

Summary of Safety and Effectiveness Data

I. GENERAL INFORMATION

Device Generic Name: Drug-Eluting Coronary Stent System (NIQ)

Device Trade Name: TAXUS[®] Liberté[®] Atom[™] Paclitaxel-Eluting Coronary Stent System (Monorail and Over-the-Wire Delivery Systems), 2.25 x 8-32 mm

Applicant's Name and Address: Boston Scientific Corporation
One Boston Scientific Place
Natick, MA 01760-1537
USA

Premarket Approval (PMA)
Application Number: P060008/S008

Date of Panel Recommendation: None

Date of FDA Notice of Approval: May 21, 2009

The original PMA (P060008) was approved on October 10, 2008 and is indicated for improving luminal diameter for the treatment of de novo lesions ≤ 28 mm in length in native coronary arteries ≥ 2.5 to ≤ 4.00 mm in diameter. The SSED to support the indication is available on the CDRH website and is incorporated by reference here: <http://www.fda.gov/cdrh/pdf6/p060008b.pdf>. This PMA supplement P060008/S008 was submitted to support expansion of the indications of the product, specifically, for improving luminal diameter for the treatment of de novo lesions in native coronary arteries ≥ 2.25 to ≤ 4.00 mm in diameter in lesions ≤ 28 mm in length.

II. INDICATIONS FOR USE

The TAXUS Liberté Paclitaxel-Eluting Coronary Stent System (Monorail and Over-the-Wire Systems) is indicated for improving luminal diameter for the treatment of de novo lesions in native coronary arteries ≥ 2.25 to ≤ 4.00 mm in diameter in lesions ≤ 28 mm in length.

III. CONTRAINDICATIONS

Use of the TAXUS Liberté Paclitaxel-Eluting Coronary Stent System is contraindicated in patients with:

- Known hypersensitivity to 316L stainless steel
- Known hypersensitivity to paclitaxel or structurally-related compounds.
- Known hypersensitivity to the polymer or its individual components.

Coronary Artery Stenting is contraindicated for use in:

- Patients who can not receive recommended anti-platelet and/or anticoagulant therapy.
- Patients judged to have a lesion that prevents complete inflation of an angioplasty balloon or proper placement of the stent or delivery device.

IV. WARNING AND PRECAUTIONS

The warnings and precautions can be found in the TAXUS Liberté Paclitaxel-Eluting Coronary Stent System Directions for Use (DFU).

V. DEVICE DESCRIPTION

The TAXUS Liberté Paclitaxel-Eluting Coronary Stent System is a device / drug combination product comprised of two regulated components: a device (Liberté Coronary Stent System) and a drug product (a formulation of paclitaxel contained in a polymer coating). The components and characteristics of the TAXUS Liberté Atom Paclitaxel-Eluting Coronary Stent System are identical to the small vessel model TAXUS Liberté Paclitaxel-Eluting Coronary Stent System approved in P060008. Please refer to the device description provided in the original SSED for additional details. The characteristics of the TAXUS Liberté Atom stent system are described in **Table 1**.

Table 1: TAXUS Liberté Stent System Product Description

	TAXUS Liberté Monorail® Stent Delivery System	TAXUS Liberté Over-the-Wire Stent Delivery System
Available Stent Lengths (mm)	8, 12, 16, 20, 24, 28, 32	
Available Stent Diameters (mm)	2.25	
Stent Material	A 316L surgical grade stainless steel Liberté® stent	
Drug Product	A conformal coating of a polymer carrier loaded with 1µg/mm ² paclitaxel in a slow release (SR)* formulation applied to the stent with a maximum nominal drug content of 155 µg on the largest stent (2.25 x 32 mm).	
Delivery System		
Working Length	140 cm	135 cm
Delivery System Y-Adapter Ports	Single access port to inflation lumen. Guidewire exit port is located approximately 25 cm from tip. Designed for guidewire ≤ 0.014"	Y-Connector (Side arm for access to balloon inflation/deflation lumen. Straight arm is continuous with shaft inner lumen). Designed for guidewire ≤ 0.014"
Stent Delivery	A balloon, nominally 0.4 mm longer than the stent, with two radiopaque markers.	
Balloon Inflation Pressure	Nominal Inflation Pressure: 9 ATM Rated Burst Inflation Pressure: 18 ATM	
Guide Catheter Inner Diameter	≥ 0.058"	≥ 0.066"
Catheter Shaft Outer Diameter	1.8F proximally and 2.7F distally	3.2F proximally, 2.7F distally

*Release rate is a function of weight/weight ratio of polymer and drug. (SR) is the formulation that was studied clinically and is used in the marketed product

VI. ALTERNATIVE PRACTICES OR PROCEDURES

Treatment of patients with coronary artery disease may include exercise, diet, drug therapy, percutaneous coronary interventions (such as angioplasty, and placement of bare metal stents, coated stents, and other drug eluting stents), and coronary artery bypass surgery (CABG).

VII. MARKETING HISTORY

The TAXUS Liberté Paclitaxel-Eluting Coronary Stent System 2.25 mm size is commercially available in the following countries:

- Albania
- Algeria
- Antigua/Barbuda
- Argentina
- Armenia
- Aruba
- Australia
- Austria
- Bahamas
- Bahrain
- Bangladesh
- Barbados
- Belarus
- Belgium
- Belize
- Bermuda
- Bolivia
- Bosnia
- Brazil
- Brunei
- Bulgaria
- Chile
- China
- Colombia
- Costa Rica
- Croatia
- Cyprus
- Czech Republic
- Denmark
- Djibouti
- Dominican Rep
- Dutch Antilles
- Ecuador
- Egypt
- El Salvador
- Estonia
- Finland
- France
- Georgia
- Germany
- Great Britain
- Greece
- Guatemala
- Guyana
- Haiti
- Honduras
- Hong Kong
- Hungary
- Iceland
- India
- Indonesia
- Iran
- Iraq
- Ireland
- Israel
- Italy
- Jamaica
- Jordan
- Kenya
- Korea
- Kuwait
- Latvia
- Lebanon
- Libya
- Liechtenstein
- Lithuania
- Luxembourg
- Macau
- Macedonia
- Malaysia
- Malta
- Martinique
- Mauritania
- Mauritius
- Mexico
- Moldavia
- Morocco
- Myanmar
- Nepal
- Netherlands
- New Zealand
- Nicaragua
- Norway
- Oman
- Pakistan
- Panama
- Paraguay
- Peru
- Philippines
- Poland
- Portugal
- Qatar
- Romania
- Russia
- Saudi Arabia
- Scotland
- Serbia/Montenegro
- Singapore
- Slovakia
- Slovenia
- South Africa
- Spain
- Sri Lanka
- Sudan
- Suriname
- Sweden
- Switzerland
- Syria
- Taiwan
- Thailand
- Trinidad/Tobago
- Tunisia
- Turkey
- United Arab Emirates
- Ukraine
- Uruguay
- Venezuela
- Vietnam
- West Bank Gaza Strip
- Yemen

