiology Devices" published by the

Interventional Cardiology Devices Branch, Division of Cardiovascular, Respiratory and Neurological Devices, Office of Device Evaluation in May 1995, and ISO 10993.

The following tests were conducted on the BeStent™ 2 stent: cytotoxicity, hemolysis, acute systemic toxicity, intracutaneous reactivity, sensitization, material mediated pyrogenicity, complement activation, coagulation, muscle implantation, genotoxicity (chromosomal aberration, bacterial reverse mutation, and mouse micronucleus) and subchronic toxicity.

The biocompatibility of the materials in the delivery catheters have been shown to be acceptable for short-term blood contact. Biocompatibility testing on Medtronic AVE's delivery systems includes cytotoxicity, hemolysis, acute systemic toxicity, intracutaneous reactivity, sensitization, material mediated pyrogenicity and complement activation.

Chronic toxicity, carcinogenicity, biodegradation and developmental/reproductive tests were not conducted due to the historical use of 316L stainless steel for implantation throughout the body (and thus exempt from these particular tests per ISO).

2. *In Vitro* Testing

In vitro testing was conducted in accordance with the FDA ODE "Guidance for the Submission of Research and Marketing Applications for Interventional Cardiology Devices: PTCA Catheters, Atherectomy Catheters, Lasers, Intravascular Stents", May 1995

Table 1: *In Vitro* Testing

Test	*Acceptance Criteria*	*BeStent™ 2 OTW*	*BeStent™ 2 RX*
Material Analysis	1) Surface Analysis – no evidence of surface contamination	Pass (N=13)	
	2) Grain Size - ≥ 7.5 ASTM No.	3.5 x 9 – 8.6 ASTM No. (minimum) (N=13)	Same
	3) Microhardness – 180 ± 20 Hv	180.9 Hv (N=13)	
	4) Material Analysis – ASTM F138 (stainless steel)	Pass	
	ASTM B562 grade 99.99 (Gold)	Pass	
Mechanical Properties	comply with ASTM F138	Pass	
	UTS - > 480 Mpa YS - > 170 Mpa Elongation - > 40%	UTS – 611.4 Mpa (N=13) YS – 328.1 Mpa (N=13) Elongation – 45.7% (N=13)	Same
Corrosion	1) Corrosion Potential – achieve stable potentials below breakdown potential	Pass (N=6)	
	2) Anodic Polarization – breakdown values above corrosion potential	Pass (N=6)	
	3) Crevice Corrosion – repassivation values above corrosion potential	Pass (N=3)	Same
	4) Cyclic Polarization – breakdown and repassivation values above corrosion potential	Pass (N=2)	
	5) Impedance Measurements – no increase in corrosion rate due to gold	Pass (N=6)	
Stent Free-area	10-25% for min and max diameters	3.0 x 9 – 16.4% (N=13) 3.5 x 15 – 16.8% (N=13) 4.0 x 30 – 14.6% (N=13)	3.0 x 9 - 16.9% (N=13) 3.5 x 9 - 17.9% (N=13) 4.0 x 9 - 15.4 % (N=13)

Test	*Acceptance Criteria*	*BeStent™ 2 OTW*	*BeStent™ 2 RX*
Stent Foreshortening	Stent Lengths 9mm & 12mm: ≤ 10% 15mm, 18mm, 24mm, 30mm: ≤ 5%	4.0 x 9 – 6.6% (N=13) 3.5 x 9 – 4.7% (N=13) 3.0 x 9 – 3.5% (N=13) 4.0 x 12 – 4.8% (N=13) 3.5 x 12 – 3.0% (N=13) 3.0 x 12 – 2.6% (N=13) 4.0 x 15 – 3.6% (N=13) 3.5 x 15 – 1.6% (N=13) 3.0 x 15 – 2.3% (N=13) 4.0 x 18 – 3.8% (N=13) 3.5 x 18 – 0.7% (N=13) 3.0 x 18 – 1.4% (N=13) 4.0 x 24 – 1.9% (N=13) 3.5 x 24 – 1.0% (N=13) 3.0 x 24 – 1.2 % (N=13) 4.0 x 30 – 1.9% (N=13) 3.5 x 30 – 1.2% (N=13) 3.0 x 30 – 0.8% (N=13)	4.0 x 9 – 6.4% (N=13) 3.5 x 9 – 3.8% (N=13) 3.0 x 9 – 2.7% (N=13) 4.0 x 15 – 3.0% (N=13) 3.5 x 15 – 1.5% (N=13) 3.0 x 15 – 1.8% (N=13) 4.0 x 30 – 1.4% (N=13) 3.5 x 30 – 0.4% (N=13) 3.0 x 30 – 0.6% (N=13)
Stent Uniformity	measured ID at proximal, mid and distal must be within ± 5% of mean	Pass (N=234)	Pass (N=117)
Radial Strength	1) Elastic Limit – 500 mmHg 2) Radial Stiffness 3) Deflection at 100 and 200 mmHg	Elastic Limit 3.0 x 30 – 862 mmHg (N=13) 3.5 x 15 – 889 mmHg (N=13) 4.0 x 30 – 700 mmHg (N=13) Radial Stiffness 3.0 x 30 – 2.67 N/mm² (N=13) 3.5 x 15 – 2.81 N/mm² (N=13) 4.0 x 30 – 2.50 N/mm² (N=13) Deflection @ 100 mmHg 3.0 – 0.0150 mm (N=13) 3.5 – 0.0166 mm (N=13) 4.0 – 0.0213 mm (N=13) Deflection @ 200 mmHg 3.0 – 0.0300 mm (N=13) 3.5 – 0.0332 mm (N=13) 4.0 – 0.0427 mm (N=13)	Same
Fatigue Testing	Withstand 10 years equivalent real time testing – 420 million cycles	Pass 420 million cycles complete (N=11)	Same
Stent Recoil	≤ 8%	3.0 x 18 – 2.24% (nominal) 1.99% (RBP) (N=13) 3.5 x 18 – 1.59% (nominal) 2.23% (RBP) (N=13) 4.0 x 30 – 1.92% (nominal) 2.61% (RBP) (N=13)	3.0 x 9 – 2.87% (nominal) 1.86% (RPB) (N=13) 3.5 x 9 – 2.71% (nominal) 2.34% (RBP) (N=13) 4.0 x 9 – 2.34% (nominal) 1.84% (RBP) (N=13)
MRI	MRI compatibility	Pass (N=1) note: labeling contains warning regarding use with MRI	Same
Stent Expansion	no crack initiation at max stent expansion at x200	Pass (N=13)	Pass (N=13)

Test	*Acceptance Criteria*	*BeStent™ 2 OTW*	*BeStent™ 2 RX*
Dimensional Verification (stent)	Stent Ring Element Width – 0.095 +0.010/-0.020 mm Stent Link Element Width – 0.070 +0.010/-0.020 mm Stent Wall Thickness 0.085 +0.0075/-0.005 mm Stent Cell Area 1.3 – 2.3 mm^2 Stent Length – Nominal +0.5/-0.75 mm	Pass (N=234 stent @ 6 measurements/stent) Pass (N=234 stent @ 6 measurements/stent) Pass (N=234) Pass (N=39) Pass (N=234)	Same
Maximum Pressure	RBP 16 atm – 3.0 & 3.5 RBP 15 atm – 4.0 mm	3.0 x 9 – 23.9 atm (N=13) 3.0 x 12 – 23.1 atm (N=13) 3.0 x 15 – 24.3 atm (N=13) 3.0 x 18 – 24.2 atm (N=13) 3.0 x 24 – 24.9 atm (N=13) 3.0 x 30 – 22.9 atm (N=13) 3.5 x 9 – 23.5 atm (N=13) 3.5 x 12 – 24.6 atm (N=13) 3.5 x 15 – 24.8 atm (N=13) 3.5 x 18 – 24.5 atm (N=13) 3.5 x 24 – 24.3 atm (N=13) 3.5 x 30 – 23.3 atm (N=13) 4.0 x 9 – 21.9 atm (N=13) 4.0 x 12 – 21.0 atm (N=13) 4.0 x 15 – 22.5 atm (N=13) 4.0 x 18 – 23.1 atm (N=13) 4.0 x 24 – 23.0 atm (N=13) 4.0 x 30 – 21.7 atm (N=13)	3.0 x 9 – 24.6 atm (N=13) 3.0 x 15 – 24.8 atm (N=13) 3.0 x 30 – 25.7 atm (N=13) 3.5 x 9 – 23.3 atm (N=13) 3.5 x 15 – 23.4 atm (N=13) 3.5 x 30 – 23.0 atm (N=13) 4.0 x 9 – 23.4 atm (N=13) 4.0 x 15 – 22.8 atm (N=13) 4.0 x 30 – 21.6 atm (N=13)
Stent Diameter vs. Pressure (stent compliance)	measured stent diameter within 10% of labeled diameter between nominal and rated burst pressures	Acceptable - see labeling (N=234)	Acceptable - see labeling (N=234)
Bond Strength	Bifurcate (OTW): >2.0 lbs. All other OTW bonds: OTW >1.5 lbs. Balloon/Tack & Intermediate (RX): >1.5 lbs. Conversion/Luer (RX): >2.5 lbs.	Proximal Balloon/Outer Shaft (2.74 lbs. min.) N=13 Intermediate/Distal (2.34 lbs. min.) N=30 Intermediate/Proximal (2.45 lbs. min.) N=30 Bifurcate Bond (4.83 lbs. min.) N=30	Balloon Bond/Tack (2.42 lbs. min.) N=270 Intermediate Bond (2.62 lbs. min.) N=270 Conversion Bond (2.67 lbs. min.) N=270 Luer Bond (7.2 lbs. min.) N=270

