SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Stent, Iliac (NIO)

Device Trade Name: Express® LD Iliac Premounted Stent System

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

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P090003

Date of FDA Notice of Approval: March 05, 2010

Expedited: Not Applicable

II. INDICATIONS FOR USE

The Express LD Iliac Premounted Stent System is indicated for the treatment of atherosclerotic lesions found in iliac arteries up to 100 mm in length, with a reference diameter of 6 mm to 10 mm.

III. CONTRAINDICATIONS

Generally, contraindications for Percutaneous Transluminal Angioplasty (PTA) are also contraindications for stent placement. Contraindications associated with the use of the Express LD Iliac Premounted Stent System include:

- Patients who exhibit persistent acute intraluminal thrombus at the treatment site, following thrombolytic therapy
- Patients with uncorrected bleeding disorders or patients who cannot receive anticoagulation or antiplatelet aggregation therapy
- Persons with known allergies to stainless steel or its components (for example nickel)
- A lesion that is within or adjacent to the proximal or distal segments of an aneurysm
- Patients who experience the complication of arterial perforation or a fusiform or sacciform aneurysm during the procedure, preceding possible stent implantation
- Patients with excessive vessel tortuosity
- Patients with perforated vessels evidenced by extravasation of contrast media

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Express LD Iliac Premounted Stent System labeling.

V. DEVICE DESCRIPTION

The Express® LD Iliac Premounted Stent System consists of a balloon expandable stent premounted on an over-the-wire balloon delivery system. The device is designed for use in patients with atherosclerotic disease of the iliac arteries.

The Express LD Iliac stent is delivered by advancing the device over a guide wire, through the peripheral vasculature to the iliac artery. Once in place, the stent is subsequently expanded with the balloon on the stent delivery system. Following stent deployment, the delivery balloon may be inflated with additional pressure to optimize the stent luminal diameter and strut apposition to the vessel wall.

The proposed product matrix for this PMA is provided in **Table 1** below. Each stent size is available on both a 75 cm and a 135 cm length delivery system. The Express LD stent models are separated into Small Vessel and Large Vessel configurations according to vessel diameter to be treated.

Table 1: Express LD Iliac Device Matrix

Balloon Length (mm)	Stent Length (mm)	Balloon/Stent Diameter (mm)				
		6	7	8	9	10
20	17	H74938046620750[1] H74938047620130[2]	H74938046720750[1] H74938047720130[2]	H74938046820750[1] H74938047820130[2]		
30	27	H74938046630750[1] H74938047630130[2]	H74938046730750[1] H74938047730130[2]	H74938046830750[1] H74938047830130[2]		
	25				H74938046920750[1] H74938047920130[2]	H74938046102070[1] H74938047120130[2]
40	37	H74938046640750[1] H74938047640130[2]	H74938046740750[1] H74938047740130[2]	H74938046840750[1] H74938047840130[2]	H74938046940750[1] H74938047940130[2]	H74938046104070[1] H74938047140130[2]
60	57	H74938046660750[1] H74938047660130[2]	H74938046760750[1] H74938047760130[2]	H74938046860750[1] H74938047860130[2]	H74938046960750[1] H74938047960130[2]	H74938046106070[1] H74938047160130[2]
		Small Vessel (SV) Stent Models			Large Vessel (LV) Stent Models	

1 75 cm Length Delivery System
2 135 cm Length Delivery System

Stent Description

The Express LD stent is a balloon expandable device fabricated from 316L stainless steel tubing. The stent is formed by laser cutting a geometric pattern from the tube. The geometric pattern consists of large and small sinusoidal bands interconnected by longitudinally oriented struts (see **Figure 1**). The stent is radiopaque under fluoroscopy.

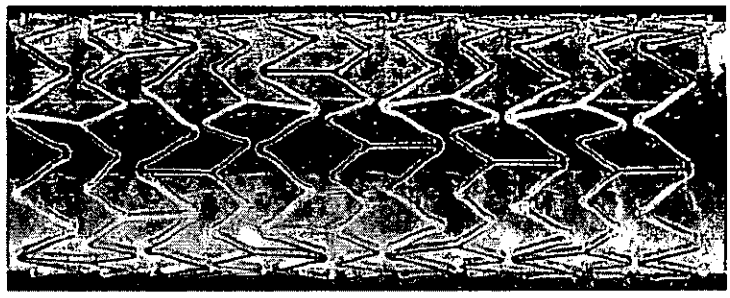


Figure 1: Photograph of Expanded Express® LD Iliac Stent

Stent Delivery System Description

The Express LD stent delivery system (SDS) is an over-the-wire balloon catheter with a dual lumen shaft and a Y-connector hub with luer lock fittings. One lumen is used to pass the catheter over 0.035" guidewires. The second lumen communicates with the balloon and is used to inflate and deflate the balloon during the procedure. The stent is centered on the balloon between two radiopaque marker bands to aid in positioning the system during the procedure. A hydrophilic coating is applied to the catheter shaft proximal to the balloon to enhance device tracking performance. The tip of the catheter is gradually tapered to facilitate advancement of the catheter through the stenosis. A drawing of the Express LD stent delivery system is shown in **Figure 2.**