As of April 2009, over 94,000 TAXUS Liberté 2.25 mm stents have been distributed outside the U.S. No products have been withdrawn from the market in any country for any reason.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Potential adverse events (in alphabetical order) which may be associated with the use of a coronary stent in native coronary arteries include but are not limited to:

- Abrupt stent closure
- Acute myocardial infarction
- Allergic reaction to anti-coagulant and/or antiplatelet therapy, contrast medium, or stent materials
- Angina
- Arrhythmias, including ventricular fibrillation (VF) and ventricular tachycardia (VT)
- Arteriovenous fistula
- Cardiac tamponade
- Cardiogenic shock/Pulmonary edema
- Coronary aneurysm
- Death
- Dissection
- Emboli, distal (air, tissue or thrombotic material or material from devices(s) used in the procedure)
- Heart failure
- Hematoma
- Hemorrhage, required transfusion
- Hypotension/Hypertension
- Infection, local or systemic
- Ischemia, myocardial
- Pain, at the access site
- Perforation or Rupture of coronary artery
- Pericardial effusion
- Pseudoaneurysm, femoral
- Renal Failure
- Respiratory Failure
- Restenosis of stented segment
- Stent embolization or migration
- Stent thrombosis/occlusion
- Stroke/cerebrovascular accident /TIA
- Total occlusion of coronary artery
- Vessel spasm
- Vessel trauma requiring surgical repair or reintervention

Potential adverse events not captured above, that may be unique to the paclitaxel drug coating:

- Allergic/immunologic reaction to drug (paclitaxel or structurally-related compounds) or the polymer stent coating (or its individual components)
- Alopecia
- Anemia
- Blood product transfusion
- Gastrointestinal symptoms
- Hematologic dyscrasia (including leukopenia, neutropenia, thrombocytopenia)
- Hepatic enzyme changes
- Histologic changes in vessel wall, including inflammation, cellular damage or necrosis
- Myalgia/Arthralgia
- Peripheral neuropathy

For the specific events that occurred in the clinical study, please see Section X.

IX. SUMMARY OF PRECLINICAL STUDIES

A series of non-clinical laboratory studies were performed – those related to the stent and the stent delivery system [i.e. the stent on either the Monorail (MR) or Over-The-Wire (OTW) stent delivery system (SDS)], the polymer substance [i.e., poly(styrene-b-isobutylene-b-styrene) (SIBS)], the drug substance (i.e., paclitaxel) and the finished combination product (i.e., TAXUS Liberté Paclitaxel-Eluting Coronary Stent).

A. Biocompatibility Studies

The biocompatibility testing information included in the original PMA submission (P060008, approved October 10, 2008) is directly applicable to this PMA supplement. Please refer to the original SSED for details regarding the biocompatibility studies.

Additional testing was conducted on SIBS coated Liberté stents to evaluate the stent and stent delivery system separately. These biocompatibility studies are summarized in **Table 2**.

Table 2: Biocompatibility Test Summary

Test Name	Test Description	Test Article and Results
Systemic Toxicity	ISO 10993-11: Systemic Toxicity (Acute)	Polymer-only coated stent: Pass (non-toxic)
	ISO 10993-11: 90-Day Chronic Toxicity (Rat, Subcutaneous Implant)	Polymer-only coated stent: Pass (non-toxic)
Pyrogenicity	ISO 10993-11: Systemic Toxicity (Material-Mediated Rabbit)	Polymer-only coated stent: Pass (non-pyrogenic)
Hemocompatibility	ISO 10993-4: Complement Activation C3a and SC5b-9 Assay	Polymer-only coated stent: Pass (Negative for C3a and SC5b-9 assays)

B. *In Vivo* Pharmacokinetics

The non-clinical chemistry information included in the original PMA submission (P060008, approved October 10, 2008) are directly applicable to this PMA Supplement; therefore, the information is not repeated herein.

C. *In Vitro* Engineering Testing

The in vitro engineering testing included in the original PMA submission (P060008, approved October 10, 2008) is directly applicable to this PMA Supplement. Therefore, only the testing information specific to the 2.25 mm diameter stent are summarized below in **Table 3**. "Pass" denotes that the test results met product specifications and/or the recommendation in the guidance documents.