Test	*Acceptance Criteria*	*BeStent™ 2 OTW*	*BeStent™ 2 RX*
Diameter and Profile	Distal Bond OD (OTW) – 0.033" max Tip OD (OTW) – 0.020"-0.022" Distal Shaft OD (OTW) – 0.035"-0.037" Intermediate Shaft OD (OTW) – 0.039"-0.041" Proximal Shaft OD (OTW) – 0.041"-0.043" All RX diameters – less than 0.058"	Distal Bond OD 4.0 x 9 – 0.025" max. (N=13) Tip OD 1.5 x 16 – 0.022" max. (N=10) 4.0 x 30 – 0.022" max. (N=10) Distal Shaft OD (0.037" max.) N=10 Intermediate Shaft OD (0.041" max.) N=10 Proximal Shaft OD (0.043" max.) N=10	Tip OD (0.033" max.) N=270 Balloon Bond OD (0.048" max.) N=270 Intermediate Bond OD (0.042" max.) N=270 Conversion Bond OD (0.048" max.) N=270 Distal Shaft OD (0.039" max.) N=270 Intermediate Shaft OD (0.042" max.) N=270 Proximal Shaft OD (0.030" max.) N=270
Balloon Deflatibility & Balloon Inflation/Deflation Time	Inflation to RBP ≤ 15s Deflation ≤ 15s for OTW; ≤ 20s for RX.	Maximum 3.0 x 30 – 9.9s (inflat.) 9.9s (deflat.) (N=13) 3.5 x 30 – 12.5s (inflat.) 5.6s (deflat.) (N=13) 4.0 x 30 – 12.3s (inflat.) 14.1s (deflat.) (N=13) Deflatibility (N=39) - acceptable	Maximum 3.0 x 30 – 11.1s (inflat.) 8.9s (deflat.) (N=13) 3.5 x 30 – 13.8s (inflat.) 9.5s (deflat.) (N=13) 4.0 x 30 – 12.4s (inflat.) 15.9s (deflat.) (N=13) Deflatibility (N=39) - acceptable
Stent Crimping	Force to move stent: ≥ 70g Delivery to target lesion and withdrawal into 6F guide catheter	3.0 x9 – 117.8 g (N=13) 3.5 x 9 – 125.5 g (N=13) 4.0 x 9 – 126.1 g (N=13) successful withdrawal into GC (N=39)	3.0 x 9 - 98.9 g (N=13) 3.5 x 9 - 106.6 g (N=13) 4.0 x 9 - 119.1 g (N=13) successful withdrawal into GC (N=39)
Crossing Profile	≤ 0.049 inches	3.0 x 24 – 0.039" (N=13) 3.5 x 24 – 0.040" (N=13) 4.0 x 24 – 0.040" (N=13) can be used with 6F GC	3.0 x 30 - 0.039" (N=13) 3.5 x 30 - 0.040" (N=13) 4.0 x 30 - 0.041" (N=13) can be used with 6F GC
Package Integrity	Seal Strength – 95% lower confidence interval (LCI) > 0.45 lbs. Seal Creep/Burst – withstand 15.46 inches of H_2O for 30s Configuration Pre/Post Transport Simulation and Impact Drop Test - must protect device	3.77 lbs. (LCI – 2.57 lbs.) pass (n=13) pass (n=13)	Pass (N=20)

Test	*Acceptance Criteria*	*BeStent™ 2 OTW*	*BeStent™ 2 RX*
Catheter Dimensional	Over-the-Wire Wire Lumen I.D. – 0.0155" patency	Pass (N=13)	
	Exit Marker Location Brachial Marker: 88 ± 2 cm	87.3mm (N=13)	
	Femoral Marker: 10 ± 0.5 cm (from Brachial)	10.0mm (N=13)	
	Useable Length - 135 +3/-2 cm	135.7mm (N=13)	
	Balloon Working Length – Reference template	Pass (N=65)	
	Radiopaque Marker Location – Reference template	Pass (N=65)	
	Rapid Exchange Intermediate Bond Length 7mm max.		Intermediate Bond Length 4.71mm (N=270)
	Conversion Bond Length 3-6mm		Conversion Bond Length 4.56mm (N=90)
	Balloon Bond Length 1.5mm min.		Balloon Bond Length 1.65mm (N=270)
	Tip Length 4.5-5.0mm		Tip Length 4.80mm (N=270)
	Tip Seal Length 1.5-2.0mm		Tip Seal Length 1.75mm (N=270)
	Tack Bond Distance 2.0mm min.		Tack Bond Distance 3.86cm (N=265)
	Intermediate Bond Distance 16-19cm		Intermediate Bond Distance 17.66cm (N=270)
	Conversion Bond Distance 26.5cm max.		Conversion Bond Distance 24.75cm (N=270)
	Perfusion Hole Diameter 0.013" max.		Perfusion Hole Diameter 0.008" (N=540)
Radiopacity	Stent, balloon (and perfusion markers – for RX only) must be equal to or darker than the distal portion of a guidewire	Pass (N=1)	Pass (N=1)
Pullability	Possible to manipulate undeployed stent back into GC without stent completely dislodging off balloon	3.0 x 9 – pass (N=13) 3.0 x 30 – pass (N=13) 3.5 x 15 – pass (N=13) 4.0 x 9 – pass (N=13) 4.0 x 30 – pass (N=13)	3.0 x 30 – pass (N=13) 3.5 x 30 – pass (N=13) 4.0 x 30 – pass (N=13)
Coating	n/a	Hydrophilic	Hydrophilic
Stent Radiopaque Marker Detachment	Detachment force: ≥ 450g	3.0 x 9 – 1741 g (N=13 stent @ 2 measurements/stent)	Same
Perfusion	1 cc/minute minimum, minimum 2cc/minute average	n/a	9mm – 3.3 cc/min (N=30) 18mm – 2.8 cc/min (N=31) 30mm – 2.7 cc/min (N=33)

* Data presented are mean results in all cases unless otherwise stated

3. *In vivo* (animal) studies

Various models have been used to evaluate the performance and biological vascular response to endovascular devices. The swine model has emerged as the most appropriate, reliable, and accepted model for the evaluation of endovascular devices. Additionally the swine is the model recommended by the FDA[1] for the evaluation of coronary stents. The rabbit is also used as an effective model to evaluate biological responses of developmental devices. The inherent differences between species and anatomical sites in these two models are as follows: arteries utilized in the rabbit model are generally the carotid and iliac arteries, which are thinner walled and more fragile elastic arteries, whereas the coronary arteries utilized in the swine model are muscular arteries and more reflective of human coronary arteries.

A non clinical research study utilizing the BeStent™ 2 coronary stent, FS19, was conducted comparing both the patency rates and biologic vascular response of the BeStent™ 2 coronary stent system with the original BeStent™. FS19 evaluated the vascular response to the BeStent™ 2 and the BeStent™ in normal porcine arteries for a duration of four weeks.