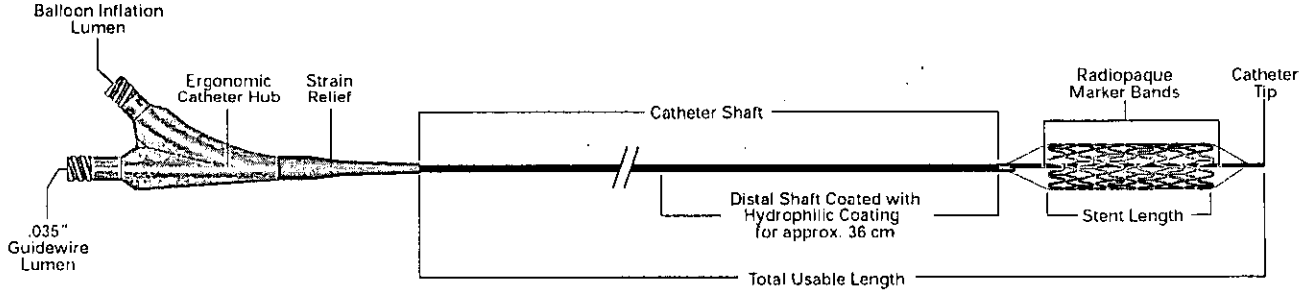


Figure 2: Express LD Stent Delivery System

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the treatment of peripheral artery disease: exercise, diet, drug therapy, percutaneous interventions, including percutaneous transluminal angioplasty (PTA) and placement of other marketed stents, and surgical bypass. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The Express LD Premounted Stent System has been commercially available as a biliary stent in the United States since October 2002. The Express LD Premounted Stent System has been available as a peripheral vascular stent since July 2002 in the following countries:

- Argentina
- Austria
- Bahrain
- Belgium
- Brazil
- Bulgaria
- Colombia
- Chile
- China
- Costa Rica
- Croatia
- Czech Rep.
- Cyprus
- Denmark
- Dominican Republic
- Egypt
- El Salvador
- Estonia
- Finland
- France
- Germany
- Greece
- Hong Kong
- Hungary
- Iceland
- India
- Indonesia
- Ireland
- Israel
- Italy
- Jordan
- Korea
- Kuwait
- Latvia
- Lebanon
- Libya
- Liechtenstein
- Lithuania
- Luxemburg
- Macedonia
- Malaysia
- Malta
- Mexico
- Moldova
- Morocco
- Netherlands
- Norway
- New Zealand
- Pakistan
- Panama
- Peru
- Philippines
- Poland
- Portugal
- Qatar
- Romania
- Saudi Arabia
- Serbia/Montenegro
- Singapore
- Slovakia
- Slovenia
- South Africa
- Spain
- Sweden
- Switzerland
- Taiwan
- Thailand
- Trinidad
- Turkey
- Ukraine
- United Kingdom
- Uruguay
- Venezuela
- Vietnam
- Virgin Islands
- Yemen

As of December 2008, approximately 204,000 units have been sold in the United States and approximately 112,000 units have been sold outside of the United States.

The Express LD Premounted Stent System has not been withdrawn from marketing in any country for any reason.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Based on literature, and the clinical and commercial history, the potential adverse events (e.g. complications) that may be associated with the implantation of stents in the iliac artery may include, but are not limited to:

- Abscess
- Aneurysm
- Arrhythmias
- AV fistula
- Bleeding / Hemorrhage
- Death
- Drug reaction, allergic reaction (including to antiplatelet agent, contrast medium, stent materials, or other)
- Embolization of device, air, plaque, thrombus, tissue, or other
- Emergency surgery to correct vascular complications
- Extremity ischemia / amputation
- Hematoma
- Hypotension or Hypertension
- Myocardial infarction
- Pseudoaneurysm formation
- Renal insufficiency or renal failure
- Restenosis of the stented artery
- Sepsis / Infection
- Stent migration
- Stent thrombosis
- Stroke, TIA, or other cerebrovascular accidents
- Vessel injury, including perforation, trauma, rupture, and dissection
- Vessel occlusion

For the specific adverse events that occurred in the clinical studies, please see Section X below.

