



Paclitaxel-Eluting Coronary Stent System

Monorail™ and Over-The-Wire Coronary Stent Delivery System

*CAUTION: Federal law restricts this device to sale by or on the order of a physician.*

INSTRUCTIONS FOR USE

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**1. TAXUS™ Express<sup>2™</sup> Paclitaxel-Eluting Coronary Stent System Product Description**

The TAXUS™ Express<sup>2™</sup> Paclitaxel-Eluting Coronary Stent System (TAXUS Express<sup>2</sup> Stent) is a device / drug combination product comprised of two components: a device (Express<sup>2™</sup> Coronary Stent System) and a drug (a formulation of paclitaxel contained in a polymer coating).

**1.1 Device Component Description**

The device component consists of the Express stent mounted onto the Express<sup>2</sup> stent delivery system (SDS). The characteristics of TAXUS™ Express<sup>2™</sup> Paclitaxel-Eluting Coronary Stent System are described in Table 1-1.

**Table 1-1 TAXUS Express<sup>2</sup> Stent Device Component Description**

	TAXUS™ Express <sup>2™</sup> Stent Monorail Stent Delivery System	TAXUS™ Express <sup>2™</sup> Stent Over-The-Wire Stent Delivery System
Available Stent Lengths (mm)	8, 12, 16, 20, 24, 28, 32	8, 12, 16, 20, 24, 28, 32
Available Stent Diameters (mm)	2.50, 2.75, 3.00, 3.50	2.50, 2.75, 3.00, 3.50
Stent Material	A 316L surgical grade stainless steel Express stent with a conformal coating of a polymer carrier loaded with 1 µg/mm <sup>2</sup> paclitaxel in a slow release formulation with a maximum nominal drug content of 209 µg on the largest stent (3.50x32mm).	
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 Balloon	A balloon enabling high pressure inflations that can be used for post stent dilatation. Two radiopaque markers which aid in the accurate placement of the stent.	
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	All model sizes are 1.8F proximally and 2.7F distally, with the exception of the 3.50mm in 24, 28, 32 lengths, which are 2.0F proximally and 2.7F distally.	3.2F proximally, 2.7F distally

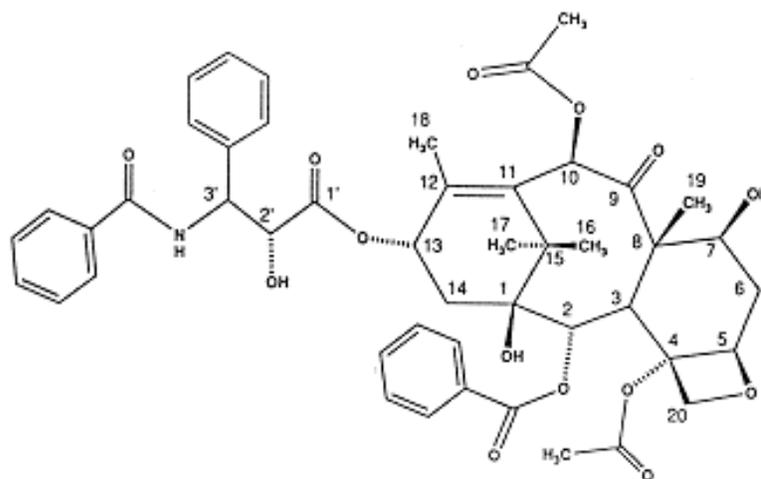
**1.2 Drug Component Description**

The TAXUS™ Express<sup>2™</sup> Paclitaxel-Eluting Coronary Stent System is a stent with the drug / polymer coating formulation consisting of paclitaxel (the active ingredient), and Translute™ polymer carrier (the inactive ingredient).

**1.2.1 Paclitaxel**

The active pharmaceutical ingredient in the TAXUS™ Express<sup>2™</sup> Paclitaxel-Eluting Coronary Stent System is paclitaxel. It is a white to off-white crystalline powder, originally isolated from the bark of the Pacific Yew tree (*Taxus brevifolia*), but currently isolated from a spectrum of *Taxus* species and hybrids cultivated specifically to provide a biomass for the manufacture of the drug. It is highly lipophilic, insoluble in water, soluble in organic solvents, and has a melting temperature of approximately 216° to 217° C (capillary melting point).

## The Chemical Structure of Paclitaxel



Paclitaxel is a diterpenoid with a characteristic taxane skeleton of 20 carbon atoms, a molecular mass of 853.91 a.m.u., and a molecular formula of  $C_{47}H_{51}NO_{14}$ .

The Chemical Abstract nomenclature for paclitaxel is:

Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-, 6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1 *H*-cyclodeca[3,4]benz[1,2-*b*]oxet-9yl ester, [2a*R*- [2a $\alpha$ ,4 $\beta$ ,4a $\beta$ ,6 $\beta$ ,9 $\alpha$  ( $\alpha$ *R*\*, $\beta$ *S*\*),11 $\alpha$ ,12 $\alpha$ ,12a $\alpha$ ,12b $\alpha$ ]]-. (2a*R*,4*S*,4a*S*,6*R*,9*S*,11*S*,12*S*,12a*R*,12b*S*)-1,2a,3,4,4a,6,9,10,11,12,12a,12b-Dodecahydro-4,6,9,11,12,12b-hexahydroxy-4a,8,13,13-tetramethyl-7,11-methano-5 *H*-cyclodeca[3,4]-benz[1,2-*b*]oxet-5-one 6,12b-diacetate, 12-benzoate, 9-ester with (2*R*,3*S*)-*N*-benzoyl-3-phenylisoserine [C.A.S. number: 33069-62-4]

Reference: Current United States Pharmacopeia (USP) monograph for Paclitaxel.

### 1.2.2 Translute™ Polymer Carrier

Translute is the release-controlling inactive ingredient of the TAXUS™ Express<sup>2™</sup> Paclitaxel-Eluting Coronary Stent System. It is an exceptionally biostable, vascular compatible, hydrophobic triblock elastomeric copolymer. Translute has a molecular weight (Mn-number average molecular weight-unitless) of 80,000 to 130,000 and a polydispersity index of 1.0 to 2.0.

### 1.2.3 Product Matrix and Paclitaxel Content

**Table 1-2 TAXUS Express<sup>2</sup> Stent product matrix and paclitaxel content**

Product Code MR	Product Code OTW	Nominal Expanded Stent ID (mm)	Nominal Un-expanded Stent Length (mm)	Nominal Paclitaxel Content (µg)
H7493897008250	H7493896808250	2.50	8	50
H7493897008270	H7493896808270	2.75	8	50
H7493897008300	H7493896808300	3.00	8	50
H7493897008350	H7493896808350	3.50	8	50
H7493897012250	H7493896812250	2.50	12	79
H7493897012270	H7493896812270	2.75	12	79
H7493897012300	H7493896812300	3.00	12	79
H7493897012350	H7493896812350	3.50	12	79
H7493897016250	H7493896816250	2.50	16	108
H7493897016270	H7493896816270	2.75	16	108
H7493897016300	H7493896816300	3.00	16	108
H7493897016350	H7493896816350	3.50	16	108
H7493897020250	H7493896820250	2.50	20	137
H7493897020270	H7493896820270	2.75	20	137
H7493897020300	H7493896820300	3.00	20	137
H7493897020350	H7493896820350	3.50	20	137
H7493897024250	H7493896824250	2.50	24	151
H7493897024270	H7493896824270	2.75	24	151
H7493897024300	H7493896824300	3.00	24	151
H7493897024350	H7493896824350	3.50	24	151
H7493897028270	H7493896828270	2.75	28	180
H7493897028300	H7493896828300	3.00	28	180
H7493897028350	H7493896828350	3.50	28	180
H7493897032270	H7493896832270	2.75	32	209
H7493897032300	H7493896832300	3.00	32	209
H7493897032350	H7493896832350	3.50	32	209

## 2. Indications

The TAXUS Express<sup>2</sup> Paclitaxel-Eluting Coronary Stent System is indicated for improving luminal diameter and reducing restenosis for the treatment of *de novo* lesions  $\leq 28$ mm in length in native coronary arteries  $\geq 2.5$  to  $\leq 3.75$  mm in diameter.

In a pivotal US trial, the TAXUS<sup>TM</sup> Express<sup>2TM</sup> Paclitaxel-Eluting Coronary Stent System has been shown to improve patient outcomes at 9 months when compared to uncoated (bare metal) stents. Specifically, the TAXUS<sup>TM</sup> Express<sup>2TM</sup> Stent has proven to significantly reduce restenosis, Target Lesion Revascularization (TLR), Target Vessel Revascularization (TVR) and late loss while allowing for sufficient tissue growth over struts of the stent.

Long-term outcomes in large, randomized, multi-center, controlled trials (beyond 12 months) for this implant are unknown at present.

### 3. **Contraindications**

The TAXUS™ Express<sup>2™</sup> Paclitaxel-Eluting Coronary Stent System is contraindicated in patients with:

- Known hypersensitivity to paclitaxel or its derivatives.
- Patients in whom anti-platelet and/or anticoagulant therapy is contraindicated.
- Patients judged to have a lesion that prevents complete inflation of an angioplasty balloon or proper placement of the stent or delivery device.
- Known allergy to stainless steel.

### 4. **Warnings**

- To maintain sterility, the inner package should not be opened or damaged prior to use.
- The use of this device carries the risks associated with coronary artery stenting, including subacute thrombosis, vascular complications, and/or bleeding events.

### 5. **Precautions**

#### 5.1. **General Precautions**

- Only physicians who have received adequate training should perform implantation of the stent.
- Stent placement should only be performed at hospitals where emergency coronary artery bypass graft surgery can be readily performed.
- Subsequent stent blockage may require repeat dilatation of the arterial segment containing the stent. The long-term outcome following repeat dilatation of endothelialized stents is not well characterized.
- Do not use in patients with history of severe reaction to contrast agents that cannot be adequately premedicated prior to the procedure.
- Do not expose the delivery system to organic solvents, such as alcohol, or detergents.
- Antiplatelet therapy is recommended for a period of 6 months post procedure.