Conclusion

The 28-day microscopic evaluation showed a low injury score for both stent designs. There were no qualitative differences in response to stents of the two designs evaluated in this study. A thick rim of neointima existed between the stent struts and the arterial lumen. The percent diameter stenosis was slightly less with the BeStent™ 2 compared to the BeStent™ control (28±2 versus 35±4, respectively). The morphometric analysis of the stents in the coronary arteries showed no statistical significant differences between the BeStent™ 2 test stents and the BeStent™ controls, the parameters evaluated included: intimal thickness, medial area, injury score, and % diameter stenosis. However, the morphometric analysis demonstrated that the lumen area and balloon size of the BeStent™ 2 stents was statistically larger compared to the BeStent™ controls.

The sponsor believes that the animal study demonstrates the *in vivo* equivalence of the BeStent™ 2 stent design to the clinically evaluated BeStent™ coronary stent in this animal model and provides support of the safety and effectiveness of the BeStent™ 2 stent and delivery system.

[1] Guidance for the Submission of Research and Marketing Applications for Interventional Cardiology Devices: PTCA Catheters, Atherectomy Catheters, Lasers, Intravascular Stents, May 1995, page 3.

X. Summary of Clinical Studies

Data to support the BeStent™ 2 OTW and RX Coronary Stent Delivery Systems were taken from the BEST randomized clinical study and the BeStent ™ 2 OTW Registry. Due to similarities in design, function, and materials the 6-month data on the BeStent™ Coronary Stent were used to support the long-term performance of the BeStent™2 coronary stent. Data from the BeStent™ 2 OTW Registry and clinical data from other Medtronic AVE Rapid Exchange delivery systems were used to support the safety and effectiveness of the BeStent™ 2 RX delivery system.

1. BeStent™ 2 OTW Registry

Title: The BeStent™ 2 OTW Registry

The BeStent™2 OTW Registry was a prospective, multi-center non-randomized trial conducted at eighteen (18) sites within the United States and three (3) Middle East sites. This registry included 227 patients with de novo and restenotic native coronary artery lesions. An independent Clinical Events Committee adjudicated all of the major clinical endpoints and clinically driven TVR.

Conclusions: The acute clinical and angiographic and 30-day clinical results demonstrated that the procedure success rate, defined as the attainment of a <50% residual stenosis (by QCA when available, or by the visual estimate when QCA was not available) using any percutaneous method and no in-hospital major adverse cardiac events (MACE, defined as death, emergent CABG, Q wave and non-Q wave MI, and target vessel revascularization), was 97.8% (222/227) for the BeStent™ 2 OTW Registry compared with 96.3% (315/327) for the Palmaz-Schatz® (PS®) arm of the BEST randomized trial. The Kaplan-Meier estimate of freedom from MACE at 30 days was 96.4% for the BeStent™2 registry compared with 96.0% for the PS® arm. The Kaplan-Meier estimate of freedom from target vessel failure (TVF, defined as death, Q wave or non-Q wave MI, and target vessel revascularization), at 30 days was 96.4% for the BeStent™2 registry compared with 96.0% for the PS® arm.

Investigative Sites: Eighteen sites within the United States and three Middle East sites contributed patients to the BeStent™ 2 Study.

Purpose: To demonstrate the safety and efficacy of the Medtronic AVE BeStent™ 2 Coronary Stent in the treatment of de novo or restenotic native coronary artery lesions. This report contains 30-day outcomes.

Design: This was a non-randomized, prospective, multi-center, consecutive-enrollment registry. Patients with symptomatic ischemic heart disease due to de novo and restenotic lesions of the native coronary

arteries that were amenable to percutaneous treatment with stenting, and who met all of the eligibility criteria were enrolled in this study.

Demographics: The BeStent™ 2 OTW Registry was comprised of 227 patients. Baseline demographics and clinical characteristics showed that patients had a mean age of 62.4 years, there was 68.3% (155/227) male gender participation (which is indicative of coronary disease), and that 27.0% (61/226) had a history of diabetes mellitus. Patient screening logs were maintained and reviewed to ensure non-bias selection.

Method: Baseline and follow-up clinical data were collected by Clinical Research Coordinators at the clinical sites on standardized case report forms. Clinical follow-up was mandated at 30 days and 6 months post-procedure for all patients. Clinical follow-up was available for 91.0% (206/227) of BeStent™ 2 patients at 25 days or greater. Baseline quantitative coronary angiography was performed pre-procedure, following device deployment and after final treatment. The pre-specified primary endpoint of this study is a composite 30-day endpoint of MACE. The secondary endpoints were the 6-month composite endpoint of TVF, and subacute stent thrombosis, acute ischemic, hemorrhagic and/or vascular complications within 30 days of the index procedure, as well as lesion success, device success and acute procedure success (see Definition of Terms for success definitions). An independent Clinical Events Committee adjudicated all of the major clinical endpoints. All endpoints were analyzed on an intent-to-treat basis.

Procedure Success: Procedure success was defined as the attainment of a <50% residual stenosis using any percutaneous method and no in-hospital MACE. If no in-stent measurements were available, in-lesion measurements were used, and if no QCA was available, visual estimates were used.

Lesion Success: Lesion success was defined as the attainment of <50% residual stenosis using any percutaneous method. If no in-stent measurements were available, in-lesion measurements were used, and if no QCA was available, visual estimates were used.

Device Success: Device success was defined as the attainment of <50% residual stenosis using only the assigned device. If no in-stent measurements were available, in-lesion measurements were used, and if no QCA was available, visual estimates were used.

Table 1.1. Baseline Demographics and Clinical Characteristics.
Medtronic AVE BeStent™ 2 OTW Registry (N=227 patients, 227 Lesions)

Patient Characteristic	BeStent™ 2 (N=227 Patients, N=227 Lesions)	PS® (N=327 Patients, N=330 Lesions)
Age (years)		
Mean±SD (N)	62.4±10.6 (227)	61.3±11.2 (327)
Range (min,max)	(36.0,83.0)	(24.0,91.0)
Number of men	68.3% (155 / 227)	68.8% (225 / 327)
Cigarette smoking during the past year	30.2% (68 / 225)	30.2% (98 / 324)
Diabetes Mellitus	27.0% (61 / 226)	24.2% (79 / 327)
Hypertension requiring treatment	64.6% (146 / 226)	56.7% (185 / 326)
Dyslipidemia requiring treatment	68.7% (147 / 214)	40.9% (132 / 323)
Prior CABG	10.6% (24 / 227)	7.3% (24 / 327)
Prior MI	35.3% (78 / 221)	39.4% (128 / 325)
Revascularization for angina or MI	83.3% (189 / 227)	93.0% (304 / 327)
Stable exertional angina	13.7% (31 / 226)	10.1% (33 / 327)
CCS* III or IV	78.7% (129 / 164)	68.4% (221 / 323)
Unstable angina	57.5% (130 / 226)	68.8% (225 / 327)
Crescendo exertional angina	31.9% (72 / 226)	34.9% (114 / 327)
Rest angina	25.7% (58 / 226)	33.9% (111 / 327)
Pain only with MI	8.0% (18 / 226)	13.8% (45 / 327)
Post MI angina	4.0% (9 / 226)	N/A
Number of Diseased, Native, Major Epicardial Coronary Arteries		
Single	59.3% (134 / 226)	68.2% (223 / 327)
Double	30.1% (68 / 226)	23.5% (77 / 327)
Triple	10.6% (24 / 226)	8.3% (27 / 327)
Ejection Fraction (%)		
Mean±SD (N)	56.4%±0.1 (197)	53.9%±10.8% (307)
Range (min,max)	(18.0%,82.0%)	(21.0%,80.0%)

Numbers are % (counts/sample size) or Mean ± SD
N/A = Not applicable
*CCS = Canadian Cardiovascular Society angina class.