Table 3: Stent and Delivery Catheter Engineering Testing

Test	Description of Test	Conclusion
Stent Dimensional and Functional Attributes		
Radial Stiffness and Radial Strength	Testing was conducted to determine the ability of the TAXUS Liberté stent to resist collapse under short term and long term loads.	Pass
Stent Delivery System Dimensional and Functional Attributes		
Delivery, Deployment and Retraction	The delivery, deployment and retraction of the TAXUS Liberté Stent System was assessed by testing guidewire movement at rated burst pressure. Testing demonstrated that the TAXUS Liberté stent system could be delivered to the target location, deployed, and retracted, thus met required product specifications.	Pass
Balloon Fatigue	TAXUS Liberté stent systems across the range of stent/balloon lengths and diameters were required to complete 10 pressurization cycles to Rated Burst Pressure (RBP). The results show statistically that, with 95% confidence, 90% of the catheters will not experience balloon, shaft, or proximal/distal seal loss of integrity at or below the maximum recommended rated balloon burst pressure.	Pass
Stent Securement for Unsheathed Stents	Testing was conducted to assess the forces required to displace a crimped TAXUS Liberté stent from the delivery systems (1) after tracking through a simulated tortuous artery model and then through a simulated lesion and (2) during non-coaxial withdrawal. All stent systems met specification.	Pass
Balloon Catheter Withdrawal Resistance	TAXUS Liberté is to have statistically lower withdrawal forces as compared to TAXUS Express ² when analyzed as a pooled population with 95% confidence.	Pass
Stent, System and Coating Durability Testing		
Accelerated Durability Testing	Overlapping stents in a curve were evaluated in an accelerated in vitro test of approximately 10 year equivalent (400 million cycles) real time and met visual requirements for coating integrity and strut damage.	Pass
Coating Durability	The coating durability of the TAXUS Liberté stent coating was assessed pre-expansion and post deployment beyond rated burst pressure. The test results demonstrate that the paclitaxel/SIBS coating displays good durability and coating integrity that will be maintained throughout the lifetime of the coated stent implant.	Pass

D. Coating Characterization Testing

The coating characterization information included in the original PMA submission (P060008, approved October 10, 2008) is directly applicable to this PMA supplement. Therefore, only the testing information specific to the 2.25 mm diameter stent is summarized below in **Table 4**.

Table 4: Coating Characterization Testing

Test	Description of Test
Material Characterization	
Particulates	Particulate levels were evaluated for the TAXUS Liberté stent system post deployment, over-expansion and simulated use.

E. Chemistry Manufacturing and Controls (CMC) Testing

The CMC information included in the original PMA submission (P060008, approved October 10, 2008) is directly applicable to this PMA Supplement; therefore, the information is not repeated herein.

F. Stability

Stability studies were conducted to establish a shelf life/expiration date for the TAXUS Liberté Atom Paclitaxel-Eluting Coronary Stent System. Based on these studies, a shelf life of 18 months is appropriate.

G. Sterilization

The TAXUS Liberté Atom Paclitaxel-Eluting Coronary Stent System (Monorail and Over-The-Wire) is sterilized using ethylene oxide sterilization and has been validated per AAMI/ISO 1135:1994 "Medical Devices – Validation and Routine Control of Ethylene Oxide Sterilization."

Results obtained from the sterilization studies show that the product satisfies a minimum Sterility Assurance Level (SAL) of 10^{-6} .

The amount of bacterial endotoxin was verified to be within the specification limit for TAXUS Liberté Atom Paclitaxel-Eluting Coronary Stent System.

H. Animal Studies

The non-clinical studies included in the original PMA submission (P060008, approved October 10, 2008) are directly applicable to this PMA Supplement; therefore, the information is not repeated herein.

X. SUMMARY OF PRIMARY CLINICAL STUDY

TAXUS ATLAS Small Vessel Trial

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of coronary drug-eluting stent implantation with the 2.25 mm TAXUS Liberté Coronary Stent System for improving luminal diameter for the treatment of de novo lesions in native coronary arteries 2.25 mm in diameter and ≤ 28 mm in length in the US under IDE #G040100. Data from this clinical study were the basis for this PMA approval decision. A summary of the clinical study is presented below.

Study Design

The TAXUS ATLAS Small Vessel (SV) trial is a prospective, multicenter, single-arm, trial to evaluate the safety and efficacy of the TAXUS Liberté 2.25 mm stent in the treatment of small (RVD ≤ 2.5 mm) *de novo* coronary artery lesions. The primary endpoint of the study is percent diameter stenosis (%DS) of the analysis segment at 9 month follow-up as determined by QCA. Patients were enrolled after successful predilation and received a TAXUS Liberté paclitaxel-eluting stent with a diameter of 2.25 mm. All patients were to have angiographic follow-up at 9 months. A total of 261 patients were enrolled in TAXUS ATLAS SV study from 23 centers in 3 countries (New Zealand, Singapore, and the United States).

The outcomes of TAXUS ATLAS SV study were compared to 2 historical controls derived from the TAXUS V *de novo* clinical trial.

The first objective of the TAXUS ATLAS Small Vessel study was to demonstrate non-inferiority for the angiographic outcome of %DS for the 2.25 mm TAXUS Liberté stent when compared to the TAXUS Express Stent. Therefore, the treatment group is compared to a case-matched Control group derived from TAXUS V *de novo*. In order to case-match this first Control group, all TAXUS V patients randomized to the TAXUS Express group with (1) a reference vessel diameter (RVD) by visual estimate ≤ 2.5 mm, (2) a lesion length by visual estimate ≥ 10 mm and ≤ 28 mm, and (3) receiving 1 planned 2.25 mm study stent were included. This resulted in inclusion of 75 out of 577 patients randomized into the TAXUS Express treatment arm of TAXUS V *de novo*.

The second objective of the TAXUS ATLAS Small Vessel study was to demonstrate superiority for the angiographic outcome of %DS for the 2.25 mm TAXUS Liberté stent when compared to the bare metal Express stent. Therefore, the treatment group is compared to a case-matched Control group derived from TAXUS V *de novo*. In order to case-match this second Control group, all TAXUS V patients randomized to the bare metal Express group with (1) a reference vessel diameter (RVD) by visual estimate ≤ 2.5 mm, (2) a lesion length by visual estimate ≥ 10 mm and ≤ 28 mm, and (3) receiving 1 planned 2.25 mm or 2.5mm study stent were included. This resulted in

inclusion of 155 out of 579 patients randomized into the bare metal Express treatment arm of TAXUS V *de novo*.

Patients were consented, and then were to be followed-up at 1, 4, and 9 months post-index procedure and 1, 2, 3, 4, and 5 years thereafter. The primary endpoint was reached after all enrolled patients had completed the 9 month follow-up.

Patients were to receive aspirin and clopidogrel or ticlopidine pre-procedure. Following the procedure patients were prescribed to mandatory clopidogrel (or ticlopidine) use for 6 months. In addition, patients were prescribed mandatory aspirin use for 9 months, with indefinite use of aspirin highly recommended.