#### 5.2. **Use of Multiple Stents**

The extent of the patient's exposure to drug and polymer is directly related to the number of stents implanted. Use of more than two TAXUS™ Express<sup>2™</sup> Stents has not been fully evaluated. When multiple stents are required, resulting in stent to-stent contact, stent materials should be of similar composition to avoid the possibility of dissimilar metal corrosion.

#### 5.3. **Brachytherapy**

The safety and effectiveness of the TAXUS™ Express<sup>2™</sup> Stent in patients with prior brachytherapy of the target lesion have not been established. The safety and effectiveness of use of brachytherapy to treat in-stent restenosis in a TAXUS™ Express<sup>2™</sup> Stent has not been established.

#### 5.4. **Use in Special Population**

- 5.4.1. **Pregnancy:** There are no adequate and well controlled studies in pregnant women or men intending to father children. Systemic levels of paclitaxel have not been demonstrated in any pre-clinical or clinical trials with the TAXUS™ Express<sup>2™</sup> Stent.

- 5.4.2. **Pediatric use:** The safety and efficacy of the TAXUS™ Express<sup>2™</sup> Stent in pediatric patients have not been established.
- 5.4.3. **Geriatric Use:** Clinical studies of the TAXUS™ Express<sup>2™</sup> Stent did not find that patients age 65 years and over differed with regard to safety and efficacy compared to younger patients.

#### 5.5. **Lesion/Vessel Characteristics**

The safety and effectiveness of the TAXUS™ Express<sup>2™</sup> Paclitaxel-Eluting Coronary Stent System have not been established in the following patient populations:

- Patients with unresolved vessel thrombus at the lesion site.
- Patients with coronary artery reference vessel diameters < 2.5 mm or > 3.75 mm.
- Patients with lesions located in the left main coronary artery, ostial lesions, or lesions located at a bifurcation.
- Patients with diffuse disease or poor overflow distal to the identified lesions.
- Patients with tortuous vessels in the region of the obstruction or proximal to the lesion.
- Patients with a recent acute myocardial infarction where there is evidence of thrombus or poor flow.

#### 5.6. **Drug Interaction**

Because systemic levels of paclitaxel have not been detected post-stent placement in clinical trials, possible interactions of paclitaxel with concomitantly administered medications have not been formally investigated. Drug interactions of systemic chemotherapeutic levels of paclitaxel with possible concomitant medications are outlined in the labeling for finished pharmaceuticals containing paclitaxel, such as Taxol®. Given that the amount of paclitaxel loaded onto each TAXUS™ Express<sup>2™</sup> Stent is at a minimum 1000 times lower than that used in oncological applications of the drug and is released at considerably lower levels than this, drug interactions are unlikely to be detectable.

#### 5.7. **Magnetic Resonance Imaging (MRI)**

Do not perform Magnetic Resonance Imaging (MRI) scan on patient's post-stent implantation until the stent has been completely endothelialized (30 days) to minimize the potential for migration. The stent may cause artifacts in MRI scans due to distortion of the magnetic field.

#### 5.8. **Stent Handling** (also see Section 13 Operator's Instructions)

- Note product "Use By" date.
- The TAXUS Express<sup>2</sup> Stent is designed for use as a unit. The stent is not to be removed from its delivery balloon. The stent is not designed to be crimped onto another balloon. Removing the stent from its delivery balloon may damage the stent and/or lead to stent embolization.
- Special care must be taken not to handle or in any way disrupt the stent position on the delivery device. This is most important during catheter removal from packaging, placement over guidewire, and advancement through hemostasis valve adapter and guide catheter hub.
- Excessive manipulation (e.g., rolling the mounted stent) may cause coating damage or dislodgment of the stent from the delivery balloon.

- In the event the TAXUS™ Express<sup>2</sup>™ Stent is not deployed, follow product returns procedures.
- Use only the appropriate balloon inflation media (see Section 13 Operator's Instructions). Do not use air or any gas medium to inflate the balloon.
- Stent contact with any fluid prior to placement is not recommended as there is a possibility of drug release. However, if it is absolutely necessary to flush the stent with sterile/isotonic saline, contact time should be limited (1 minute maximum).

### 5.9. Stent Placement

- Do not prepare or pre-inflate balloon prior to stent deployment other than as directed. Use balloon purging technique described in Section 13, Operator's Instructions.
- Implanting a stent may lead to dissection of the vessel distal and/or proximal to the stented portion, and may cause acute closure of the vessel requiring additional intervention (e.g., CABG, further dilation, placement of additional stents, or other).
- When treating multiple lesions, the distal lesion should be initially stented, followed by stenting of the more proximal lesion(s). Stenting in this order alleviates the need to cross the proximal stent in placement of the distal stent and reduces the chances for dislodging the proximal stent.
- Do not expand the stent if it is not properly positioned in the vessel (see 5.10 Stent System Removal).
- Placement of the stent has the potential to compromise side branch patency.
- The vessel should be pre-dilated with an appropriate sized balloon.
- Balloon pressures should be monitored during inflation. Do not exceed rated burst pressure as indicated on product label (see Table 14-1 Typical TAXUS Express<sup>2</sup> Stent and Balloon Compliance). Use of pressures higher than specified on product label may result in a ruptured balloon and potential intimal damage and dissection. The stent I.D. should approximate 1.1 times the reference diameter of the vessel.
- If unusual resistance is felt at any time during lesion access before stent implantation, the Stent System and the guide catheter should be removed as a single unit (See 5.10 Stent System Removal).
- Do not attempt to pull an unexpanded stent back into the guide catheter while engaged in the coronary arteries, as stent damage or stent dislodgment from the balloon may occur (See 5.10 Stent System Removal).
- An unexpanded stent should be introduced into the coronary arteries one time only. An unexpanded stent should not be subsequently moved in and out through the distal end of the guide catheter as stent damage or stent dislodgment from the balloon may occur.
- Stent retrieval methods (use of additional wires, snares and/or forceps) may result in additional trauma to the vascular site. Complications can include bleeding, hematoma or pseudoaneurysm.

### 5.10. Stent System Removal

- If unusual resistance is felt at any time during lesion access before stent implantation, the Stent System and the guide catheter should be removed as a single unit.
- Do not attempt to pull an unexpanded stent back into the guide catheter while engaged in the coronary arteries, as stent damage or stent dislodgment from the balloon may occur.

When removing the entire Stent System and guide catheter as a single unit (NOTE: The following steps should be executed under direct visualization using fluoroscopy):

- Maintain guidewire placement across the lesion during the entire removal process. Carefully pull back the Stent System until the proximal balloon marker of the Stent System is aligned with the distal tip of the guide catheter.
- The Stent System and the guide catheter should be pulled back until the tip of the guide catheter is just distal to the arterial sheath, allowing the guide catheter to straighten. Carefully retract the Stent System into the guide catheter and remove the Stent System and the guide catheter from the patient as a single unit while leaving the guidewire across the lesion.

Failure to follow these steps, and/or applying excessive force to the Stent System can potentially result in stent damage, stent dislodgment from the balloon and/or damage to the Delivery System.

#### 5.11. Post Implant

- Care must be exercised when crossing a newly deployed stent with an intravascular ultrasound (IVUS) catheter, a coronary guidewire, or a balloon catheter to avoid disrupting the stent placement, apposition, geometry, and/or coating.
- Do not perform Magnetic Resonance Imaging (MRI) scan on patient's post-stent implantation until the stent has been completely endothelialized (30 days) to minimize the potential for migration. The stent may cause artifacts in MRI scans due to distortion of the magnetic field.
- Prescribe an antiplatelet therapy (i.e. clopidogrel or ticlopidine) for a period of 6 months to reduce the risk of stent thrombosis.

## 6. Drug Information

### 6.1. Mechanism of Action

The mechanism of action by which a TAXUS Express<sup>2</sup> Paclitaxel-Eluting Coronary Stent reduces or reverses neointima formation and proliferation, leading to restenosis, as demonstrated in clinical studies has not been established. It is known that paclitaxel promotes the assembly of microtubules from tubulin dimers and stabilizes microtubules by preventing depolymerization. This stability results in the inhibition of the normal dynamic reorganization of the microtubule network that is essential for vital interphase and mitotic cellular functions.

### 6.2. Pharmacokinetics of the TAXUS<sup>TM</sup> Express<sup>2TM</sup> Paclitaxel-Eluting Coronary Stent System

With local drug-delivery using the TAXUS stent system, systematic paclitaxel levels have not been above the limit of detection using high sensitivity assays in various clinical and preclinical studies. In the human trials TAXUS I, II, and III, no paclitaxel levels were detected at various time points after stent implantation using an assay system with a LLOQ of 10 ng/ml. These findings were confirmed in preclinical studies using multiple stents with total loaded doses above the clinically available stent system and an assay system with

an LLOQ of 0.03 ng/ml. Hence, in the absence of any systemically detectable levels, standard pharmacokinetic studies have not been performed for the TAXUS<sup>TM</sup> Express<sup>2TM</sup> Paclitaxel-Eluting Coronary Stent because systemic levels of paclitaxel have not been detected post-stent placement in clinical trials or in small animal pre-clinical studies. In the absence of detectable paclitaxel blood levels, standard pharmacokinetic parameters ( $t_{\max}$ ,  $C_{\max}$ ,  $t_{1/2}$ , AUC, CL) are not able to be calculated. The actual amount of paclitaxel incorporated into each TAXUS<sup>TM</sup> Express<sup>2TM</sup> Stent is, at a minimum, 1000 times lower than that used systemically in oncological applications.

$t_{\max}$  = time peak blood concentration occurs

$C_{\max}$  = peak blood concentration

$t_{1/2}$  = terminal-phase half-life

AUC = area under the concentration-time curve

CL = total blood clearance

### 6.3. Drug Interactions

Formal drug interaction studies have not been conducted with the TAXUS<sup>TM</sup> Express<sup>2TM</sup> Paclitaxel-Eluting Coronary Stent System. Systemic levels of paclitaxel following implantation of the TAXUS<sup>TM</sup> Express<sup>2TM</sup> Stent have not been detected in any clinical or preclinical studies, therefore drug interactions are unlikely. See section 6.2, Pharmacokinetics of the TAXUS<sup>TM</sup> Express<sup>2TM</sup> Paclitaxel-Eluting Coronary Stent System.