Table 1.2. Baseline Lesion Characteristics.
Medtronic AVE BeStent™ 2 OTW Registry (N=227 patients, 227 Lesions)

Lesion Characteristic	BeStent™ 2 (N=227 Patients, N=227 Lesions)	PS® (N=327 Patients, N=330 Lesions)
Pre-Procedure Reference Vessel Diameter (RVD, in mm)		
Mean±SD (N)	2.91±0.53 (225)	3.02±0.53 (324)
Range (min,max)	(1.71,4.64)	(1.61,5.12)
Pre-Procedure Minimal Lumen Diameter (MLD, in mm)		
Mean±SD (N)	1.15±0.49 (225)	1.03±0.45 (324)
Range (min,max)	(0.00,2.74)	(0.00,3.22)
Pre-Procedure Percent Diameter Stenosis (% DS)		
Mean±SD (N)	60.7%±14.4% (225)	65.4%±14.6% (324)
Range (min,max)	(25.6%,100.0%)	(21.9%,100.0%)
Lesion Length (mm)		
Mean±SD (N)	11.08±4.97 (222)	11.90±5.01 (317)
Range (min,max)	(2.03,35.00)	(2.52,38.02)
Target Lesion Vessel		
LAD	39.1% (88 / 225)	35.8% (116 / 324)
Circumflex (LCX)	21.8% (49 / 225)	22.8% (74 / 324)
RCA	38.7% (87 / 225)	41.0% (133 / 324)
LMCA	0.4% (1 / 225)	0.3% (1 / 324)
Restenotic Lesion	4.4% (10 / 227)	3.3% (11 / 330)
Calcification (moderate-severe)	8.0% (18 / 225)	9.9% (32 / 323)
Thrombus	3.1% (7 / 225)	2.8% (9 / 322)
Eccentric Lesion	49.8% (112 / 225)	32.6% (105 / 322)
Angulation >45°	5.3% (12 / 225)	6.5% (21 / 321)
ACC/AHA* Lesion Class		
A	12.0% (27 / 225)	13.8% (44 / 324)
B1	30.2% (68 / 225)	30.2% (98 / 324)
B2 (or higher grade B)	52.4% (118 / 225)	47.8% (155 / 324)
C	5.3% (12 / 225)	8.3% (27 / 324)

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

*American College of Cardiology/American Heart Association Lesion Class.

All variables are from assessment by the Angiographic Core Laboratory except Restenotic Lesion which is derived from Case Report Forms.

Table 1.3. Principal Effectiveness and Safety Results (to 30 days). Medtronic AVE BeStent™ 2 OTW Registry (N=227)

Efficacy Measures	BeStent™ 2 (N=227 Patients, N=227 Lesions)	PS® (N=327 Patients, N=330 Lesions)
Lesion Success	100.0% (227 / 227)	98.8% (326 / 330)
Device Success	95.2% (216 / 227)	93.9% (307 / 327)
Procedure Success	97.8% (222 / 227)	96.3% (315 / 327)
Post-Procedure In-Stent Minimal Lumen Diameter (MLD, in mm)		
Mean±SD (N)	2.61±0.46 (224)	2.80±0.41 (321)
Range (min,max)	(1.69,4.15)	(1.61,4.31)
Post-Procedure In-Stent Percent Diameter Stenosis (% DS)		
Mean±SD (N)	3.8%±9.6% (224)	8.0%±10.5% (321)
Range (min,max)	(-25.7%,27.0%)	(-29.3%,36.8%)
Post-Procedure In-Lesion Minimal Lumen Diameter (MLD, in mm)		
Mean±SD (N)	2.44±0.48 (224)	2.50±0.51 (323)
Range (min,max)	(1.26,4.06)	(0.00,4.15)
Post-Procedure In-Lesion Percent Diameter Stenosis (% DS)		
Mean±SD (N)	16.8%±9.1% (224)	18.3%±12.0% (323)
Range (min,max)	(-8.6%,50.4%)	(-16.5%,100.0%)
TLR-free to 30 days*	99.6%	98.5%
TVR-free to 30 days*	98.7%	98.5%
TVF-free to 30 days*	96.4%	96.0%
MACE-free to 30 days*	96.4%	96.0%
Safety Measures and Other Clinical Events		
In-Hospital MACE	2.2% (5 / 227)	2.8% (9 / 327)
Out-of-Hospital MACE to 30 days	1.3% (3 / 227)	1.2% (4 / 327)
Combined In- and Out-of-Hospital MACE to 30 days	3.5% (8 / 227)	4.0% (13 / 327)
Stent Thrombosis to 30 days	0.9% (2 / 227)	1.5% (5 / 327)
Abrupt Closure to 30 days	0.4% (1 / 227)	1.2% (4 / 327)
Subacute Closure to 30 days	0.0% (0 / 227)	0.6% (2 / 327)
CVA to 30 days	0.0% (0 / 227)	0.9% (3 / 327)
Bleeding Complications to 30 days	1.8% (4 / 227)	0.6% (2 / 327)
Vascular Complications to 30 days **	0.4% (1 / 227)	4.9% (16 / 327)

N/A = Not applicable

Lesion Success = Attainment of <50% residual stenosis using any percutaneous method. If no in-stent measurements were available, in-lesion measurements were used, and if no QCA was available, visual estimates were used.

Device Success = Attainment of <50% residual stenosis using only the assigned device. If no in-stent measurements were available, in-lesion measurements were used, and if no QCA was available, visual estimates were used.

Procedure Success = Attainment of a <50% residual stenosis using any percutaneous method and no in-hospital MACE. If no in-stent measurements were available, in-lesion measurements were used, and if no QCA was available, visual estimates were used.

*Survival estimates by Kaplan-Meier methods. Standard error estimates by Peto formula.

TLR-Free = No target lesion revascularization.

TVR-Free = No target vessel revascularization.

TVF-Free = No death, MI, or target vessel revascularization.

MACE= Death, Q wave or non-Q wave MI, emergent CABG, or target vessel revascularization.

In-Hospital MACE = Death, Q wave or non-Q wave MI, emergent CABG, or target vessel revascularization prior to discharge as determined by the independent Clinical Events Committee.

Out-of-Hospital MACE = Death, Q wave or non-Q wave MI, emergent CABG, or target vessel revascularization from hospital discharge through the 30-day contact, as determined by the independent Clinical Events Committee.

Stent Thrombosis = Angiographic thrombus or subacute closure within the stented vessel at the time of the clinically driven angiographic restudy for documented ischemia. Any death not attributed to a non-cardiac cause within the first 30 days was considered a surrogate for stent thrombosis in the absence of documented angiographic stent patency.

Abrupt Closure = Occurrence of new reduced flow (TIMI 0 or 1) within the target vessel that persisted and required rescue by a non-assigned treatment strategy or resulted in myocardial infarction or death.

Subacute Closure = Abrupt closure that occurred after the index procedure was completed (and the patient left the catheterization laboratory) and before the 30-day follow-up endpoint.

CVA = Sudden onset of vertigo, numbness, aphasia, or dysarthria due to vascular lesions of the brain such as hemorrhage, embolism, thrombosis, or rupturing aneurysm, that persisted >24 hours.

Bleeding Complications = Transfusions of blood products due to blood loss resulting from the percutaneous revascularization procedure.

Vascular Complications = Hematoma (>5 cm for BeStent 2 patients and >4 cm for PS patients), false aneurysm, AV fistula, retroperitoneal bleed, peripheral ischemia/nerve injury, procedure related transfusion or vascular surgical repair.

**Due to the difference in definition for hematoma between the BEST and BeStent 2 OTW trials, it was confirmed that none of the vascular complications in either trial involved a hemotoma.

Table 1.4. Major Adverse Events In-Hospital and Out-of-Hospital (to 30 days). Medtronic AVE BeStent™ 2 OTW Registry (N=227)

	BeStent™ 2 (N=227 Patients, N=227 Lesions)		PS® (N=327 Patients, N=330 Lesions)	
In-Hospital Complications	**Number**	**%**	**Number**	**%**
MACE (Death, MI, Emergent CABG, TVR)	5	2.2%	9	2.8%
Death	0	0.0%	0	0.0%
Myocardial Infarction (Q or Non-Q)	3	1.3%	8	2.4%
Q Wave MI	1	0.4%	2	0.6%
Non-Q Wave MI	2	0.9%	6	1.8%
Emergent CABG	1	0.4%	2	0.6%
Target Lesion Revascularization	1	0.4%	4	1.2%
TL-CABG	1	0.4%	2	0.6%
TL-PTCA	0	0.0%	2	0.6%
Target Vessel Revascularization (not involving the TL)	1	0.4%	0	0.0%
TV/non-TL-CABG	0	0.0%	0	0.0%
TV/non-TL-PTCA	1	0.4%	0	0.0%
Stent Thrombosis	0	0.0%	2	0.6%
Abrupt Closure	1	0.4%	4	1.2%
Subacute Closure	0	0.0%	2	0.6%
CVA	0	0.0%	2	0.6%
Bleeding Complications	3	1.3%	2	0.6%
Vascular Complications	1	0.4%	15	4.6%
Out-of-Hospital Complications (to 30 days)	**Number**	**%**	**Number**	**%**
MACE (Death, MI, Emergent CABG, TVR)	3	1.3%	4	1.2%
Death	2	0.9%	3	0.9%
Myocardial Infarction (Q or Non-Q)	0	0.0%	1	0.3%
Q Wave MI	0	0.0%	1	0.3%
Non-Q Wave MI	0	0.0%	0	0.0%
Emergent CABG	0	0.0%	0	0.0%
Target Lesion Revascularization	0	0.0%	1	0.3%
TL-CABG	0	0.0%	0	0.0%
TL-PTCA	0	0.0%	1	0.3%
Target Vessel Revascularization (not involving the TL)	1	0.4%	0	0.0%
TV/non-TL-CABG	0	0.0%	0	0.0%
TV/non-TL-PTCA	1	0.4%	0	0.0%
Stent Thrombosis (to 30 days)	2	0.9%	3	0.9%
Subacute Closure (to 30 days)	0	0.0%	0	0.0%
CVA	0	0.0%	1	0.3%
Bleeding Complications	1	0.4%	0	0.0%
Vascular Complications	0	0.0%	2	0.6%

Target Vessel Revascularization not involving the Target Lesion was defined as target vessel revascularization at a site other than the target site with or without concomitant target lesion revascularization.