The trial utilized a clinical event committee (CEC) to adjudicate potential Major Adverse Clinical Events (MACE), including all reported death and stent thromboses. During the course of the trial, a data monitoring committee (DMC) reviewed aggregate safety data to monitor for incidence of MACE and other trends that may warrant modification of the trial. A core lab was used for central assessment of angiography.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the TAXUS ATLAS Small Vessel study was limited to patients who met the following inclusion criteria:

1. Patient is ≥ 18 years old.
2. Eligible for percutaneous coronary intervention (PCI)
3. Documented stable angina pectoris (Canadian Cardiovascular Society [CCS] Classification 1, 2, 3, or 4) or unstable angina pectoris with documented ischemia (Braunwald Class IB-C, IIB-C, or IIIB-C), or documented silent ischemia
4. Left ventricular ejection fraction (LVEF) of $\geq 25\%$
5. Acceptable candidate for coronary artery bypass grafting (CABG)
6. Patient or legal guardian understands the study requirements and the treatment procedures and provides written Informed Consent before any study-specific tests or procedures are performed
7. Willing to comply with all specified follow-up evaluations

Patients were not permitted to enroll in the TAXUS ATLAS Small Vessel study if they met any of the following exclusion criteria:

1. Known sensitivity to paclitaxel
2. Any previous, concurrent or planned treatment with a non-study anti-restenotic drug-coated or DES
3. Planned use of both the study stent and a non-study stent, (i.e., commercial stent) in the treatment of the target vessel

4. Previous or planned treatment with intravascular brachytherapy in the target vessel
5. Planned CABG \leq 9-months post-index procedure
6. MI within 72 hours prior to the index procedure and/or creatine kinase (CK) $>2x$ the local laboratory's ULN (refers to a measured value twice the upper limits of normal on the day of the index procedure) unless CK-MB is $<2x$ ULN. A CK-MB laboratory result must be available on the day of the procedure prior to treatment for patients with recent MI (72 hours to 30 days) or unstable angina if the CK is $2x$ ULN. Patients with stable angina may be enrolled without lab results being received; however, baseline CK must be drawn immediately pre-procedure
7. Cerebrovascular Accident (CVA) within the past 6 months
8. Cardiogenic Shock characterized by systolic pressure <80 mm Hg and/or central filling pressure >20 mm Hg, or cardiac index <1.8 liters/minute/ m^2 or intra-aortic balloon pump or intravenous inotropes were needed to maintain a systolic pressure >80 mm Hg and a cardiac index >1.8 liters/minute/ m^2
9. Acute or chronic renal dysfunction (creatinine >2.0 mg/dL or $177 \mu\text{mol/L}$)
10. Contraindication to ASA, or to both clopidogrel and ticlopidine
11. Leukopenia (leukocyte count $<3.5 \times 10^9/\text{liter}$)
12. Thrombocytopenia (platelet count $<100,000/\text{mm}^3$) or thrombocytosis ($>750,000/\text{mm}^3$)
13. Active peptic ulcer or active gastrointestinal (GI) bleeding
14. Known allergy to stainless steel
15. Any prior true anaphylactic reaction to contrast agents; defined as known anaphylactoid or other non-anaphylactic allergic reactions to contrast agents that cannot be adequately pre-medicated prior to the index procedure
16. Patient was currently, or had been treated with paclitaxel or other chemotherapeutic agents within 12-months of the index procedure
17. Anticipated treatment with paclitaxel or oral rapamycin during any period in the 9-months after the index procedure
18. Male or female with known intention to procreate within 3 months after the index procedure
19. Female of childbearing potential with a positive pregnancy test within 7 days before the index procedure, or lactating
20. Life expectancy of less than 24 months due to other medical conditions
21. Co-morbid condition(s) that could limit the patient's ability to participate in the study, compliance with follow-up requirements or impact the scientific integrity of the study
22. Currently participating in another investigational drug or device study that has not completed the primary endpoint or that clinically interferes with the endpoints of this study

2. Follow-up Schedule

Follow-up included clinical assessments at 1, 4 and 9 months. All patients were to undergo angiographic follow-up at 9 months. In addition, patients agreed to annual telephone follow-up for clinical parameters through 5 years post-procedure.

3. Clinical Endpoints

The primary endpoint for the study was the percent diameter stenosis (%DS) of the analysis segment at 9 months, as determined by QCA. Secondary endpoints included clinical procedural and technical success, utilization parameters (e.g., procedure and fluoroscopic time), MACE rates at each follow-up time point, stent thrombosis rate, target vessel failure, target vessel revascularization, and QCA measurements (binary restenosis, in-stent %DS, MLD and late loss).