The following summarizes the drug interactions of systemic chemotherapeutic levels of paclitaxel. In Phase I trials, myelosuppression was observed when paclitaxel was administered following cisplatin. While no formal drug interaction studies have been done, caution should be used when administering paclitaxel concomitantly with known substrates or inhibitors of the cytochrome P450 isoenzymes CYP2C8 and CYP3A4. A potential for interactions between paclitaxel, a substrate of CYP3A4 and protease inhibitors exists, but has not been evaluated in clinical trials. The literature suggests that plasma levels in doxorubicin may be increased when paclitaxel is used in combination with this drug. For a complete description of drug interactions and pharmacokinetics, please refer to the Taxol<sup>®</sup> labeling.

### 6.4. Carcinogenicity, Genotoxicity, and Reproductive Toxicology

Carcinogenicity, genotoxicity and reproductive toxicology are not expected with the low paclitaxel concentrations of the TAXUS<sup>TM</sup> Express<sup>2TM</sup> Stent.

Formal long-term carcinogenicity testing of paclitaxel in animals has not been published. However, the potential for secondary malignancies is considered to be remote based on the long clinical history of paclitaxel use in cancer chemotherapy without any reported secondary malignancies and on the observation that this microtubule stabilizer does not cause DNA damage. In addition, histopathological evaluation of TAXUS<sup>TM</sup> Express<sup>2TM</sup> Stent implant sites from animals at one year showed no evidence of any pre-neoplastic or neoplastic cells. Histological evaluation of the Translute<sup>TM</sup> polymer alone in a 2 year canine vascular model also indicated no evidence of pre-neoplastic or neoplastic cells.

Genotoxicity studies were conducted across a broad range (0.06 to 0.6 ng/mg) of paclitaxel concentrations bracketing those found in animal tissues following stenting with the TAXUS<sup>TM</sup> Express<sup>2TM</sup> Paclitaxel-Eluting Coronary Stent System. Paclitaxel at all doses tested was shown to be non-mutagenic and non-clastogenic in the *in vitro* bacterial reverse mutation assay (Ames mutagenicity), the standard chromosomal aberration assay in Chinese hamster ovary cells, the standard chromosomal aberration in human lymphocyte assay and the mouse micronucleus assay.

The effects of paclitaxel on human coronary smooth muscle cells, a more relevant cell type for this application, was evaluated over a broad range of paclitaxel concentrations. The data showed no evidence of apoptosis and provided evidence for a cytostatic mechanism in the inhibition of proliferation of human coronary smooth muscle cells.

The reproductive toxicity of paclitaxel has been studied in the rat at doses as high as 1.0 mg/kg. Results were reported by Bristol-Myers-Squibb Pharmaceutical Corporation (Lochry, 1995). It is estimated that the TAXUS<sup>TM</sup> Express<sup>2TM</sup> Paclitaxel-Eluting Coronary Stent System (one 3.5mm x 32mm stent and an additional 3.5mm x 24mm stent) would deliver a total systemic paclitaxel dose of 5.1 µg/kg to a patient (based on a 70 kg patient) if the entire amount of paclitaxel is released from the stent. Because the reproductive toxicity studies conducted for Taxol<sup>®</sup> used approximately 1000 times higher doses than those to which a patient would be exposed from a TAXUS Stent, additional studies at these lower doses were not performed.

## 7. Adverse Events

### 7.1. Observed Adverse Events

Observed adverse event experience comes from three clinical studies, TAXUS I, II and IV. See Section 8 Clinical Studies for more complete descriptions of the study designs and results. All three studies were multi-center, double-blind, randomized clinical trials in patients with symptomatic ischemic coronary artery disease due to *de novo* lesions in native coronary arteries. Patients were randomized to either a TAXUS<sup>TM</sup> Paclitaxel-Eluting Coronary Stent System or to a Control stent (a matched uncoated 316L stainless steel stent). Eligibility was based on visual estimates of vessel diameter and lesion length. Following treatment, patients were treated with aspirin indefinitely and either clopidogrel or ticlopidine for 6 months. Evaluations included clinical and angiographic and/or IVUS outcomes. Major study characteristics are summarized in Table 7-1. Principal adverse events are shown in Table 7-2. The TAXUS II trial studied two dose release formulations, slow release (SR) and moderate release (MR). For TAXUS II, results are only presented for the SR treatment group (Cohort I) and corresponding control. No statistically significant differences for any safety or efficacy parameters were observed between Cohort I (SR) or Cohort II (MR).

**Table 7-1 Clinical Studies Major Characteristics**

	<b>TAXUS I (Feasibility)</b>	<b>TAXUS II (Supportive)</b>	<b>TAXUS IV (Pivotal)</b>
Study Type	<ul style="list-style-type: none"> <li>prospective</li> <li>multi-center</li> <li>randomized</li> <li>double-blind</li> </ul>	<ul style="list-style-type: none"> <li>prospective</li> <li>multi-center</li> <li>randomized</li> <li>double-blind</li> <li>two sequential cohorts</li> </ul>	<ul style="list-style-type: none"> <li>prospective</li> <li>multi-center</li> <li>randomized</li> <li>double-blind</li> </ul>
Number of Patients	Total 61 (31 TAXUS Stent, 30 control)	Total 536 (Cohort I: 131 TAXUS Stent, 136 Control; Cohort II: 135 TAXUS Stent, 134 Control)	Total 1,326
Dose Release Formulation	SR (1 µg /mm <sup>2</sup> )	Cohort I =SR (1 µg /mm <sup>2</sup> ) Cohort II = MR (1 µg /mm <sup>2</sup> )	SR (1 µg /mm <sup>2</sup> )
Lesion Criteria	<ul style="list-style-type: none"> <li><i>De novo</i> lesions in native coronary artery</li> <li>≤12mm in length</li> <li>≥3.0mm to ≤3.5mm in diameter</li> </ul>	<ul style="list-style-type: none"> <li><i>De novo</i> lesions in native coronary artery</li> <li>≤12mm in length</li> <li>≥3.0mm to ≤3.5mm in diameter</li> </ul>	<ul style="list-style-type: none"> <li><i>De novo</i> lesions in native coronary artery</li> <li>≥<u>10mm</u> and &lt;u&gt;28mm in length</li> <li>≥2.5mm to ≤3.75mm in diameter</li> </ul>
Antiplatelet Therapy	6 month regimen of aspirin and clopidogrel	6 month regimen of aspirin and clopidogrel	6 month regimen of aspirin and clopidogrel

**Table 7-2 Principal Adverse Events**

	TAXUS IV (SR) to 270 Days		TAXUS II (SR) to 365 Days		TAXUS I (SR) to 24 Months	
	TAXUS stent	Control Stent	TAXUS stent	Control Stent	TAXUS Stent	Control Stent
<b>In-Hospital</b>						
MACE	2.4% (16/662)	2.1% (14/ 652)	1.5% (2/131)	4.4% (6/136)	0.0% (0/31)	0.0% (0/30)
Death	0.0% (0/662)	0.3% (2/652)	0.0% (0/131)	0.7% (1/136)	0.0% (0/31)	0.0% (0/30)
Myocardial Infarction	2.4% (16/662)	2.1% (14/652)	1.5% (2/131)	3.7% (5/136)	0.0% (0/31)	0.0% (0/30)
Q-wave	0.2% (1/662)	0.2% (1/662)	0.0% (0/131)	0.7% (1/136)	0.0% (0/31)	0.0% (0/30)
Non Q-wave	2.3% (15/662)	2.0% (13/652)	1.5% (2/131)	2.9% (4/136)	0.0% (0/31)	0.0% (0/30)
Target Vessel Revascularization (TVR)	0.0% (0/662)	0.2% (1/652)	0.8% (1/131)	0.0% (0/136)	0.0% (0/31)	0.0% (0/30)
Target Lesion Revascularization (TLR)	0.0% (0/662)	0.2% (1/652)	0.8% (1/131)	0.0% (0/136)	0.0% (0/31)	0.0% (0/30)
TVR Remote	0.0% (0/662)	0.0% (0/652)	0.0% (0/131)	0.0% (0/136)	0.0% (0/31)	0.0% (0/30)
TVR, CABG	0.0% (0/662)	0.0% (0/652)	0.0% (0/131)	0.0% (0/136)	0.0% (0/31)	0.0% (0/30)
Stent Thrombosis	0.0% (0/662)	0.3% (2/652)	0.8% (1/131)	0.0% (0/136)	0.0% (0/31)	0.0% (0/30)
<b>Out-of-Hospital</b>						
MACE	6.2% (41/ 662)	13.0% (85/ 652)	9.2% (12/131)	17.8% (24/135)	3.2% (1/31)	10.0% (3/30)
Death	1.4% (9/ 662)	0.8% (5/652)	0.0% (0/131)	0.7% (1/135)	0.0% (0/31)	0.0% (0/30)
Myocardial Infarction	1.1% (7/662)	1.5% (10/652)	0.8% (1/131)	2.2% (3/135)	0.0% (0/31)	0.0% (0/30)
Q-wave	0.6% (4/662)	0.2% (1/652)	0.8% (1/131)	1.5% (2/135)	0.0% (0/31)	0.0% (0/30)
Non Q-wave	0.5% (3/662)	1.4% (9/652)	0.0% (0/131)	0.7% (1/135)	0.0% (0/31)	0.0% (0/30)
Target Vessel Revascularization (TVR)	4.7% (31/662)	11.8% (77/652)	9.2% (12/131)	15.6% (21/135)	3.2% (1/31)	10.0% (3/30)
Target Lesion Revascularization (TLR)	3.0% (20/662)	11.2% (73/652)	3.8% (5/131)	12.6% (17/135)	0.0% (0/31)	10.0% (3/30)
TVR Remote	1.7% (11/662)	1.1% (7/652)	3.1% (4/131)	3.0% (4/135)	3.2% (1/31)	0.0% (0/30)
TVR, CABG	0.5% (3/662)	0.3% (2/652)	3.1% (4/131)	0.7% (1/135)	0.0% (0/31)	3.3% (1/30)
Stent Thrombosis	0.6% (4/662)	0.5% (3/652)	0.8% (1/131)	0.0% (0/135)	0.0% (0/31)	0.0% (0/30)

Numbers are % (Count/Sample Size).