Table 1.4. (Continued) Major Adverse Events In-Hospital and Out-of-Hospital (to 30 days). Medtronic AVE BeStent™ 2 Revascularization Trial (N=227)

	BeStent™ 2 (N=227 Patients, N=227 Lesions)		PS® (N=327 Patients, N=330 Lesions)	
Combined In and Out-of-Hospital Complications (to 30 days)	Number	%	Number	%
MACE (Death, MI, Emergent CABG, TVR)	8	3.5%	13	4.0%
Death	2	0.9%	3	0.9%
Myocardial Infarction (Q or Non-Q)	3	1.3%	9	2.8%
Q Wave MI	1	0.4%	3	0.9%
Non-Q Wave MI	2	0.9%	6	1.8%
Emergent CABG	1	0.4%	2	0.6%
Target Lesion Revascularization	1	0.4%	5	1.5%
TL-CABG	1	0.4%	2	0.6%
TL-PTCA	0	0.0%	3	0.9%
Target Vessel Revascularization (not involving the TL)	2	0.9%	0	0.0%
TV/non-TL-CABG	0	0.0%	0	0.0%
TV/non-TL-PTCA	2	0.9%	0	0.0%
Stent Thrombosis (to 30 days)	2	0.9%	5	1.5%
Abrupt Closure	1	0.4%	4	1.2%
Subacute Closure (to 30 days)	0	0.0%	2	0.6%
CVA	0	0.0%	3	0.9%
Bleeding Complications	4	1.8%	2	0.6%
Vascular Complications	1	0.4%	16	4.9%

Target Vessel Revascularization not involving the Target Lesion was defined as target vessel revascularization at a site other than the target site with or without concomitant target lesion revascularization.

2.0 BeStent™ (BEST) Trial

Title: BEST. An Evaluation of the Medtronic Model 6326 BeStent™ Coronary Stent System.

Conclusions: The acute and 180-day angiographic and clinical results demonstrated that the BeStent™ was not significantly different from the Palmaz-Schatz® (PS®) Stent with respect to procedural success, defined as the attainment of a <50% residual stenosis (by QCA or visual estimate) and no in-hospital major adverse cardiac (MACE) events (defined as death, Q wave or non-Q wave MI, target vessel revascularization, or emergent CABG), the 180-day incidence of MACE, and the in-stent restenosis rate (defined as >50% in-stent diameter stenosis at the follow-up angiogram). Procedure success was 95.4% (310/325) for the BeStent™ arm and 96.3% (315/327) for the PS® arm (95% C.I. of difference [-4.0%, 2.1%]). The 180-day cumulative incidence of MACE was 9.2% (30/325) for the BeStent™ arm and 12.5% (41/327) for the PS® arm (95% C.I. of difference –3.3% [-8.1%, 1.5%]). The in-stent restenosis rate in the angiographic subset was 16.5% (17/103) for the BeStent™ arm and 26.5% (27/102) for the PS® arm (95% C.I. of difference [-21.1%, 1.2%]). The Kaplan-Meier estimate of freedom from target vessel failure at 180 days was 90.5% for the BeStent™ arm and 87.0% for the PS® arm.

Investigative sites: 32 sites within the United States contributed patients to the randomized cohort.

Purpose: To show equivalence in late-term clinical outcomes between the Medtronic Model 6326 BeStent™ Coronary Stent and the Palmaz-Schatz® Stent (PS®) in *de novo* and restenotic native coronary lesions. This report contains 180-day outcomes.

Design: This was a randomized, multi-center comparison of the Medtronic Model 6326 BeStent™ Coronary Stent to the PS® Stent in *de novo* and restenotic native coronary artery lesions, preceded by a non-randomized roll-in phase.

Demography: The randomized trial was composed of 652 patients, 325 in the BeStent™ Coronary Stent arm and 327 in the PS® Stent arm. Seventy-six roll-in patients were enrolled. Baseline demographics and clinical characteristics for the randomized trial showed that the mean age was 60.4 years, 67.1% (218/325) male participation, and 19.4% (63/324) with a history of diabetes mellitus in the BeStent™ arm, and 61.3 years, 68.8% (225/327) male participation, and 24.2% (79/327) with a history of diabetes mellitus in the PS® arm. Baseline demographics and clinical characteristics for the roll-in phase revealed a mean age of 60.9 years, 69.7% (53/76) male participation (which is indicative of coronary disease), and 18.4% (14/76) with a history of diabetes mellitus. Patient screening logs were maintained and reviewed to ensure non-bias selection.

Method: Baseline and follow-up clinical data were collected by clinical coordinators at the clinical sites on standardized case report forms. Clinical follow-up was mandated at 1, 6, and 12 months post-procedure for all patients. Clinical follow-up at 180 days is available for 76.9% (250/325) of patients in the BeStent™ arm and for 78.9% (258/327) of patients in the PS® arm. Baseline quantitative coronary angiography was performed pre-procedure, following device deployment, and after final treatment. The pre-specified primary endpoint for this trial was a combined clinical endpoint of TVF (target vessel revascularization, MI, and death) at 6 months. The secondary endpoints were acute success, acute ischemic, hemorrhagic, and vascular complications, MACE at 30 days, and binary angiographic restenosis (defined as >50% diameter stenosis) and loss index at 6 months for patients in the angiographic subset of the randomized trial (the first 302 patients randomized), and procedural minimal luminal diameter. An independent Clinical Events Committee, blinded to treatment assignment, adjudicated all of the major clinical endpoints. All endpoints were analyzed on an intent-to-treat basis.

Procedure Success: Procedure success was defined as the attainment of a <50% residual stenosis using any percutaneous method and no in-hospital MACE. If no in-stent measurements were available, in-lesion measurements were used, and if no QCA was available, visual estimates were used.

Lesion Success: Lesion success was defined as the attainment of <50% residual stenosis using any percutaneous method. If no in-stent measurements were available, in-lesion measurements were used, and if no QCA was available, visual estimates were used.

Device Success: Device success was defined as the attainment of <50% residual stenosis using only the assigned device. If no in-stent measurements were available, in-lesion measurements were used, and if no QCA was available, visual estimates were used.

Table 2.1. Baseline Demographics and Clinical Characteristics
All Randomized Patients Treated (N=652 Patients, 657 Lesions)