A. Accountability of PMA Cohort

Figure 1: TAXUS ATLAS Small Vessel Group versus DES Control

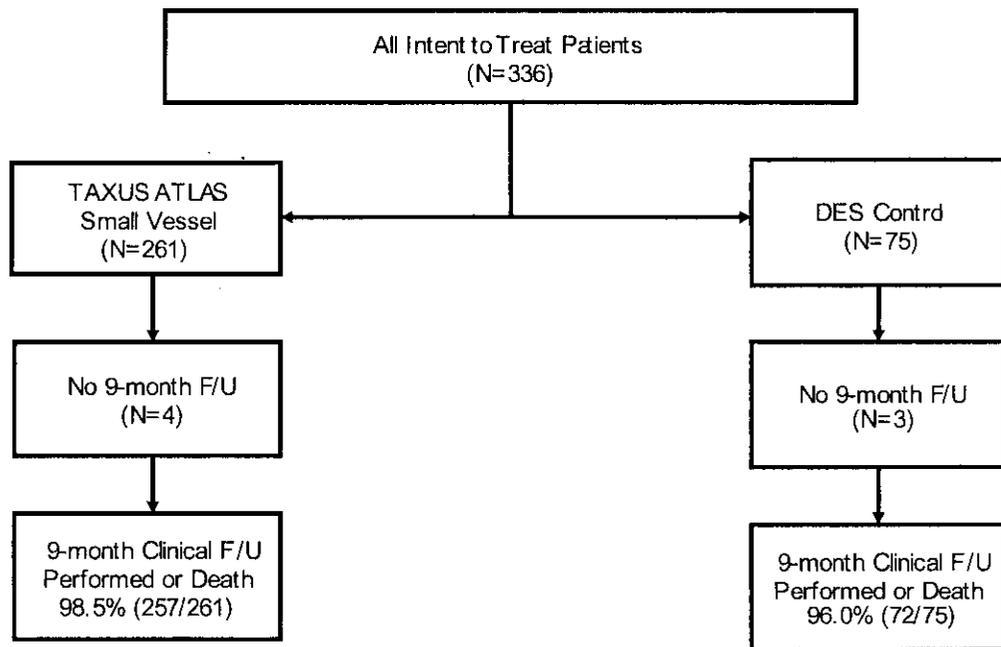
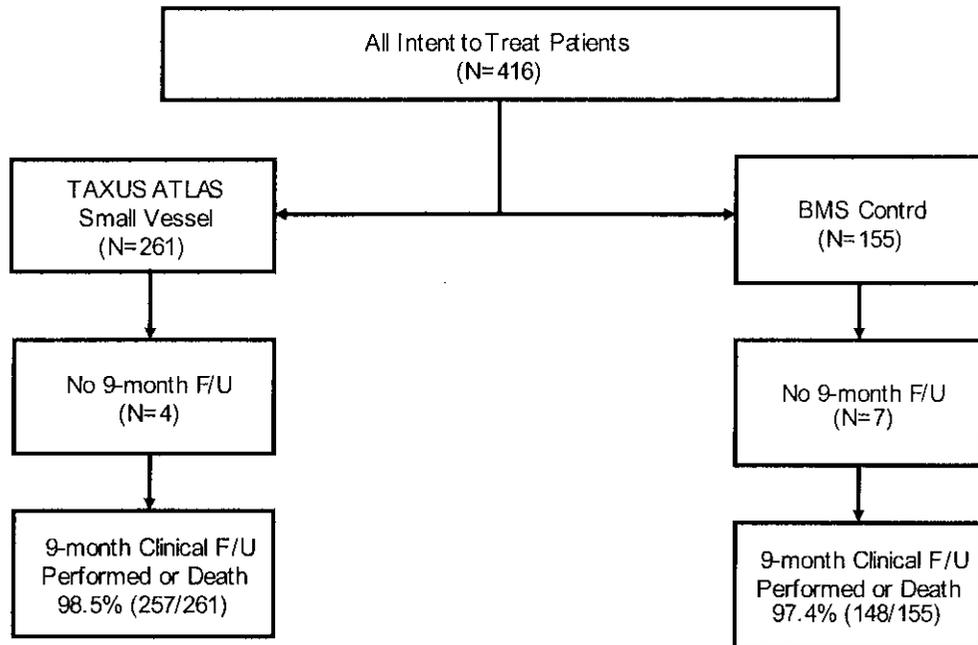


Figure 2: TAXUS ATLAS Small Vessel Group versus BMS Control



B. Study Population Demographics and Baseline Parameters

TAXUS ATLAS Small Vessel versus DES Control

Baseline characteristics were comparable between the 2 groups with no statistically significant differences in demographics, cardiac history and cardiac risk factors. In terms of comorbidities, more patients in the DES Control Group had a known history of peripheral vascular disease (PVD) (13.3%) as compared with patients in the TAXUS ATLAS Small Vessel Group (5.7%, $P=0.0274$).

Most of the baseline angiographic lesion characteristics assessed by the Core Lab were comparable between the 2 groups. However, patients in the TAXUS ATLAS Small Vessel Group had lesions that were longer (14.53 ± 6.89 mm) than those observed in the DES Control Group (11.84 ± 5.69 mm, $P=0.0025$), and a greater proportion had ACC/AHA Category C lesions (34.5% versus 16.2%, respectively, $P=0.0026$). Lesion location demonstrated a significant difference between the groups, with more target lesions in the TAXUS ATLAS Small Vessel group being in the mid portion of the target vessels, and more lesions in the DES Control group being in the proximal portion of the target vessel. Eccentric lesions were observed more frequently in the DES Control Group (59.5% versus 28.7% for the TAXUS ATLAS Small Vessel Group, $P<0.0001$). Notably, differences in baseline characteristics were not expected to affect the primary endpoint due to propensity-score adjustment.

TAXUS ATLAS Small Vessel versus BMS Control

The groups were well matched with respect to most baseline patient characteristics. As compared with the BMS Control Group, a larger proportion of patients in the TAXUS ATLAS Small Vessel Group were with CCS Class 1 angina (4.5% versus 10.0%, respectively, $P=0.0469$), however, patients with clinically more significant angina class 2, 3 or 4 were similarly distributed between the 2 groups.

Several differences between study groups were noted. Although inclusion criteria for RVD were identical in the TAXUS ATLAS Small Vessel study and for the TAXUS V patients included in the BMS Control group, based on the angiographic analysis at the Core Lab, patients in the TAXUS ATLAS Small Vessel Group had lesions with a smaller RVD than those in the BMS Control Group (2.02 ± 0.30 mm versus 2.20 ± 0.34 mm, respectively, $P<0.0001$). Patients in the TAXUS ATLAS Small Vessel Group had a smaller %DS ($67.26\pm 10.91\%$ versus $72.10\pm 10.69\%$, respectively, $P<0.0001$). Patients with a BMS had more complex target lesions as compared with the TAXUS ATLAS Small Vessel Group (59.4% were eccentric lesions versus 28.7% for patients in the TAXUS ATLAS Small Vessel Group, $P<0.0001$, and 79.4% were classified as B2/C as compared with 69.0% in the TAXUS ATLAS Small Vessel Group, $p=0.0213$). These differences were not expected to affect outcomes variables, as propensity score adjustments were made.

For patients with only study stents implanted, maximum diameter implanted was greater in the BMS Control Group (2.39 ± 0.17 mm) versus the TAXUS ATLAS Small Vessel Group (2.25 ± 0.00 mm, $P<0.0001$), as expected, due to the differences in protocol design. The total length implanted in patients in the BMS Control Group (23.3 ± 7.9 mm) was greater than that implanted in the TAXUS ATLAS Small Vessel Group (21.5 ± 7.0 mm, $P=0.0173$).