MACE: Major Adverse Cardiac Events, comprised of Cardiac Death, MI and TVR.

TVR: Target Vessel Revascularization, defined as Ischemia-driven repeat percutaneous intervention of the target vessel or bypass surgery of the target vessel. A TVR will be considered as ischemia-driven if the target vessel diameter stenosis is  $\geq 50\%$  by QCA and any of the following are present:

- the patient had a positive functional study corresponding to the area served by the target vessel;
- ischemic ECG changes at rest in a distribution consistent with the target vessel;
- ischemic symptoms referable to the target lesion.

Primary endpoint of TAXUS IV: 9-month TVR.

**Table 7-3 Frequency of Incomplete Stent Apposition**

	TAXUS IV (SR) Trial		TAXUS II (SR) Trial	
	TAXUS Stent	Control Stent	TAXUS Stent	Control Stent
Incomplete Stent apposition Rate Post-Procedure	11.6% (13/112)	6.4% (7/109)	11.1% (14/126)	9.3% (12/129)
Incomplete Stent apposition Rate at Follow-up	4.0% (4/99)	3.0% (3/100)	12.5% (15/120)	7.9% (10/127)
Resolved	6.4% (6/94)	5.4% (5/93)	6.8% (8/118)	4.9% (6/123)
Persistent	3.2% (3/94)	1.1% (1/93)	4.2% (5/118)	4.1% (5/123)
Late Acquired	1.1% (1/94)	2.2% (2/93)	8.5% (10/118)	4.1% (5/123)

Numbers are % (Count/Sample Size).

IA = Incomplete Apposition, BL = Baseline, FU = Follow-up.

Resolved = # patients with BL IA and without FU IA ÷ # patients evaluable at baseline and follow-up.

Persistent = # patients with BL IA and with FU IA ÷ # patients evaluable at baseline and follow-up.

Late Acquired = # patients without BL IA and with FU IA ÷ # patients evaluable at baseline and follow-up.

Incomplete Apposition variables are from assessment by IVUS core laboratory.

## 7.2. Potential Adverse Events

### 7.2.1. 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 antithrombotic therapy or contrast medium
- Angina
- Aneurysm
- Arrhythmias, including ventricular fibrillation (VF) and ventricular tachycardia (VT)
- Arteriovenous fistula
- Cardio tamponade
- Cardiogenic shock
- Death
- Dissection
- Emboli, distal (air, tissue or thrombotic emboli)
- Emergent Coronary Artery Bypass Surgery (CABG)
- Heart failure
- Hematoma
- Hemorrhage, requiring transfusion
- Hypotension/Hypertension
- Infection
- Infection and/or pain at the access site
- Ischemia, myocardial
- Perforation or Rupture
- Pericardial effusion
- Pseudoaneurysm, femoral
- Renal Failure
- Respiratory Failure

- Restenosis of stented segment
- Shock/Pulmonary edema
- Spasm
- Stent embolization
- Stent thrombosis/occlusion
- Stroke/cerebrovascular accident/TIA
- Total occlusion of coronary artery
- Vessel trauma requiring surgical repair or reintervention

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

- Allergic/immunologic reaction to drug or stent coating
- 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

There may be other potential adverse events that are unforeseen at this time.

## **8. Clinical Studies**

### **8.1 Overview of Clinical Studies**

TAXUS I was a randomized, double-blind, controlled feasibility study comparing the slow rate-release formulation of the TAXUS NIRx™ Paclitaxel-Eluting Coronary Stent System (TAXUS™ NIRx™ Stent) with the NIR™ Conformer uncoated (bare metal) control stent in *de novo* lesions. IVUS guidance during the index procedure and at 6-month follow up was required. Patients received a 6 month regimen of acetylsalicylic acid (ASA) and clopidogrel (Plavix™) 75 mg p.o. QD. In brief, 61 patients were enrolled by 3 centers in Germany. Baseline demographic, lesion characteristics were similar between the 2 groups. The primary endpoint was 30-Day Major Adverse Cardiac Event (MACE). Patients remain in follow-up for clinical parameters from 1 to 5 years.

TAXUS II was a randomized, double-blind, controlled study of the safety and performance of the 1 µg /mm<sup>2</sup> (loaded drug/stent surface area) TAXUS™ NIRx™ Paclitaxel-Eluting Coronary Stent System (TAXUS™ NIRx™ Stent), in which two sequential cohorts of patients with standard risk, *de novo* coronary artery lesions were treated. The slow rate-release (SR) formulation was studied in Cohort I and the moderate rate-release (MR) formulation in Cohort II. A total of 536 patients in 15 countries were enrolled. Patients in each cohort were randomized (1:1) to the TAXUS™ NIRx™ Stent or the NIR Conformer uncoated control stent. The primary endpoint for the study was mean percent in-stent net volume obstruction at 6 months as measured by IVUS. Secondary endpoints included 6-month clinical and angiographic parameters. Post procedure ASA and clopidogrel are

required for 6 months. Patients will continue follow-up for clinical parameters from 1 to 5 years with an additional angiographic follow-up scheduled at the 2 year time-point. For TAXUS II, results are only presented for the SR treatment group (Cohort I) and corresponding control as no statistically significant differences for any safety or efficacy parameters were observed between Cohort I (SR) or Cohort II (MR).

TAXUS IV was a randomized, double-blind, controlled study of the safety and performance of the 1 µg /mm<sup>2</sup> slow rate-release formulation TAXUS<sup>TM</sup> Express<sup>TM</sup> Paclitaxel-Eluting Coronary Stent System (TAXUS<sup>TM</sup> Express<sup>TM</sup> Stent) in patients with standard risk, *de novo* coronary artery lesions. A total of 1,326 patients at 73 U.S. sites were enrolled with patients randomized 1:1 to the TAXUS<sup>TM</sup> Express<sup>TM</sup> Stent or the uncoated Express stent control. The primary endpoint for the study was the 9-month ischemia driven TVR rate. Secondary endpoints included 9-month clinical assessments for all patients and analysis of angiographic and IVUS parameters in a subset of patients. Post procedure ASA and clopidogrel were required for 6 months. Patients will continue follow-up for clinical parameters from 1 to 5 years.

**Table 8-1 Clinical Trial Comparison**

	<b>TAXUS I (Feasibility)</b>	<b>TAXUS II (Supportive)</b>	<b>TAXUS IV (Pivotal)</b>
<b>Study Type</b>	<ul style="list-style-type: none"> <li>prospective</li> <li>multi-center randomized</li> <li>double-blind</li> </ul>	<ul style="list-style-type: none"> <li>prospective</li> <li>multi-center randomized</li> <li>double-blind</li> <li>two sequential cohorts</li> </ul>	<ul style="list-style-type: none"> <li>prospective</li> <li>multi-center randomized</li> <li>double-blind</li> </ul>
<b>Number of Patients</b>	Total 61 (31 TAXUS Stent, 30 control)	Total 536 (Cohort I: 131 TAXUS, 136 Control) Cohort II: 135 TAXUS Stent, 134 Control)	Total 1314 Treatment A:662 Treatment B:652
<b>Dose Release Formulation</b>	SR (1 µg /mm <sup>2</sup> )	Cohort I = SR (1 µg /mm <sup>2</sup> ) Cohort II = MR (1 µg /mm <sup>2</sup> )	SR (1 µg /mm <sup>2</sup> )
<b>Lesion Criteria</b>	<i>De novo</i> lesions in native coronary artery ≤12mm in length and vessel diameter ≥3.0mm to ≤3.5mm in diameter	<i>De novo</i> lesions in native coronary artery artery ≤12mm in length and vessel diameter ≥3.0mm to ≤3.5mm in diameter	<i>De novo</i> lesions in native coronary artery artery <u>≥10mm and &lt;28mm</u> in length and vessel diameter ≥2.5mm to ≤3.75mm in diameter
<b>Stent Used</b>	NIR Stent	NIR Stent	Express Stent
<b>Antiplatelet Therapy</b>	6 month regimen of aspirin and clopidogrel.	6 month regimen of aspirin and clopidogrel.	6 month regimen of aspirin and clopidogrel.
<b>Follow-Up</b>	30 days, 6 months, 1 year – 5 years	30 days, 6 months, 1 year – 5 years	30 days, 4 months, 9 months, 1year – 5 years

## 8.2. TAXUS IV Pivotal Clinical Trial

**Objective:** The primary objective of this study was to demonstrate superiority of the TAXUS stent over bare metal control stent for reduction of the target vessel revascularization rate (TVR) 9 months post index procedure.

**Design:** This was a multi-center, prospective, randomized, double-blind study. Eligible patients were those presenting for stenting of de novo lesions of a single native coronary artery (RVD 2.5 to 3.75 mm) with a target lesion 10 to 28 mm in length and stenosis  $\geq 50\%$  in diameter, who were eligible for percutaneous transluminal coronary angioplasty (PTCA) and coronary artery bypass grafting (CABG), and had documented angina pectoris or functional ischemia. Patients were randomized to receive either a paclitaxel-eluting TAXUS Express™ slow-release (SR) coronary stent or uncoated Express™ coronary stent (bare metal control). Patients were followed-up at study visits at 1, 4, and 9 months post procedure. Extended follow-up via telephone call will be performed annually from year 1 to 5. Angiography and IVUS were performed at the 9-month follow-up visit for a subset of patients. The patients were substratified for medically treated diabetes and reference vessel diameter (RVD)  $< 3.0$  mm. In addition, there was a pre-specified sample size of 200 patients in the 32-mm stent group.

**Demographics:** A total of 1314 patients (ITT population) were enrolled and evaluable in this study: 662 in the TAXUS group and 652 in the Control group. Patients were well matched for baseline demographics with no statistically significant differences between groups.