Patient Characteristic	BeStent™ (N=325 Patients, N=327 Lesions)	PS® (N=327 Patients, N=330 Lesions)	All Randomized (N=652 Patients, N=657 Lesions)	Difference [95% C.I.]
Age (years)				
Mean±SD (N)	60.4±11.3 (325)	61.3±11.2 (327)	60.8±11.3 (652)	-0.8 [-2.6,0.9]
Range (min,max)	(32.0,90.0)	(24.0,91.0)	(24.0,91.0)	
Number of men	67.1% (218 / 325)	68.8% (225 / 327)	67.9% (443 / 652)	-1.7% [-8.9%,5.4%]
Current cigarette use	29.1% (94 / 323)	24.1% (78 / 323)	26.6% (172 / 646)	5.0% [-1.9%,11.8%]
Diabetes Mellitus	19.4% (63 / 324)	24.2% (79 / 327)	21.8% (142 / 651)	-4.7% [-11.0%,1.6%]
Hypertension requiring treatment	54.6% (177 / 324)	56.7% (185 / 326)	55.7% (362 / 650)	-2.1% [-9.8%,5.5%]
Dyslipidemia requiring treatment	40.6% (131 / 323)	40.9% (132 / 323)	40.7% (263 / 646)	-0.3% [-7.9%,7.3%]
Prior CABG	4.9% (16 / 325)	7.3% (24 / 327)	6.1% (40 / 652)	-2.4% [-6.1%,1.3%]
Prior MI	34.8% (112 / 322)	39.4% (128 / 325)	37.1% (240 / 647)	-4.6% [-12.0%,2.8%]
Revascularization for angina or MI	90.5% (294 / 325)	93.0% (304 / 327)	91.7% (598 / 652)	-2.5% [-6.7%,1.7%]
Stable exertional angina	4.6% (15 / 325)	10.1% (33 / 327)	7.4% (48 / 652)	-5.5% [-9.5%,-1.5%]
CCS* III or IV	63.6% (204 / 321)	68.4% (221 / 323)	66.0% (425 / 644)	-4.9% [-12.2%,2.4%]
Unstable angina	74.2% (241 / 325)	68.8% (225 / 327)	71.5% (466 / 652)	5.3% [-1.6%,12.3%]
Cresc. exertional angina	40.9% (133 / 325)	34.9% (114 / 327)	37.9% (247 / 652)	6.1% [-1.4%,13.5%]
Rest angina	33.2% (108 / 325)	33.9% (111 / 327)	33.6% (219 / 652)	-0.7% [-8.0%,6.5%]
Pain only with MI	11.4% (37 / 325)	13.8% (45 / 327)	12.6% (82 / 652)	-2.4% [-7.5%,2.7%]
Number of Diseased, Native, Major Epicardial Coronary Arteries				
Single	68.9% (224 / 325)	68.2% (223 / 327)	68.6% (447 / 652)	0.7% [-6.4%,7.9%]
Double	22.5% (73 / 325)	23.5% (77 / 327)	23.0% (150 / 652)	-1.1% [-7.5%,5.4%]
Triple	8.6% (28 / 325)	8.3% (27 / 327)	8.4% (55 / 652)	0.4% [-3.9%,4.6%]
Ejection Fraction (%)				
Mean±SD (N)	54.4%±0.1 (302)	53.9%±10.8% (307)	54.1%±10.3% (609)	0.5% [-1.1%,2.2%]
Range (min,max)	(30.0%,86.0%)	(21.0%,80.0%)	(21.0%,86.0%)	

Numbers are % (counts/ sample size) or Mean ± SD. CI = Confidence Interval
Difference = BE – PS® SE = $\text{sqrt}(p_1*q_1/n_1+p_2*q_2/n_2)$ CI = Diff±1.96*SE
*CCS = Canadian Cardiovascular Society angina class.

Table 2.2. Baseline Lesion Characteristics
All Randomized Lesions Treated (652 Patients, 657 Lesions)

Lesion Characteristic	BeStent™ (N=325 Patients, N=327 Lesions)	PS® (N=327 Patients, N=330 Lesions)	All Randomized (N=652 Patients, N=657 Lesions)	Difference [95% C.I.]
Pre-Procedure Reference Vessel Diameter (RVD, in mm)				
Mean±SD (N)	3.00±0.47 (321)	3.02±0.53 (324)	3.01±0.50 (645)	-0.03 [-0.10,0.05]
Range (min,max)	(1.91,4.87)	(1.61,5.12)	(1.61,5.12)	
Pre-Procedure Minimal Lumen Diameter (MLD, in mm)				
Mean±SD (N)	1.03±0.45 (321)	1.03±0.45 (324)	1.03±0.45 (645)	0.00 [-0.07,0.07]
Range (min,max)	(0.00,2.76)	(0.00,3.22)	(0.00,3.22)	
Pre-Procedure Percent Diameter Stenosis (% DS)				
Mean±SD (N)	65.5%±13.7% (321)	65.4%±14.6% (324)	65.5%±14.1% (645)	0.0% [-2.2%,2.2%]
Range (min,max)	(18.3%,100.0%)	(21.9%,100.0%)	(18.3%,100.0%)	
Lesion Length (mm)				
Mean±SD (N)	11.84±5.71 (320)	11.90±5.01 (317)	11.87±5.37 (637)	-0.06 [-0.90,0.78]
Range (min,max)	(2.90,60.00)	(2.52,38.02)	(2.52,60.00)	
Target Lesion Vessel				
LAD	42.9% (138 / 322)	35.8% (116 / 324)	39.3% (254 / 646)	7.1% [-0.5%,14.6%]
Circumflex (LCX)	21.4% (69 / 322)	22.8% (74 / 324)	22.1% (143 / 646)	-1.4% [-7.8%,5.0%]
RCA	35.4% (114 / 322)	41.0% (133 / 324)	38.2% (247 / 646)	-5.6% [-13.1%,1.8%]
LMCA	0.3% (1 / 322)	0.3% (1 / 324)	0.3% (2 / 646)	0.0% [-0.9%,0.9%]
SVG	0.0% (0 / 322)	0.0% (0 / 324)	0.0% (0 / 646)	0.0% [—,—]
Restenotic Lesion	2.8% (9 / 326)	3.3% (11 / 330)	3.0% (20 / 656)	-0.6% [-3.2%,2.1%]
Calcification (moderate-severe)	9.3% (30 / 321)	9.9% (32 / 323)	9.6% (62 / 644)	-0.6% [-5.1%,4.0%]
Thrombus	0.6% (2 / 321)	2.8% (9 / 322)	1.7% (11 / 643)	-2.2% [-4.2%,-0.2%]
Eccentric Lesion	30.8% (99 / 321)	32.6% (105 / 322)	31.7% (204 / 643)	-1.8% [-9.0%,5.4%]
Angulation >45°	8.4% (27 / 321)	6.5% (21 / 321)	7.5% (48 / 642)	1.9% [-2.2%,5.9%]
ACC/AHA* Lesion Class				
A	14.6% (47 / 321)	13.6% (44 / 324)	14.1% (91 / 645)	1.1% [-4.3%,6.4%]
B1	34.9% (112 / 321)	30.2% (98 / 324)	32.6% (210 / 645)	4.6% [-2.6%,11.9%]
B2 (or higher grade B)	43.6% (140 / 321)	47.8% (156 / 324)	45.7% (295 / 645)	-4.2% [-11.9%,3.5%]
C	6.9% (22 / 321)	8.3% (27 / 324)	7.6% (49 / 645)	-1.5% [-5.6%,2.6%]

Numbers are % (counts/ sample size) or Mean ± SD. CI = Confidence Interval

Difference = BE–PS® SE = $\text{sqrt}(p_1*q_1/n_1+p_2*q_2/n_2)$ CI = Diff±1.96*SE

*American College of Cardiology/American Heart Association Lesion Class.

All variables are from assessment by the Angiographic Core Laboratory except Restenotic lesion which is derived from Case Report Forms.

Table 2.3. Principal Effectiveness and Safety Results
All Randomized Patients Treated (N=652 Patients, 657 Lesions)