C. Safety and Effectiveness Results

Major Adverse Cardiac Events (MACE) reported in the TAXUS ATLAS Small Vessel Study are presented in **Table 5** below. Please note that this study was not powered to assess clinical outcomes; however, the following safety outcomes were observed:

- MI rates (both Q-wave and non-Q-wave) were comparable between the two groups at 9 months (overall MI rate was 2.7% in the TAXUS ATLAS Small Vessel group versus 4.1% in the DES Control group,).
- Cardiac death rates were also comparable between the two groups at 9 months (0.8% in the TAXUS ATLAS Small Vessel group versus 2.7% in the DES Control group,).
- Stent thrombosis events were comparable between the two groups at 9 months (0.4% in the TAXUS ATLAS Small Vessel group versus 1.4% in the DES Control group,).

**Table 5: TAXUS ATLAS Small Vessel Major Adverse Cardiac Events (MACE)
From Post-Procedure to Latest Follow-Up**

	TAXUS ATLAS Small Vessel 2.25 mm to 1 Year		
	TAXUS ATLAS Small Vessel (N=261)	TAXUS Express DES Control (N=75)	Express BMS Control (N=155)
In-Hospital MACE	1.9% (5/261)	2.7% (2/75)	1.9% (3/155)
30-Day MACE, overall	1.9% (5/261)	4.1% (3/74)	2.6% (4/154)
9-Month MACE, overall	12.8% (33/258)	20.5% (15/73)	21.6% (33/153)
Cardiac Death	0.8% (2/258)	2.7% (2/73)	0.7% (1/153)
MI	2.7% (7/258)	4.1% (3/73)	2.6% (4/153)
Q-Wave MI	0.8% (2/258)	1.4% (1/73)	0.0% (0/153)
Non-Q-Wave MI	1.9% (5/258)	2.7% (2/73)	2.6% (4/153)
TVR, Overall	10.1% (26/258)	17.8% (13/73)	19.6% (30/153)
TLR, Overall	5.8% (15/258)	13.7% (10/73)	17.6% (27/153)
Non-TLR, Overall	6.6% (17/258)	6.8% (5/73)	5.9% (9/153)
1-Year MACE	13.4% (33/247)	26.8% (19/71)	28.4% (42/148)
Cardiac Death	1.2% (3/247)	4.2% (3/71)	0.7% (1/148)
MI	2.4% (6/247)	4.2% (3/71)	2.7% (4/148)
Q-Wave MI	0.8% (2/247)	1.4% (1/71)	0.0% (0/148)
Non-Q-Wave MI	1.6% (4/247)	2.8% (2/71)	2.7% (4/148)
TVR, Overall	10.5% (26/247)	22.5% (16/71)	26.4% (39/148)
TLR, Overall	6.1% (15/247)	16.9% (12/71)	22.3% (33/148)
Non-TLR, Overall	6.9% (17/247)	8.5% (6/71)	8.8% (13/148)
1-Year Stent Thrombosis	0.4% (1/243)	1.5% (1/67)	1.4% (2/146)

TAXUS ATLAS Small Vessel versus DES Control

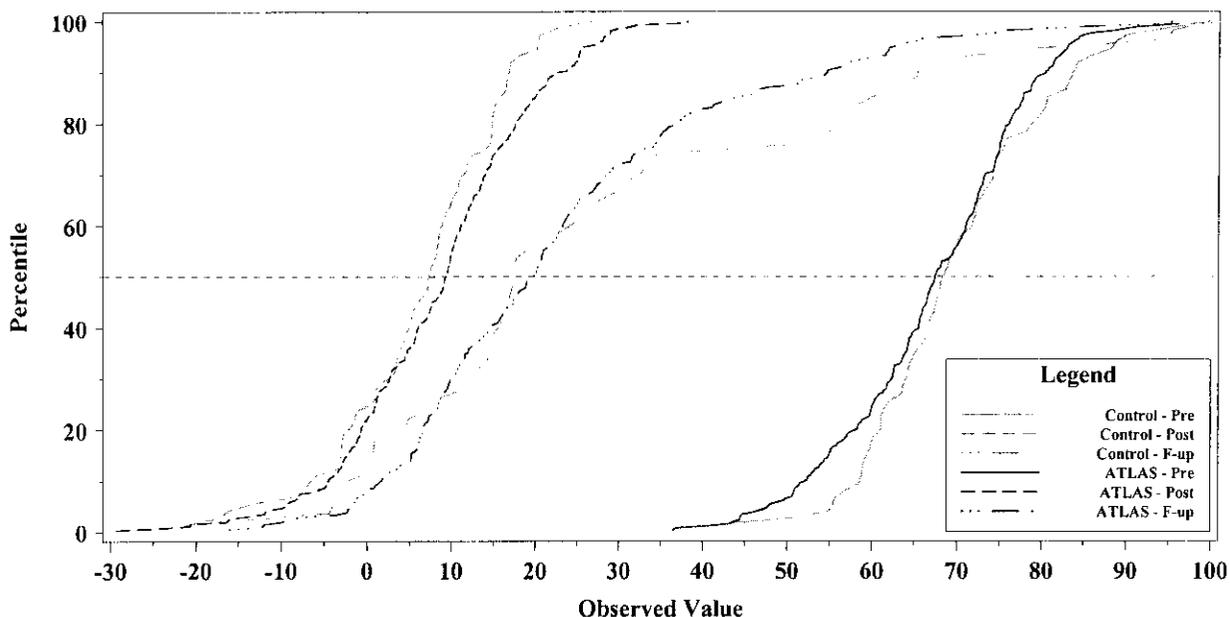
The pre-specified primary endpoint of non-inferiority of in-segment %DS in the 2.25 mm TAXUS Liberté stent versus the TAXUS Express stent was met with propensity score adjustment. The 9-month difference in the in-segment %DS was -7.3%. As the upper 1-sided 95% confidence bound for the difference was -0.8%, this was less than the pre-specified non-inferiority margin of 10.00% ($P < 0.0001$). In addition, the primary endpoint was met without propensity score adjustment. Non-inferiority testing was also performed in the ITT population, which was met with and without adjustment for propensity score (**Table 6**).