**Results:** The primary endpoint, 9-month ischemia-driven TVR rate, was met with a reduction of 61% in the TAXUS group (4.7%) in the TAXUS group compared with 12.0% in Control ( $P < 0.001$ ). The cumulative MACE rate at 9 months was significantly ( $P < 0.001$ ) reduced from 15.0% (98/652) in the Control group to 8.5% (56/662) in the TAXUS group. The rate of TLR was significantly ( $P < 0.001$ ) reduced from 11.3% (74/652) in the Control group to 3.0% (20/662) in the TAXUS group. Stent thrombosis rates were low and comparable between groups. Nine-month angiographic follow-up was completed in 292 TAXUS and 267 Control patients. The in-stent binary restenosis rate was significantly lower in the TAXUS group (5.5% [16/291]) compared with Control (24.4% [65/266];  $P < 0.001$ ). The binary restenosis rate in the analysis segment was significantly lower in the TAXUS group (7.9% [23/291]) compared with Control (26.6% [71/267];  $P < 0.001$ ). Statistically significant improvements were also observed in late loss (in-stent and at the proximal and distal edges), minimal lumen diameter (MLD), and % diameter stenosis (%DS). Rates of aneurysm at 9 months were low and comparable between groups (0.7% [2/290] in TAXUS and 0.7% [2/267] in Control;  $P = 1.000$ ). Mean lumen volume at 9 months was significantly ( $P = 0.001$ ) larger in the TAXUS group (123.44 mm<sup>3</sup>) compared with Control (103.89 mm<sup>3</sup>), which resulted in a 55% reduction in neointimal volume from 41.48 mm<sup>3</sup> in Control to 17.56 mm<sup>3</sup> in TAXUS ( $P < 0.001$ ). Percent in-stent net volume obstruction (normalized vessel volume) was reduced 59%, from 29.4% in Control to 12.2% in TAXUS for ( $P < 0.001$ ). Rates of late-acquired incomplete apposition at 9 months were low and comparable between groups (1.1% [1/94] in TAXUS and 2.2% [2/93] in Control;  $P = 0.621$ ).

**Conclusion:** In selected patients, the TAXUS stent significantly reduced the rate of 9-month TVR rate (primary endpoint) as compared to control. This reduction was exclusively attributable to reduction in revascularization procedures (PCI and CABG) performed on the target lesion (TLR). QCA and IVUS analyses confirm this beneficial effect of the TAXUS stent with reductions of 55% to 77% in binary restenosis rate, MLD, %DS, late loss, and % in-stent net volume obstruction. These benefits within the TAXUS stent were achieved without increased edge stenosis and late loss at the proximal and distal edges, which were significantly lower in the TAXUS group. In addition, lower MACE rates in the TAXUS group, along with low and comparable rates of stent thrombosis, aneurysm and incomplete apposition between groups demonstrates the safety of the TAXUS stent.

**Table 8-2 TAXUS IV Principal Effectiveness and Safety Results**

	TAXUS (N=662)	Control (N=652)	Relative Risk [95% CI]	Difference [95% CI]	P
<b>Effectiveness Measures</b>					
Clinical Procedural Success	97.3% (643/661)	97.4% (635/652)	1.00 [0.98, 1.02]	-0.1% [-1.9%, 1.6%]	1.000
Technical Success	97.3% (643/ 661)	97.4% (635/ 652)	1.00 [0.98, 1.02]	-0.1% [-1.9%, 1.6%]	1.000
9-month Target Vessel Revascularization	4.7% (31/ 662)	12.0% (78/ 652)	0.39 [0.26, 0.59]	-7.3% [-10.2%, -4.3%]	<0.001
9-month In-stent restenosis	5.5% (16/ 291)	24.4% (65/ 266)	0.23 [0.13, 0.38]	-18.9% [-24.7%, -13.1%]	<0.001
9-month Analysis segment restenosis	7.9% (23/ 291)	26.6% (71/ 267)	0.30 [0.19, 0.46]	-18.7% [-24.8%, -12.5%]	<0.001
MLD (mm), Stented Segment					
Post-Procedure	2.65 +/- 0.42 ( 373) (1.53 , 3.92 )	2.67 +/- 0.41 ( 351) (1.67 , 3.76 )	NA	-0.01 [ -0.07,0.05]	0.658
9-Month	2.26 +/- 0.58 (291) ( 0.00,3.88 )	1.75 +/- 0.65 (266) ( 0.00,3.36)	NA	0.51 [ 0.41,0.61]	<0.001
MLD (mm), Analysis Segment					
Post Procedure	2.26 +/- 0.48 (374) ( 1.28,3.66)	2.29 +/- 0.50 (356) ( 1.01,3.62)	NA	-0.03 [ -0.10,0.04]	0.456
9-Month	2.03 +/- 0.55 (291) ( 0.00,3.32)	1.68 +/- 0.61 (267) ( 0.00,3.15)	NA	0.35 [0.26, 0.45]	<0.001
Diameter Stenosis, Stented Segment (%)					
Post Procedure	4.21 +/- 10.84 (373) (-35.16,31.35)	5.16 +/- 11.41 (351) (-54.40,40.86 )	NA	-0.95 [ -2.57, 0.67]	0.250
9-Month	17.43 +/-17.71 (291) (-27.83,100.00)	37.24 +/- 19.76 (266) (-7.61,100.00)	NA	-19.82 [-22.93,16.70]	<0.001
Diameter Stenosis, Analysis Segment (%)					
Post Procedure	19.16 +/- 9.67 (374) (-12.48,49.61 )	19.33 +/- 10.45 (356) ( -3.64,59.27 )	NA	-0.17 [ -1.63, 1.29]	0.822
9-Month	26.29 +/- 15.45 (291) ( 0.36,100.00 )	39.79 +/- 18.45 (267) ( 4.13,100.00 )	NA	-13.50 [-16.31,-10.68]	<0.001
Late Loss, Stented Segment (mm)	0.39 +/- 0.50 (291) ( -0.85 , 2.68 )	0.92 +/- 0.58 (266) ( -0.95 , 2.84 )	NA	-0.53 [ -0.62, -0.44]	<0.001
Late Loss, Analysis Segment (mm)	0.23 +/- 0.44 (291) ( -0.69 , 2.68 )	0.61 +/- 0.57 (267) ( -0.56 , 2.75 )	NA	-0.38 [ -0.47, -0.30]	<0.001
9-Month % Net Volume Obstruction	12.20 +/- 12.44 (81) (0.00 , 53.96)	29.40 +/- 14.05 (80) (0.00 , 64.46)	NA	-17.19 [-21.29,-13.10]	<0.001
9-Month Minimum Lumen Area	5.20 +/- 2.25 (88) (1.50, 13.50)	4.20 +/- 1.63 (86) (1.00, 7.90)	NA	1.00 [ 0.41, 1.58]	0.001
9-Month Neointimal Volume	18.41 +/- 18.71 ( 88 ) (0.00, 66.40)	41.08 +/- 23.52 (86) (0.00, 121.00)	NA	-22.67 [-28.98,-16.36]	<0.001

	TAXUS (N=662)	Control (N=652)	Relative Risk [95% CI]	Difference [95% CI]	P
<b>Safety Measures</b>					
In-hospital MACE	2.4% (16/662)	2.1% (14/ 652)	1.13 [0.55, 2.29]	0.3% [-1.3%, 1.9%]	0.854
Out-of-Hospital MACE to 9-months	6.2% (41/ 662)	13.0% (85/ 652)	0.48 [0.33, 0.68]	-6.8% [-10.0%, -3.7%]	<0.001
MACE to 9-months	8.5% (56/ 662)	15.0% (98/ 652)	0.56 [0.41, 0.77]	-6.6% [-10.0%, -3.1%]	<0.001
TVR to 9-months (Primary Endpoint)	4.7% (31/ 662)	12.0% (78/ 652)	0.39 [0.26, 0.59]	-7.3% [-10.2%, -4.3%]	<0.001
Stent Thrombosis (to 30 days)	0.3% (2/ 662)	0.3% (2/ 652)	0.98 [0.14, 6.97]	-0.0% [-0.6%, 0.6%]	1.000
Stent Thrombosis (to 9 months)	0.6% (4/ 662)	0.8% (5/ 652)	0.79 [0.21, 2.92]	-0.2% [-1.1%, 0.7%]	0.751
CVA to 9 months	1.5% (10/ 662)	0.8% (5/ 652)	1.97 [0.68, 5.73]	0.7% [-0.4%, 1.9%]	0.299
Serious Bleeding Complications	2.6% (17/ 662)	1.8% (12/ 652)	1.40 [0.67, 2.90]	0.7% [-0.9%, 2.3%]	0.454
Serious Vascular Complications	1.5% (10/ 662)	1.8% (12/ 652)	0.82 [0.36, 1.89]	-0.3% [-1.7%, 1.1%]	0.673
Platelet Disorders	0.6% (4/ 662)	0.8% (5/ 652)	0.79 [0.21, 2.92]	-0.2% [-1.1%, 0.7%]	0.751
Hematological Dyscrasia to 9 months	1.5% (10/ 662)	0.5% (3/ 652)	3.28 [0.91, 11.9]	1.1% [-0.0%, 2.1%]	0.091

Numbers are % (Count/Sample Size) or Mean±SD (N) (Min, Max). CI = Confidence Interval.

Difference = TAXUS SR – Control. Relative Risk (RR) = TAXUS SR / Control. SE of RR =  $\sqrt{\{(1-p_1)/n_{11} + (1-p_2)/n_{21}\}}$ .

SE of Difference =  $\sqrt{(p_1q_1/n_1 + p_2q_2/n_2)}$  for proportions, =  $\sqrt{[(1/n_1 + 1/n_2)\{(n_1-1)s_1^2 + (n_2-1)s_2^2\}]/(N-2)}$  for continuous variables.

95% CI of Difference = Diff±1.96·SE. 95% CI of RR = RR·exp(±1.96·SE).

P-values are two-sided and from Student's t test for continuous variables and Fisher's exact test for discrete variables.