Efficacy Measures	BeStent™ (N=325 Patients, N=327 Lesions)	PBS (N=327 Patients, N=330 Lesions)	All Randomized (N=652 Patients, N=657 Lesions)	Relative Risk [95% C.I.]	Difference [95% C.I.]
Lesion Success	98.7% (323 / 327)	99.0% (326 / 330)	98.2% (652 / 657)	1.01 [1.00,1.02]	0.0% [-0.4%,2.2%]
Device Success	93.2% (309 / 329)	93.6% (307 / 327)	93.6% (616 / 652)	0.99 [0.96,1.03]	-0.7% [-4.4%,3.1%]
Procedure Success	96.4% (313 / 325)	98.3% (315 / 327)	96.9% (625 / 652)	0.99 [0.96,1.02]	-0.9% [-4.0%,2.1%]
Post-Procedure In-Stent Minimal Lumen Diameter (MLD, in mm)					
Mean±SD (N)	2.82±0.40 (319)	2.80±0.41 (321)	2.81±0.41 (640)	N/A	0.02 [-0.06,0.09]
Range (min,max)	(1.82,4.49)	(1.61,4.31)	(1.61,4.49)		
Post-Procedure In-Stent Percent Diameter Stenosis (% DS)					
Mean±SD (N)	6.9%±9.7% (319)	8.0%±10.5% (321)	7.5%±10.1% (640)	N/A	-1.0% [-2.8%,0.8%]
Range (min,max)	(-30.7%,42.8%)	(-29.3%,38.8%)	(-30.7%,42.8%)		
180-day Follow-up In-Stent Minimal Lumen Diameter (MLD, in mm)					
Mean±SD (N)	2.06±0.78 (183)	1.87±0.72 (162)	1.98±0.75 (206)	N/A	0.18 [-0.03,0.39]
Range (min,max)	(0.00,3.52)	(0.00,3.73)	(0.00,3.73)		
180-day Follow-up In-Stent Percent Diameter Stenosis (% DS)					
Mean±SD (N)	32.9%±22.9% (183)	38.1%±21.9% (162)	35.5%±22.3% (206)	N/A	-5.2% [-11.3%,0.9%]
Range (min,max)	(-12.9%,100.0%)	(-7.1%,100.0%)	(-12.9%,100.0%)		
180-day Follow-up In-Stent Binary Restenosis Rate	16.5% (17 / 103)	26.5% (27 / 102)	21.5% (44 / 205)	0.62 [0.37,1.06]	-10.0% [-21.1%,1.2%]
Post-Procedure In-Lesion Minimal Lumen Diameter (MLD, in mm)					
Mean±SD (N)	2.51±0.48 (322)	2.50±0.51 (323)	2.50±0.49 (645)	N/A	0.01 [-0.07,0.09]
Range (min,max)	(1.31,4.18)	(0.00,4.15)	(0.00,4.18)		
Post-Procedure In-Lesion Percent Diameter Stenosis (% DS)					
Mean±SD (N)	17.7%±11.1% (322)	18.3%±12.0% (323)	18.0%±11.5% (645)	N/A	-0.6% [-2.4%,1.2%]
Range (min,max)	(-31.9%,51.1%)	(-18.9%,100.0%)	(-31.9%,100.0%)		
180-day Follow-up In-Lesion Minimal Lumen Diameter (MLD, in mm)					
Mean±SD (N)	1.66±0.71 (183)	1.76±0.68 (162)	1.82±0.69 (206)	N/A	0.13 [-0.06,0.32]
Range (min,max)	(0.00,3.18)	(0.00,3.34)	(0.00,3.34)		
180-day Follow-up In-Lesion Percent Diameter Stenosis (% DS)					
Mean±SD (N)	38.2%±21.0% (103)	41.8%±19.7% (102)	40.0%±20.4% (205)	N/A	-3.8% [-8.4%,1.8%]
Range (min,max)	(-6.0%,100.0%)	(10.4%,100.0%)	(-6.0%,100.0%)		
180-day Follow-up In-Lesion Binary Restenosis Rate	21.4% (22 / 103)	27.5% (28 / 102)	24.4% (50 / 205)	0.78 [0.48,1.28]	-6.1% [-17.8%,5.6%]
TLR-free to 180 days*	95.9%	90.8%	93.3%	1.06 [1.01,1.11]	5.1% [0.8%,9.4%]
TVR-free to 180 days*	94.5%	89.4%	92.0%	1.06 [1.00,1.11]	5.1% [0.4%,9.8%]
TVF-free to 180 days*	90.3%	87.0%	88.7%	1.04 [0.98,1.11]	3.3% [-2.0%,8.1%]
Safety Measures and Other Clinical Events					
In-Hospital MACE	4.3% (14 / 328)	2.8% (9 / 327)	3.5% (23 / 652)	1.57 [0.68,3.64]	1.5% [-1.3%,4.4%]
Out-of-Hospital MACE to 180 days	4.9% (16 / 325)	10.1% (33 / 327)	7.5% (49 / 652)	0.48 [0.28,0.86]	-5.2% [-9.2%,-1.1%]
Combined In- and Out-of-Hospital MACE to 180 days	9.2% (30 / 325)	12.5% (41 / 327)	10.9% (71 / 652)	0.74 [0.47,1.16]	-3.3% [-8.1%,1.5%]
Stent Thrombosis to 30 days	0.6% (2 / 325)	1.8% (6 / 327)	1.2% (8 / 652)	0.60 [0.15,2.47]	-0.9% [-2.9%,1.1%]
Abrupt Closure	0.0% (0 / 325)	1.2% (4 / 327)	0.6% (4 / 652)	0.00 [—,—]	-1.2% [-2.4%,0.0%]
Subacute Closure to 30 days	0.6% (2 / 325)	0.0% (2 / 327)	0.0% (4 / 652)	1.01 [0.14,7.11]	0.0% [-1.2%,1.2%]
CVA to 180 days	0.9% (3 / 325)	0.0% (0 / 327)	0.5% (3 / 652)	1.01 [0.20,4.95]	0.0% [-1.5%,1.5%]
Bleeding Complications to 180 days	1.8% (6 / 325)	0.6% (2 / 327)	1.2% (8 / 652)	3.02 [0.60,13.71]	1.2% [-0.5%,2.9%]
Vascular Complications to 180 days	6.2% (20 / 325)	4.9% (16 / 327)	5.5% (36 / 652)	1.26 [0.66,2.38]	1.3% [-2.2%,4.8%]

Numbers are % (counts/sample size) or Mean ± SD. CI = Confidence Interval

Relative Risk = BE/PS* SE = $\text{sqrt}\{(1-p_1)/n_{11}+(1-p_2)/n_{21}\}$ CI = $RR*\exp(\pm 1.96*SE)$

Difference = BE–PS* SE = $\text{sqrt}(p_1*q_1/n_1+p_2*q_2/n_2)$ CI = Diff±1.96*SE

N/A = Not applicable.

Lesion Success = Attainment of <50% residual stenosis using any percutaneous method. If no in-stent measurements were available, in-lesion measurements were used, and if no QCA was available, visual estimates were used.

Device Success = Attainment of <50% residual stenosis using only the assigned device. If no in-stent measurements were available, in-lesion measurements were used, and if no QCA was available, visual estimates were used.

Procedure Success = Attainment of a <50% residual stenosis using any percutaneous method and no in-hospital MACE. If no in-stent measurements were available, in-lesion measurements were used, and if no QCA was available, visual estimates were used.

TLR-Free = No target lesion revascularization.

TVR-Free = No target vessel revascularization.

TVF-Free = No death, MI, or target vessel revascularization.

MACE= Death, Q wave or non-Q wave MI, emergent CABG, or target vessel revascularization.

In-Hospital MACE = Death, Q wave or non-Q wave MI, emergent CABG, or target vessel revascularization prior to discharge as determined by the independent Clinical Events Committee.

Out-of-Hospital MACE = Death, Q wave or non-Q wave MI, emergent CABG, or target vessel revascularization from hospital discharge through the 180-day contact, as determined by the independent Clinical Events Committee.

Stent Thrombosis = Angiographic thrombus or subacute closure within the stented vessel at the time of the clinically driven angiographic restudy for documented ischemia. Any death not attributed to a non-cardiac cause within the first 30 days was considered a surrogate for stent thrombosis in the absence of documented angiographic stent patency.

Abrupt Closure = Occurrence of new reduced flow (TIMI 0 or 1) within the target vessel that persisted and required rescue by a non-assigned treatment strategy or resulted in myocardial infarction or death.

Subacute Closure = Abrupt closure that occurred after the index procedure was completed (and the patient left the catheterization laboratory) and before the 30-day follow-up endpoint.

CVA = Acute neurological deficits due to vascular lesions of the brain such as hemorrhage, embolism, thrombosis, or rupturing aneurysm that persisted >24 hours.

Bleeding Complications = Transfusions of blood products due to blood loss resulting from the percutaneous revascularization procedure.

Vascular Complications = Hematoma >4 cm, false aneurysm, AV fistula, retroperitoneal bleed, peripheral ischemia/nerve injury, procedure related transfusion or vascular surgical repair.

*Survival estimates by Kaplan-Meier method; Standard Error estimates by Peto formula.