Table 6: TAXUS ATLAS Small Vessel Primary Endpoint with DES Control

Per Protocol Population	TAXUS Liberté® Atom™ (N=254)	TAXUS® Express® DES Control (N=73)	Difference [Upper 1- Sided 95% CL]	P-Value	Δ
Follow-up In-Segment Percent Diameter Stenosis					
Adjusted for the propensity score	32.2	39.6	-7.3 [-0.8]	<0.0001	10.00%
Unadjusted	31.70±18.23 (207) (4.07, 100.00)	37.69±23.32 (54) (5.36, 100.00)	-5.99 [-1.10]	<0.0001*	10.00%
Intent-to-Treat Population	TAXUS Liberté Atom (N=261)	TAXUS Express DES Control (N=75)	Difference [Upper 1- Sided 95% CL]	P-Value	Δ
Follow-up In-Segment Percent Diameter Stenosis					
Adjusted for the propensity score	32.4	40.1	-7.7 [-1.1]	<0.0001	10.00%
Unadjusted	32.09±18.38 (211) (4.07, 100.00)	38.36±23.64 (55) (5.36, 100.00)	-6.27 [-1.38]	<0.0001*	10.00%

*Variances unequal: Satterthwaite's approximate t statistic.

Figure 3: Cumulative Frequency Distribution of In-Stent Percent Diameter Stenosis by QCA, Intent-to-Treat, All Patients (N=336)



	Post-Procedure		Follow-Up		Pre-Procedure	
	TAXUS [®] Liberté [®] Atom [™] (N=261)	TAXUS [®] Express [®] DES Control (N=75)	TAXUS Liberté Atom (N=261)	TAXUS Express DES Control (N=75)	TAXUS Liberté Atom (N=261)	TAXUS Express DES Control (N=75)
N	255	72	207	54	261	74
Median	9.43	7.41	20.04	17.40	67.45	68.56
Minimum	-29.41	-21.17	-16.12	-18.31	36.49	41.29
Maximum	38.19	26.90	100.00	100.00	95.37	100.00
Mean	8.64	6.36	23.35	27.73	67.26	69.97
SD	11.10	9.60	20.89	28.12	10.91	10.59
COV	128.51%	150.91%	89.47%	101.43%	16.22%	15.14%
Diff (95% CI)	2.28 [-0.55, 5.10]		-4.38 [-11.14, 2.38]		-2.71 [-5.51, 0.08]	

COV = coefficient of variation.

Post-Procedure and Follow-up measurements are in-stent measurements.

Clinical evaluations and survival analyses demonstrate that MACE, TVR, and TVF were similar for patients in the TAXUS ATLAS Small Vessel Group and the DES Control Group. The 9-month TLR rates were statistically significantly lower in TAXUS ATLAS Small Vessel Group (5.8%) as compared with the DES Control Group (13.7%, $P=0.0244$) (Table 7). After propensity score adjustment, the differences no longer remained statistically significant (6.5% versus 12.6%, $P=0.1472$). The safety profile of the 2.25 mm TAXUS Liberté stent is similar to that of the DES Control stent. The rates for MACE and MACE components (cardiac death, MI, and TVR) demonstrate that the TAXUS Liberté stent is as safe as the commercially-available TAXUS Express stent for use in small vessels.

Table 7: TAXUS ATLAS Small Vessel Clinical Results

	9 months (ITT population)			1 year (per protocol population**)		
	TAXUS ATLAS Small Vessel (N=261)	TAXUS Express DES Control (N=75)	P-Value	TAXUS ATLAS Small Vessel (N=254)	TAXUS Express DES Control (N=73)	P-Value
EFFICACY						
TVR, Overall	10.1% (26/258)	17.8% (13/73)	0.0705	10.5% (26/247)	22.5% (16/71)	0.0084
TLR, Overall	5.8% (15/258)	13.7% (10/73)	0.0244	6.1% (15/247)	16.9% (12/71)	0.0039
TLR, PCI	5.8% (15/258)	12.3% (9/73)	0.0581	6.1% (15/247)	15.5% (11/71)	0.0107
TLR, CABG	0.0% (0/258)	1.4% (1/73)	0.2205*	0.0% (0/247)	1.4% (1/71)	0.2233*
Non-TLR, Overall	6.6% (17/258)	6.8% (5/73)	1.0000*	6.9% (17/247)	8.5% (6/71)	0.6530
Non-TLR, PCI	6.6% (17/258)	6.8% (5/73)	1.0000*	6.9% (17/247)	8.5% (6/71)	0.6530
Non-TLR, CABG	0.4% (1/258)	0.0% (0/73)	1.0000*	0.4% (1/247)	0.0% (0/71)	1.0000*
SAFETY						
Total Death	1.2% (3/259)	2.7% (2/73)	0.3035*	2.8% (7/249)	4.3% (3/69)	0.4569*
Cardiac Death or MI	3.5% (9/258)	5.5% (4/73)	0.4938*	3.6% (9/247)	7.0% (5/71)	0.3204*
Cardiac Death	0.8% (2/258)	2.7% (2/73)	0.2123*	1.2% (3/247)	4.2% (3/71)	0.1275*
MI	2.7% (7/258)	4.1% (3/73)	0.4643*	2.4% (6/247)	4.2% (3/71)	0.4234*
Q-wave MI	0.8% (2/258)	1.4% (1/73)	0.5277*	0.8% (2/247)	1.4% (1/71)	0.5327*
Non-Q-wave MI	1.9% (5/258)	2.7% (2/73)	0.6519*	1.6% (4/247)	2.8% (2/71)	0.6187*
Stent Thrombosis	0.4% (1/256)	1.4% (1/72)	0.3914*	0.4% (1/243)	1.5% (1/67)	0.3861*

* P-values are two-sided from Fisher's exact test; p-values without * are two-sided from the Chi-square test.