Undef = Undefined.

All event data were adjudicated by the independent Clinical Events Committee (CEC). All QCA data were assessed by the Angiographic Core Laboratory. All IVUS data were assessed by the IVUS Core Laboratory

Primary endpoint is 9-month TVR.

Clinical Procedural Success: using the assigned study device to achieve an in-target-lesion diameter stenosis <30% in the average of 2 near-orthogonal projections, as visually assessed by the physician, without the occurrence of in-hospital MACE.

Technical success: successful delivery and deployment of the study stent to the target lesion, without balloon rupture, embolization, or use of a device outside the treatment strategy.

MLD = Minimum Lumen Diameter

9-Month MACE: the proportion of patients who experience a MACE up to the 9-month follow-up. MACE includes cardiac death, myocardial infarction (MI) including Q- and non-Q-wave MI, and target vessel revascularization (TVR).

30-Day MACE: binary MACE rate to 30 days post-procedure.

9-Month Restenosis: the proportion of patients who demonstrate ≥50% diameter stenosis of the target lesion by Quantitative Coronary Analysis (QCA) performed at the Angiographic Core Laboratory at the 9-month follow-up.

The Analysis Segment consists of the proximal edge, stent, and the distal edge, where each edge segment contains up to 5mm immediately outside the stent.

Serious Bleeding Complications included: hemorrhage (gastric ulcer, mediastinal, rectal, upper GI, and GI not specified), hematuria, hemoptysis, and hemothorax. Serious Vascular Complications included: hematoma (catheter site and not specified), hemorrhage (catheter site and retroperitoneal), arterial injury, and vascular pseudoaneurysm. Platelet disorders included thrombocytopenia. Hematologic dyscrasia included: anemia, and pancytopenia.

### 8.3. TAXUS II

**Objective:** The primary objective of this study was to evaluate the safety and effectiveness of the TAXUS NIRx™ Paclitaxel-Eluting Coronary Stent Systems (1 µg /mm<sup>2</sup> of paclitaxel incorporated into slow-release formulation) compared with a matched uncoated control stent.

**Design:** This was a prospective, double-blind comparison of the safety and effectiveness of the TAXUS NIRx™ (SR) with a uncoated control (bare metal) stent. Eligible patients had documented angina pectoris and a single *de novo* lesion in a native coronary artery measuring ≤ 12 mm in length with a visual reference diameter ≥ 3.0 mm and ≤ 3.5 mm. Time points assessed were 1, 6, and 12 months, and every year for 4 more years after stent placement (at 12 months telephone interviews replaced site visits and only MACE clinical parameters were assessed).

**Demographics (Cohort I Slow Release):** A total of 131 patients were randomized to the TAXUS NIRx™ (SR) Stent group and 136 patients to the uncoated control group. There were no clinically significant differences between groups with respect to baseline

demographics or clinical characteristics. A statistically significantly higher Canadian Cardiovascular Society Classification (CCS) Class was noted in the uncoated control group as compared to the TAXUS-SR group ( $P=0.0104$ ).

**Results:** 6-month percent in-stent net volume obstruction (primary endpoint) as determined by IVUS was statistically significantly lower in the TAXUS NIRx™ (SR) Stent treatment group as compared with the uncoated control group (7.85% versus 23.17%, respectively,  $p<0.0001$ ). In-stent restenosis, defined as restenosis occurring in the stented segment only and determined by Quantitative Coronary Angiography (QCA) analysis for the TAXUS NIRx™ (SR) Stent treatment group was 2.3% as compared to 17.9% for the uncoated control group. This difference was statistically significant ( $p<0.0001$ ). Analysis segment restenosis, defined as restenosis occurring in the stented segment and the area of the vessel  $\pm 5$  mm proximal and distal to the stent was 5.5% for the TAXUS NIRx™ (SR) Stent group as compared to 20.1% for the uncoated control group. At the 6-month time-point, statistically significant improvements were also observed in late loss, minimal lumen diameter (MLD), and % diameter stenosis (%DS) for the TAXUS NIRx™ (SR) Stent group as compared to the uncoated control group. Statistically significantly lower rates for MACE were observed in the TAXUS NIRx™ (SR) Stent group as compared with the uncoated control group at 6-months follow-up (8.5% versus 19.5%, respectively,  $p=0.0125$ ), and 12-month follow-up (10.9% versus 22.0%, respectively,  $p=0.0191$ ) (Table 8-3). MACE-free survival was statistically significantly improved in the TAXUS-SR group as compared with the uncoated control group at both 6 and 12 months.

**Conclusion:** The slow-release formulation of the TAXUS NIRx™ (SR) Stent was safe in this population, and effectively reduced the processes that lead to restenosis. The primary efficacy endpoint was achieved in the TAXUS NIRx™ (SR) Stent treatment group and there were significant improvements versus the uncoated control group for other secondary efficacy endpoints. There were significant improvements in overall MACE rates as well as reintervention procedures required in the target lesion. No substantial differences were observed as compared to the uncoated control group with respect to safety assessments.

**Table 8-3 TAXUS II Principal Effectiveness and Safety Results**

	TAXUS II (SR) (N=131)	Control (N=136)	Relative Risk [95% CI]	Difference [95% CI]	P Value
<b>Effectiveness Measures</b>					
Clinical Procedural Success	95.4% (125/131)	93.4% (127/136)	1.02 [0.96, 1.08]	2.0% [-3.5%, 7.5%]	0.5976
Technical Success	97.7% (128/131)	98.5% (134/136)	0.99 [0.96, 1.03]	-0.8% [-4.1%, 2.4%]	0.6794
6-Month % Net Volume Obstruction	7.85±9.87 (118) (-0.05, 47.95)	23.17±18.19 (125) (-0.00, 77.07)	NA	-15.32 [-19.03, -11.61]	<0.0001
6-month In-stent restenosis	2.3% (3/128)	17.9% (24/134)	0.13 [0.04, 0.42]	-15.6% [-22.6%, -8.6%]	<0.0001
6-month Analysis segment restenosis	5.5% (7/128)	20.1% (27/134)	0.27 [0.12, 0.60]	-14.7% [-22.5%, -6.8%]	0.0004
<b>MLD (mm), Stented Segment</b>					
Post-Procedure	2.53±0.29 (128) (1.77, 3.19)	2.58±0.37 (135) (1.73, 3.57)	NA	-0.05 [-0.13, 0.03]	0.2132
6-Month	2.23±0.47 (128) (0.00, 3.39)	1.79±0.54 (134) (0.51, 3.02)	NA	0.44 [0.32, 0.56]	<0.0001
<b>MLD (mm), Analysis Segment</b>					
Post Procedure	2.15±0.37 (128) (1.10, 2.99)	2.23±0.43 (135) (1.27, 3.26)	NA	-0.08 [-0.17, 0.02]	0.1202
6-Month	2.01±0.46 (128) (0.00, 3.18)	1.70±0.49 (134) (0.51, 3.02)	NA	0.31 [0.20, 0.43]	<0.0001
<b>Diameter Stenosis, Stented Segment (%)</b>					
Post Procedure	10.90±6.52 (128) (-5.00, 29.00)	10.20±5.94 (135) (-6.00, 25.00)	NA	0.70 [-0.81, 2.20]	0.3659
6-Month	19.53±12.71 (128) (-3.00, 100.00)	31.77±17.11 (134) (-9.00, 79.00)	NA	-12.25 [-15.91, -8.59]	<0.0001
<b>Diameter Stenosis, Analysis Segment (%)</b>					
Post Procedure	23.07±9.27 (128) (7.50, 54.50)	21.24±8.41 (135) (5.00, 52.00)	NA	1.83 [-0.31, 3.97]	0.0943
6-Month	26.79±12.78 (128) (5.00, 100.00)	35.11±15.09 (134) (7.00, 79.00)	NA	-8.32 [-11.71, -4.93]	<0.0001
6-Month Late Loss (mm), Stented Segment	0.31±0.38 (127) (-0.54, 2.20)	0.79±0.45 (134) (-0.11, 2.09)	NA	-0.48 [-0.58, -0.38]	<0.0001
<b>Safety Measures</b>					
30-Day MACE	2.3% (3/131)	4.4% (6/136)	0.52 [0.13, 2.03]	-2.1% [-6.4%, 2.2%]	0.5010
6-Month MACE	8.5% (11/130)	19.5% (26/133)	0.43 [0.22, 0.84]	-11.1% [-19.4%, -2.8%]	0.0125
12-Month MACE	10.9% (14/129)	22.0% (29/132)	0.49 [0.27, 0.89]	-11.1% [-20.0%, -2.2%]	0.0191
TLR Free to 365 days	95.4%	87.4%	1.09 [1.01, 1.18]	8.0% [1.3%, 14.7%]	0.020
Stent Thrombosis ≤ 1 Day	0.8% (1/131)	0.0% (0/136)	Undef [Undef, Undef]	0.8% [-0.7%, 2.3%]	0.4906
Stent Thrombosis ≤ 365 Days	1.5% (2/131)	0.0% (0/136)	Undef [Undef, Undef]	1.5% [-0.6%, 3.6%]	0.2398

Numbers are % (Count/Sample Size) or Mean±SD (N) (Min, Max). CI = Confidence Interval.

Difference = TAXUS SR stent – Control. Relative Risk (RR) = TAXUS SR stent / Control. SE of RR =  $\sqrt{\{(1-p_1)/n_{11} + (1-p_2)/n_{21}\}}$ .

SE of Difference =  $\sqrt{(p_1q_1/n_1 + p_2q_2/n_2)}$  for proportions, =  $\sqrt{[(1/n_1 + 1/n_2)\{(n_1-1)s_1^2 + (n_2-1)s_2^2\} / (N-2)]}$  for continuous variables.

95% CI of Difference = Diff±1.96·SE. 95% CI of RR = RR·exp(±1.96·SE).

P-values are two-sided and from Student's t test for continuous variables and Fisher's exact test for discrete variables.

Undef = Undefined.

Primary endpoint is 6-Month Percent Stented Segment Net Volume Obstruction, determined by IVUS.