Table 2.4. Major Adverse Events – In-Hospital vs. Out-of-Hospital (to 180 days)
All Randomized Patients Treated (N=652 Patients, 657 Lesions)

	BeStent™ (N=325 Patients, N=327 Lesions)		PS® (N=327 Patients, N=330 Lesions)		All Randomized (N=652 Patients, N=657 Lesions)		[95% C.I.]
In-Hospital Complications	Number	%	Number	%	Number	%	
MACE (Death, MI, Emergent CABG, TVR)	14	4.3%	9	2.8%	23	3.5%	1.6% [-1.3%,4.4%]
Death	0	0.0%	0	0.0%	0	0.0%	0.0% [—,—]
Myocardial Infarction (Q or Non-Q)	12	3.7%	8	2.4%	20	3.1%	1.2% [-1.4%,3.9%]
Q Wave MI	4	1.2%	2	0.6%	6	0.9%	0.6% [-0.8%,2.1%]
Non-Q Wave MI	8	2.5%	6	1.8%	14	2.1%	0.6% [-1.6%,2.9%]
Emergent CABG	3	0.9%	2	0.6%	5	0.8%	0.3% [-1.0%,1.7%]
Target Lesion Revascularization	4	1.2%	4	1.2%	8	1.2%	0.0% [-1.7%,1.7%]
TL-CABG	3	0.9%	2	0.6%	5	0.8%	0.3% [-1.0%,1.7%]
TL-PTCA	1	0.3%	2	0.6%	3	0.5%	-0.3% [-1.3%,0.7%]
Target Vessel Revascularization (not involving the TL)	1	0.3%	0	0.0%	1	0.2%	0.3% [-0.3%,0.9%]
TV-CABG	0	0.0%	0	0.0%	0	0.0%	0.0% [—,—]
TV-PTCA	1	0.3%	0	0.0%	1	0.2%	0.3% [-0.3%,0.9%]
Stent Thrombosis	2	0.6%	2	0.6%	4	0.6%	0.0% [-1.2%,1.2%]
Abrupt Closure	0	0.0%	4	1.2%	4	0.6%	-1.2% [-2.4%,0.0%]
Subacute Closure	2	0.6%	2	0.6%	4	0.6%	0.0% [-1.2%,1.2%]
CVA	1	0.3%	2	0.6%	3	0.5%	-0.3% [-1.3%,0.7%]
Bleeding Complications	6	1.8%	2	0.6%	8	1.2%	1.2% [-0.5%,2.9%]
Vascular Complications	18	5.5%	15	4.5%	33	5.1%	1.0% [-2.4%,4.3%]
Out-of-Hospital Complications (to 180 days)	Number	%	Number	%	Number	%	
MACE (Death, MI, Emergent CABG, TVR)	16	4.9%	33	10.1%	49	7.5%	-5.2% [-9.2%,-1.1%]
Death	2	0.6%	3	0.9%	5	0.8%	-0.3% [-1.6%,1.0%]
Myocardial Infarction (Q or Non-Q)	1	0.3%	4	1.2%	5	0.8%	-0.9% [-2.3%,0.4%]
Q Wave MI	1	0.3%	3	0.9%	4	0.6%	-0.6% [-1.8%,0.6%]
Non-Q Wave MI	0	0.0%	1	0.3%	1	0.2%	-0.3% [-0.9%,0.3%]
Emergent CABG	0	0.0%	0	0.0%	0	0.0%	0.0% [—,—]
Target Lesion Revascularization	9	2.8%	25	7.6%	34	5.2%	-4.9% [-8.3%,-1.5%]
TL-CABG	1	0.3%	9	2.8%	10	1.5%	-2.4% [-4.3%,-0.6%]
TL-PTCA	9	2.8%	17	5.2%	26	4.0%	-2.4% [-5.4%,0.6%]
Target Vessel Revascularization (not involving the TL)	5	1.5%	9	2.8%	14	2.1%	-1.2% [-3.4%,1.0%]
TV-CABG	1	0.3%	2	0.6%	3	0.5%	-0.3% [-1.3%,0.7%]
TV-PTCA	4	1.2%	7	2.1%	11	1.7%	-0.9% [-2.9%,1.1%]
Stent Thrombosis (to 30 days)	1	0.3%	3	0.9%	4	0.6%	-0.6% [-1.8%,0.6%]
Abrupt Closure	0	0.0%	0	0.0%	0	0.0%	0.0% [—,—]
Subacute Closure (to 30 days)	0	0.0%	0	0.0%	0	0.0%	0.0% [—,—]
CVA	2	0.6%	1	0.3%	3	0.5%	0.3% [-0.7%,1.3%]
Bleeding Complications	0	0.0%	0	0.0%	0	0.0%	0.0% [—,—]
Vascular Complications	2	0.6%	2	0.6%	4	0.6%	0.0% [-1.2%,1.2%]
Combined In and Out-of-Hospital Complications (to 180 days)	Number	%	Number	%	Number	%	
MACE (Death, MI, Emergent CABG, TVR)	30	9.2%	41	12.5%	71	10.9%	-3.3% [-8.1%,1.5%]
Death	2	0.6%	3	0.9%	5	0.8%	-0.3% [-1.6%,1.0%]
Myocardial Infarction (Q or Non-Q)	13	4.0%	12	3.7%	25	3.8%	0.3% [-2.6%,3.3%]
Q Wave MI	5	1.5%	5	1.5%	10	1.5%	0.0% [-1.9%,1.9%]
Non-Q Wave MI	8	2.5%	7	2.1%	15	2.3%	0.3% [-2.0%,2.6%]
Emergent CABG	3	0.9%	2	0.6%	5	0.8%	0.3% [-1.0%,1.7%]
Target Lesion Revascularization	13	4.0%	29	8.9%	42	6.4%	-4.9% [-8.8%,-1.1%]
TL-CABG	4	1.2%	11	3.4%	15	2.3%	-2.1% [-4.4%,0.2%]
TL-PTCA	10	3.1%	19	5.8%	29	4.4%	-2.7% [-5.9%,0.4%]
Target Vessel Revascularization (not involving the TL)	6	1.8%	9	2.8%	15	2.3%	-0.9% [-3.2%,1.4%]
TV-CABG	1	0.3%	2	0.6%	3	0.5%	-0.3% [-1.3%,0.7%]
TV-PTCA	5	1.5%	7	2.1%	12	1.8%	-0.6% [-2.7%,1.5%]
Stent Thrombosis (to 30 days)	3	0.9%	5	1.5%	8	1.2%	-0.6% [-2.3%,1.1%]
Abrupt Closure	0	0.0%	4	1.2%	4	0.6%	-1.2% [-2.4%,0.0%]
Subacute Closure (to 30 days)	2	0.6%	2	0.6%	4	0.6%	0.0% [-1.2%,1.2%]
CVA	3	0.9%	3	0.9%	6	0.9%	0.0% [-1.5%,1.5%]
Bleeding Complications	6	1.8%	2	0.6%	8	1.2%	1.2% [-0.5%,2.9%]
Vascular Complications	20	6.2%	16	4.9%	36	5.5%	1.3% [-2.2%,4.8%]

Target Vessel Revascularization not involving the Target Lesion was defined as target vessel revascularization at a site other than the target site with or without concomitant target lesion revascularization.

XI. Conclusions Drawn from Studies

Discussion of Valid Scientific Evidence

The *in vitro* and *in vivo* nonclinical laboratory studies, together with the BeStent™ 2 OTW clinical investigation, and the BeStent™ long term clinical data provides valid scientific evidence and reasonable assurance that the BeStent™ 2 OTW and RX Coronary Stent Delivery Systems are safe and effective.

Discussion of Data on Safety and Effectiveness

The safety and effectiveness of the BeStent™ 2 OTW and RX devices has been demonstrated by the BeStent™ 2 OTW acute procedure success and Major Adverse Cardiac Events (defined as death, MI, emergent CABG, or target vessel revascularization) at 30 days. This report presents data for 227 subjects enrolled at eighteen (18) clinical investigational sites within the United States and three (3) Middle East sites. In addition, the BEST trial which enrolled 652 randomized patients at 32 investigative centers in the United States provides the additional long-term data, Major Adverse Cardiac Events at 6 months to further support the safety and effectiveness of the BeStent™ 2 OTW and RX devices.

Risk/Benefit Analysis

The clinical investigation results demonstrate that the BeStent™ 2 OTW and RX devices, when used in the treatment of subjects experiencing symptomatic ischemic heart disease due to single de novo lesions (no greater than 30 mm in length) in native coronary arteries with reference vessel diameters ranging from 3.0 mm to 4.0 mm, does not pose any additional risk to the patient population treated.

The *in vitro* and *in vivo* pre-clinical laboratory studies, together with the clinical investigation, provides valid scientific evidence and reasonable assurance that the BeStent™ 2 with Discrete Technology™ OTW and RX Coronary Stent Delivery Systems are safe and effective.

XII. Panel 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 Device Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. CDRH Decision

CDRH issued an approval order on October 16, 2000. The applicant's manufacturing facility was inspected and found to be in complicance with the device Quality System Regulation.

XIV. Approval Specifications

Directions for Use: See device labeling

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

Postapproval Requirements and Restrictions: See approval order