**After 9 months, the TAXUS ATLAS Small Vessel study population was reduced to a pre-specified cohort (per protocol population), which consists of all patients who received a study stent at baseline

The secondary endpoints included several angiographic parameters, including in-stent percent diameter stenosis, binary restenosis, MLD, and late loss. Nine-month MLD in the analysis segment was statistically significantly greater in the TAXUS ATLAS Small Vessel Group versus the DES Control Group (1.41±0.45 mm versus 1.26±0.51 mm, respectively, $P=0.0323$). Late loss (both in-stent and in the analysis segment) was statistically significantly lower for patients in the TAXUS ATLAS Small Vessel Group versus the DES Control Group (in-stent late loss: 0.28±0.45 mm for the TAXUS ATLAS Small Vessel Group versus 0.44±0.61 mm for the DES

Control Group, $P=0.0297$; analysis segment late loss 0.16 ± 0.40 mm for the TAXUS ATLAS Small Vessel Group versus 0.33 ± 0.52 mm for the DES Control Group, $P=0.0085$), although these p-values have not been adjusted for multiple comparisons. A summary of the angiographic results are provided in **Table 8**.

Table 8: TAXUS ATLAS Small Vessel 9-Month Angiographic Results

Angiographic Outcomes ^a	TAXUS ATLAS Small Vessel (N=261)	TAXUS Express DES Control (N=75)	P-Value
MLD (mm), In-stent			
Post-Procedure	1.88±0.26(255)	1.93±0.26(72)	0.1603
9-Month	1.59±0.48(207)	1.47±0.60(54)	0.1365
MLD (mm), Analysis Segment			
Post-Procedure	1.58±0.33(261)	1.59±0.34(74)	0.8459
9-Month	1.41±0.45(211)	1.26±0.51(55)	0.0323
% DS, In-stent			
Post-Procedure	8.64±11.10(255)	6.36±9.60(72)	0.1148
9-Month	23.35±20.89(207)	27.73±28.12(54)	0.2051
% DS, Analysis Segment			
Post-Procedure	23.96±10.38(261)	23.59±10.68(74)	0.7918
9-Month	32.09±18.38(211)	38.36±23.64(55)	0.0351
Late Loss, In-stent (mm)	0.28±0.45(207)	0.44±0.61(54)	0.0297
Late Loss, Analysis Segment (mm)	0.16±0.40(211)	0.33±0.52(55)	0.0085
Binary Restenosis			
In-stent restenosis	13.0% (27/207)	25.9% (14/54)	0.0205
Analysis segment restenosis	18.5% (39/211)	32.7% (18/55)	0.0219

^a Includes all patients in the angiographic subset.

P-values are not adjusted for multiple comparisons.

This trial was not adequately powered to compare the rate of low frequency events to a bare metal control group, nor was it sized to determine the rate of low frequency events with a pre-specified precision.

TAXUS ATLAS Small Vessel versus BMS Control

The pre-specified primary endpoint of superiority of in-segment %DS in the 2.25 mm TAXUS Liberté stent versus the bare metal Express stent with propensity score adjustment was met. The 9-month %DS in the TAXUS ATLAS Small Vessel Group was 31.9% versus 45.3% in the BMS Control Group ($P<0.0001$). In addition, the primary endpoint was met without propensity score adjustment (**Table 9**).

Table 9: TAXUS ATLAS Small Vessel Primary Endpoint with BMS Control

Per Protocol Population	TAXUS Liberté® Atom™ (N=254)	Express® BMS Control (N=152)	Difference [95% CI]	P-Value
Follow-up In-Segment Percent Diameter Stenosis				
Adjusted for the propensity score	31.9	45.3	-13.4 [-18.7,-8.0]	<0.0001
Unadjusted	31.70±18.23 (207) (4.07, 100.00)	45.61±23.48 (105) (7.29, 100.00)	-13.91 [-18.64, -9.18]	<0.0001
Intent-to-Treat Population	TAXUS Liberté Atom (N=261)	Express BMS Control (N=155)	Difference [Upper 1-Sided 95% CL]	P-Value
Follow-up In-Segment Percent Diameter Stenosis				
Adjusted for the propensity score	31.9	45.9	-13.9 [-19.6,-8.3]	<0.0001
Unadjusted	32.09±18.38 (211) (4.07, 100.00)	45.61±23.48 (105) (7.29, 100.00)	-13.53 [-18.26, -8.80]	<0.0001

Subgroup Analyses

There were no subgroup analyses performed in the TAXUS ATLAS Small Vessel clinical study.

XI. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

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

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

The data in this application support the reasonable assurance of safety and effectiveness of the TAXUS Liberté Atom MR and OTW Coronary Stent Systems when used in accordance with the indications for use. Non-clinical studies, including biocompatibility, pharmacokinetics, engineering testing, coating characterization, chemistry, manufacturing and controls information, and stability testing demonstrate that the stent is adequate and will perform as intended. Clinical study data demonstrate that the TAXUS Liberté Atom MR and OTW Coronary Stent Systems are safe and effective for their intended use. The TAXUS Liberté Atom stent was determined to be statistically non-inferior to the TAXUS Express small vessel stent and statistically superior to the Express bare metal stent with respect to in-segment percent diameter stenosis, the primary study endpoint. In addition, the rates for MACE and MACE components (cardiac death, MI, and TVR) demonstrate that the TAXUS Liberté Atom stent was comparable to the TAXUS Express small vessel stent.

XIII. CDRH DECISION

CDRH issued an approval order on May 21, 2009. The final conditions of approval cited in the approval order are described below:

The applicant should collect and report to the Agency on an annual basis clinical outcomes through 5 years post-procedure on at least 80% of patients enrolled (excluding those discontinued due to death) from the TAXUS ATLAS Small Vessel study. When appropriate or as requested by FDA, the applicant should submit PMA supplements requesting approval to update their IFU to include these data.

The applicant's manufacturing and sterilization facilities were inspected and were found to be in compliance with the Quality System Regulation (21 CFR 820 and pharmaceutical current Good Manufacturing Practice (cGMP) regulations.

XIV. APPROVAL SPECIFICATIONS

Directions for Use: See product labeling.

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

Post Approval Requirements and Restrictions: See approval order.