Event/success rates are number of patients with the outcome ÷ the number of patients evaluable for the outcome.

Clinical Procedural Success: using the assigned study device to achieve an in-target-lesion diameter stenosis <30% in the average of 2 near-orthogonal projections, as visually assessed by the physician, without the occurrence of in-hospital MACE.

6-Month MACE: the proportion of patients who experience a MACE up to the 6-month follow-up. MACE includes cardiac death, myocardial infarction (MI) including Q- and non-Q-wave MI, and target vessel revascularization (TVR).

30-Day MACE: binary MACE rate to 30 days post-procedure.

12-Month MACE: binary MACE rate to 365 days post-procedure.

6-Month Restenosis: the proportion of patients who demonstrate ≥50% diameter stenosis of the target lesion by Quantitative Coronary Analysis (QCA) performed at the Angiographic Core Laboratory at the 6-month follow-up.

The Analysis Segment consists of the proximal edge, stent, and the distal edge, where each edge segment contains up to 5mm immediately outside the stent.

#### 8.4. TAXUS I

**Objective:** The primary objective of this study was to demonstrate the 30-day safety and performance of coronary stenting using the TAXUS NIRx™ Paclitaxel-Eluting Coronary Stent System (TAXUS™ NIRx™ Stent) coated with  $1 \mu\text{g}/\text{mm}^2$  of paclitaxel incorporated into a slow-rate release formulation of Translute™ polymer for the treatment of *de novo* and restenotic coronary lesions, as compared to an uncoated NIR™ Stent control.

**Design:** This was a multi-center, prospective, randomized, double-blind study. Eligible patients were those presenting for stenting of *de novo* or restenotic lesions of a native coronary artery (with a target lesion  $\leq 12$  mm in length and stenosis between 50% and 99% in diameter), who were eligible for percutaneous transluminal coronary angioplasty (PTCA) and coronary artery bypass grafting (CABG), and had documented angina pectoris or functional ischemia. Patients were randomized to receive either a paclitaxel-eluting TAXUS NIRx™ (SR) Stent or an uncoated NIR™ Stent control.

Patients were followed during study visits at 1, 6, 9, 12 months, and 2 years post-procedure. Angiography and IVUS were performed at the 6-month follow-up visit for all patients. Extended follow-up will be performed annually from 2 to 5 years after the procedure by telephone call.

**Demographics:** Sixty-one patients were enrolled in the study: 31 in the TAXUS NIRx™ (SR) Stent group and 30 in the control group. Although there were more patients with Canadian Cardiovascular Society (CCS) Class III or IV angina in the control group, there were no statistically significant differences between groups with respect to baseline and demographic characteristics. The procedural, technical and acute clinical success was 100% for both groups.

**Results:** The primary endpoint, the 30-day MACE rate, was zero in both groups. The cumulative MACE rate at 180 days was 0% in the TAXUS NIRx™ Stent group compared with 7% (2/30) in the control group, and was 3% (1/31) and 10% (3/30), respectively at the 12-month time-point. No additional MACE events were reported in either the TAXUS NIRx™ (SR) Stent treatment group or control group. No additional MACE events were reported in either the TAXUS NIRx™ Stent treatment group or control group at two years and the rates remain unchanged at 3% (1/31) for TAXUS™ NIRx™ Stent and 10% (3/30) for control.

**Conclusion:** The TAXUS NIRx™ Stent coated with  $1 \mu\text{g}/\text{mm}^2$  paclitaxel in a slow-rate release formulation was safe and performance was superior to the uncoated NIR™ Stent control.

**Table 8-4 TAXUS I Principal Effectiveness and Safety Results**

Safety Measures and Other Clinical Events	TAXUS NIRx™ (SR) N=31	NIR™ Control N=30	p-value
<b>MACE (30-day)</b>	0% (0/31)	0% (0/30)	NA
<b>Cardiac Death</b>	0% (0/31)	0% (0/30)	NA
<b>Q-Wave MI</b>	0% (0/31)	0% (0/30)	NA
<b>TVR (CABG and/or PCI)</b>	0% (0/31)	0% (0/30)	NA
<b>MACE (12-Month )</b>	3% (1/31)	10% (3/30)	0.612
<b>Cardiac Death</b>	0% (0/31)	0% (0/30)	NA
<b>Q-Wave MI</b>	0% (0/31)	0% (0/30)	NA
<b>TVR (CABG and/or PCI)</b>	3% (1/31)	10% (3/30)	0.612
<b>MACE (2-Year)</b>	3% (1/31)	10% (3/30)	0.612
<b>Cardiac Death</b>	0% (0/31)	0% (0/30)	NA
<b>Q-Wave MI</b>	0% (0/31)	0% (0/30)	NA
<b>TVR (CABG and/or PCI)</b>	3% (1/31)	10% (3/30)	0.612
<b>Stent Thrombosis to 2 years</b>	0% (0/31)	0% (0/31)	NA
<b>QCA In-Stent Lesion Characteristics</b>			
<b>Pre-procedure</b>			
RVD, mm	2.99±0.46 (31)	2.94±0.52 (29)	0.699
MLD, mm	1.30±0.43 (31)	1.23±0.43 (29)	0.558
%DS	56.51±12.26 (31)	57.82±13.24 (29)	0.692
Lesion length, mm	10.70±3.27 (31)	11.89±4.93 (29)	0.272
<b>Post-procedure</b>			
MLD, mm			0.414
%DS	6.12±9.49 (31)	2.95±0.34 (31)	0.096
<b>6-Month follow-up</b>			
RVD, mm	3.02±0.47 (30)	3.01±0.53 (29)	0.899
MLD, mm	2.60±0.49 (30)	2.19±0.65 (29)	0.008
%DS	13.56±11.77 (30)	27.23±16.69 (29)	<0.001
Restenosis Rate ≥50%	0% (0/30)	10% (3/29)	0.112
Late lumen loss, mm	0.36±0.48 (30)	0.71±0.47 (26)	0.009
Loss index	0.22±0.29 (30)	0.45±0.29 (26)	0.004

Numbers are % (Count/Sample Size) or Mean±SD (N).

P-values are two-sided and from Student's t test for continuous variables and Fisher's exact test for discrete variables.

All event data were adjudicated by the independent Clinical Events Committee (CEC). All QCA data were assessed by the Angiographic Core Laboratory. All IVUS data were assessed by the IVUS Core Laboratory

Primary endpoint is 30-day MACE.

Event/success rates are number of patients with the outcome ÷ the number of patients evaluable for the outcome.

MLD = Minimum Lumen Diameter

RVD = Reference Vessel Diameter

% DS = Percent diameter stenosis

MACE includes cardiac death, myocardial infarction (MI) including Q- and non-Q-wave MI, and target vessel revascularization (TVR). binary MACE rate to 30 days post-procedure

MACE (30-day): the proportion of patients who experience a MACE up 30 days post-procedure

MACE (6-Months): the proportion of patients who experience a MACE up to 6 months post-procedure

MACE (12-month): the proportion of patients who experience a MACE up to 12 months post-procedure

MACE (2-year): the proportion of patients who experience a MACE up to 2 years post-procedure

Restenosis rate: the proportion of patients who demonstrate ≥50% diameter stenosis of the target lesion by Quantitative Coronary Analysis (QCA) performed at the Angiographic Core Laboratory at the 6-month follow-up.

## 9. Individualization of Treatment

See also 5.4 Precautions, Use in Special Populations and 5.5 Precautions, Lesion/Vessel Characteristics.

The risks and benefits should be carefully considered for each patient before use of the TAXUS Express<sup>2</sup> Paclitaxel-Eluting Coronary Stent System. Patient selection factors to be assessed should include a judgment regarding risk of prolonged anticoagulation. Stenting is generally avoided in those patients at heightened risk of bleeding (e.g., those patients with recently active gastritis or peptic ulcer disease).

Premorbid conditions that increase the risk of poor initial results or the risks of emergency referral for bypass surgery (diabetes mellitus, renal failure, and severe obesity) should be reviewed.

## 10. Specific Patient Populations

The safety and effectiveness of the TAXUS Express<sup>2</sup> Paclitaxel-Eluting Coronary Stent System has not been established for patients with any of the following characteristics:

- Patients with unresolved vessel thrombus at the lesion site.
- Patients with coronary artery reference vessel diameters < 2.5 mm or > 3.75 mm.
- Patients with lesions located in the saphenous vein grafts, in the unprotected left main coronary artery, ostial lesions, or lesions located at a bifurcation.
- Patients with diffuse disease or poor outflow distal to the identified lesions.
- Patients with a recent acute myocardial infarction where there is evidence of thrombus or poor flow.
- Patients with more than two overlapping stents.
- Patients for longer than 9 months follow-up.

The safety and effectiveness of using atherectomy devices or laser angioplasty catheters, to treat in-stent stenosis have not been established.

## 11. Patient Counseling Information

Physicians should consider the following in counseling patients about this product:

- Discuss the risks associated with stent placement.
- Discuss the risks associated with a paclitaxel-eluting stent.
- Discuss the risks/benefits issues for this particular patient.
- Discuss alteration to current lifestyle immediately following the procedure and over the long term.

## 12. How Supplied

**STERILE:** This device is sterilized with ethylene oxide gas. It is intended for single use only. Do not resterilize. Non-pyrogenic. Do not use if package is opened or damaged.

**CONTENTS** for (1) TAXUS Express<sup>2</sup> Over-The-Wire Stent System  
One (1) TAXUS Express<sup>2</sup> Over-The-Wire Stent System  
One (1) Instructions for Use Manual  
One (1) Patient Guide with Patient Implant Card

**CONTENTS** for (1) TAXUS Express<sup>2</sup> Monorail™ Stent System

- One (1) TAXUS Express<sup>2</sup> Monorail™ Stent System
- One (1) Instructions for Use Manual
- Two (2) CLIPIT® hypotube clips
- One (1) Flushing needle with luer fitting
- One (1) Patient Guide with Patient Implant Card

**STORAGE:** Protect from light. Do not remove from carton until ready to use. Store in a cool, dark, dry place. Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F).

**DISPOSAL INSTRUCTIONS:** After use, dispose of product and packaging in accordance with hospital, administrative and/or local government policy.

**13. Operators Instructions**

**13.1. Inspection Prior to Use**

Carefully inspect the sterile package before opening. Do not use after the “Use By” date. If the integrity of the sterile package has been compromised prior to the product “Use By” date (e.g., damage of the package), contact your local Boston Scientific Representative for return information. Do not use if any defects are noted.

**NOTE:** At any time during use of the Premounted Stent System, if the stainless steel proximal shaft has been bent or kinked, do not continue to use the catheter.

**13.2. Materials Required** (not included in Stent System package)

<b>Quantity</b>	<b>Material</b>
N/A	Appropriate guide catheter (see Table 1-1 – Device Component Description)
2-3	20 ml (cc) syringe
1,000u / 500cc	Normal heparinized saline
1	≤ 0.014 in. / 0.36 mm guidewire
1	Rotating hemostatic valve
N/A	Diluted contrast medium 1:1 with normal heparinized saline
1	Inflation device
1	Torque device
1	Pre-deployment dilation catheter
1	Three-way stopcock
1	Appropriate arterial sheath

**13.3. Preparation**

**13.3.1. Packaging Removal**

<b>Step</b>	<b>Action</b>
1.	Carefully remove the delivery system from its protective tubing for preparation of the delivery system. When using a Monorail™ system, do not bend or kink hypotube during removal.
2.	Remove the product mandrel and stent protector by grasping the catheter just proximal to the stent (at the proximal balloon bond site),

- and with the other hand, grasp the stent protector and gently remove distally.
3. A Monorail Catheter may be coiled once and secured using the coil clip (Clipit®) provided in the catheter package. Only the proximal shaft should be inserted into the Clipit® device; the clip is not intended for the distal end of the catheter.

NOTE: Care should be taken not to kink or bend the shaft upon application or removal of the coil clip.

### 13.3.2. Guidewire Lumen Flush

- | Step | Action   |
|------|--|
| 1.   | Flush Stent System guidewire lumen with normal heparinized saline. Use flushing needle supplied for the Monorail™ system.  |
| 2.   | Verify that the stent is positioned between the proximal and distal balloon markers. Check for bends, kinks and other damage. Do not use if any defects are noted. |

NOTE: Avoid manipulation of the stent during flushing of the guidewire lumen, as this may disrupt the placement of the stent on the balloon.

### 13.3.3. Balloon Preparation

- | Step | Action   |
|------|--|
| 1.   | Stent contact with any fluid is not recommended, as there is a possibility of initiating drug release. However, if it is absolutely necessary to flush the stent with saline, contact time should be limited (1 minute maximum). |
| 2.   | Prepare inflation device/syringe with diluted contrast medium.   |
| 3.   | Attach inflation device/syringe to stopcock; attach to inflation port. Do not bend the hypotube when connecting to inflation device/syringe.   |
| 4.   | With tip down, orient Stent System vertically.   |
| 5.   | Open stopcock to Stent System; pull negative for 15 seconds; release to neutral for contrast fill.   |
| 6.   | Close stopcock to Stent System; purge inflation device/syringe of all air.   |
| 7.   | Repeat steps 4 through 6 until all air is expelled. If bubbles persist, do not use device.   |
| 8.   | If a syringe was used, attach a prepared inflation device to stopcock.   |
| 9.   | Open stopcock to Stent System.   |
| 10.  | Leave on neutral.  |

### 13.4. Delivery Procedure

- | Step | Action  |
|------|---|
| 1.   | Prepare the vascular access site according to standard PTCA practice. |
| 2.   | Predilate the lesion/vessel with appropriate diameter balloon.        |

3. Maintain neutral pressure on inflation device attached to stent system.
4. Backload Stent System onto proximal portion of guidewire while maintaining guidewire position across target lesion.
5. Fully open rotating hemostatic valve to allow for easy passage of the stent and prevent damage to the stent.
6. Carefully advance the Stent System into the hub of the guide catheter. When using a Monorail™ system be sure to keep the hypotube straight. Ensure guide catheter stability before advancing the Stent System into the coronary artery.

NOTE: If unusual resistance is felt before the stent exits the guide catheter, do not force passage. Resistance may indicate a problem, and use of excessive force may result in stent damage or stent dislodgment from the balloon. Maintain guidewire placement across the lesion, and remove the Stent System and guide catheter as a single unit.

7. Advance the Stent System over the guidewire to target lesion under direct fluoroscopic visualization. Utilize the proximal and distal radiopaque balloon markers as a reference point. If the position of the stent is not optimal, it should be carefully repositioned or removed (See 5.10 Stent System Removal). The inside edges of the marker bands indicate both the stent edges and balloon shoulders. Expansion of the stent should not be undertaken if the stent is not properly positioned in the target lesion segment of the vessel.

NOTE: If unusual resistance is felt at any time during lesion access before stent implantation, the Stent System and the guide catheter should be removed as a single unit. (See 5.10 Stent System Removal).

8. Sufficiently tighten the rotating hemostatic valve. The stent is now ready to be deployed.

### 13.5. Deployment Procedure

Step	Action
------	--------

- |    |  |
|----|--|
| 1. | Inflate the delivery system expanding the stent to a minimum pressure of 9 atm (stent nominal pressure). Higher pressure may be necessary to optimize stent apposition to the arterial wall. Accepted practice generally targets an initial deployment pressure that would achieve a stent ID of about 1.1 times the reference vessel diameter (see Table 14-1). Balloon pressure must not exceed rated burst pressure of 18 atm (see Table 14-1). |
| 2. | Maintain inflation pressure for 15-30 seconds for full expansion of the stent.   |
| 3. | Deflate balloon by pulling negative on inflation device until balloon is fully deflated.   |
| 4. | Confirm stent position and deployment using standard angiographic techniques. For optimal results, the entire stenosed arterial segment should be covered by the stent. Fluoroscopic visualization during stent expansion should be used in order to properly judge the optimum expanded stent diameter as compared to the proximal and distal coronary artery diameter(s). Optimal expansion requires that  |

- the stent be in full contact with the artery wall. Stent wall contact should be verified through routine angiography or intravascular ultrasound (IVUS).
5. If stent sizing/apposition requires optimization, readvance the Stent System balloon, or another high-pressure, non-compliant balloon catheter of the appropriate size, to the stented area using standard angioplasty techniques.
  6. Inflate the balloon to the desired pressure while observing under fluoroscopy. Deflate the balloon (refer to product labeling and/or Table 14-1 for proper stent inflation pressure).
  7. If more than one TAXUS Express stent is needed to cover the lesion and balloon treated area, it is suggested that, to avoid the potential for gap restenosis, the stents be adequately overlapped. To ensure that there are no gaps between stents the balloon marker bands of the second TAXUS Express stent should be positioned inside of the deployed stent prior to expansion.
  8. Reconfirm stent position and angiographic result. Repeat inflations until optimal stent deployment is achieved.

### 13.6. Removal Procedure

- | <b>Step</b> | <b>Action</b>   |
|-------------|---|
| 1.          | Ensure balloon is fully deflated before device withdrawal.  |
| 2.          | Fully open rotating hemostatic valve.   |
| 3.          | While maintaining guidewire position and negative pressure on inflation device, withdraw Delivery System.   |
| 4.          | Monorail™ catheters may be coiled once and secured using the coil clip (Clipit®) (see 13.3 Preparation).  |
| 5.          | Repeat angiography to assess the stented area. If an adequate expansion has not been obtained, exchange back to the original stent delivery catheter or exchange to another balloon catheter of appropriate balloon diameter to achieve proper stent apposition to the vessel wall. |

14. **In Vitro Information**

**Table 14-1: Typical TAXUS Express Stent and Balloon Compliance**

Pressure (Atm)	2.50 mm Stent I.D. (mm)	2.75 mm Stent I.D. (mm)	3.00 mm Stent I.D. (mm)	3.50 mm Stent I.D. (mm)
9.0	2.50	2.75	3.00	3.50
10.0	2.55	2.81	3.06	3.57
11.0	2.60	2.86	3.12	3.64
12.0	2.65	2.91	3.17	3.69
13.0	2.69	2.95	3.21	3.75
14.0	2.72	2.99	3.26	3.80
15.0	2.76	3.03	3.30	3.85
16.0	2.79	3.06	3.33	3.89
17.0	2.82	3.10	3.37	3.93
18.0	2.85*	3.13*	3.40*	3.97*

\* Rated Burst Pressure. DO NOT EXCEED.

15. **Reuse Precaution Statement**

Contents supplied STERILE using an ethylene oxide (EO) process. Do not use if sterile barrier is damaged. If damage is found call your Boston Scientific representative.

For single patient use only. Do not reuse, reprocess or resterilize. Reuse, reprocessing or resterilization may compromise the structural integrity of the device and/or lead to device failure which, in turn, may result in patient injury, illness or death. Reuse, reprocessing or resterilization may also create a risk of contamination of the device and/or cause patient infection or cross-infection, including, but not limited to, the transmission of infectious disease from one patient to another. Contamination of the device may lead to injury, illness or death of the patient.

16. **Patient Information**

The following information is included in the package for physicians to provide to their patients.

- A Patient Information Guide which includes information on coronary artery disease, the implant procedure and the TAXUS Express<sup>2</sup>™ Paclitaxel-Eluting Coronary Stent System.
- A Patient Implant Card that includes both patient information and stent implant information.

17. **Warranty**

Boston Scientific Corporation (BSC) warrants that reasonable care has been used in the design and manufacture of this instrument. This warranty is in lieu of and excludes all other warranties not expressly set forth herein, whether express or implied by operation of law or otherwise, including, but not limited to, any implied warranties of merchantability or fitness for a particular purpose. Handling, storage, cleaning and sterilization of this instrument as well as other factors relating to the patient, diagnosis, treatment, surgical procedures, and other matters beyond BSC's control directly affect the instrument and the results obtained from its use. BSC's obligation under this warranty is limited to the repair or replacement of this instrument and BSC shall not be liable for any incidental or consequential loss, damage, or expense directly or

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