IX. SUMMARY OF PRECLINICAL STUDIES

Following is a summary of the preclinical studies performed with the Express LD Premounted Stent System. Testing included: biocompatibility testing, *in vitro* (physical) device testing, sterility testing, shelf-life testing, packaging testing and animal studies.

A. Laboratory Studies

Biocompatibility Testing

A series of biocompatibility tests and USP Physiochemical tests were conducted to demonstrate that the components of the Express LD device are non-toxic. Tests were conducted on ethylene oxide (EO) sterilized bare metal stents and stent delivery systems. In all of these test systems, the materials were non-reactive and produced no greater response than the negative control employed in each test system.

All biocompatibility testing was conducted in accordance with:

- FDA Guidance for Industry and Staff: Non-Clinical Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems, January 13, 2005
- ISO 10993-1:2003, Biological Evaluation of Medical Devices: Evaluation and Testing

The tests summarized in **Table 2** have been conducted in support of the Express LD stent component as recommended for a permanent implant device contacting circulating blood.

Table 2: Stent Biocompatibility Testing Summary

Test Performed	Test Description	Results
Cytotoxicity	MEM Elution (ISO 10993-5)	Pass (non-cytotoxic)
Hemocompatibility	Hemolysis Direct Contact (ISO 10993-4)	Pass (non-hemolytic)
Genotoxicity	Bacterial Mutagenicity Test - Ames Assay (ISO 10993-3)	Pass (non-mutagenic)
	In Vitro Mouse Lymphoma (ISO 10993-3)	Pass (non-mutagenic)
Implantation	180-Day Porcine Direct Implantation Study including Thrombogenicity (ISO 10993-6)	Pass (no thrombosis)
	14-Day Rabbit Intramuscular Study (ISO 10993-6)	Pass (non-toxic)
	30-Day Rabbit Intramuscular Study (ISO 10993-6)	Pass (non-toxic)
	14-Day Mouse Repeat Dose Intravenous Toxicity (Subacute) (ISO 10993-11)	Pass (non-toxic)
	90-Day Rat Chronic Toxicity Study following Subcutaneous Implantation (ISO 10993-6 and ISO 10993-11)	Pass. (No evidence of systemic toxicity. Non-irritant.)
Metal Extracts	Saline Leaching of Solid Samples by ICP OES	Cr, Ni and Pt are non-detectable. Fe at 0.016 µg/mL

The tests summarized in **Table 3** have been performed in support of the Express LD Premounted Stent System as recommended for a limited exposure, externally communicating, circulating blood contact device. With the exception of the Direct Contact Hemolysis testing, all tests were performed on the stent delivery system with the stent loaded.

Table 3: Delivery System Biocompatibility Testing Summary

Test Performed	Test Description	Results
Cytotoxicity	MEM Elution (ISO 10993-5)	Pass (non-cytotoxic)
Sensitization	Sensitization (Kligman Maximization) (ISO 10993-10)	Pass (non-sensitizing)
Intracutaneous Reactivity	Irritation (ISO 10993-10)	Pass (non-irritant)
Acute Systemic Toxicity	Systemic Toxicity (Acute) (ISO 10993-11)	Pass (non-toxic)
Pyrogenicity	Systemic Toxicity: Materials Mediated Rabbit Pyrogen (ISO 10993-11)	Pass (non-pyrogenic)

Test Performed	Test Description	Results
Hemocompatibility	ASTM Hemolysis Assay – Extract Method (ISO 10993-4)	Pass (non-hemolytic)
	Partial Thromboplastin Time (ISO 10993-4)	Pass (Results comparable to negative control)
	In Vitro Hemocompatibility Assay (ISO 10993-4)	Results comparable to Negative Control. WBC: 85% RBC: 87% Hemoglobin: 87% Hematocrit: 87% Platelet: 93%
	Hemolysis Direct Contact (SDS only) (ISO 10993-4)	Pass (non-hemolytic)
Complement Activation	C3a and SC5b-9 Complement Activation Assay (ISO 10993-4)	Pass (negative for assay)
Volatile/Metal Extracts	USP Physicochemical Extracts	Pass
FTIR	NA	N/A – testing conducted for information purposes only.
Latex Detection	ASTM D6499-03 ELISA Inhibition Assay for Antigenic Protein (Natural Rubber Latex)	Below detection

In Vitro (Physical) Testing

A brief summary of the in vitro (physical) testing and analytical modeling performed is provided in **Table 4**. The table includes the device component tested, name of the test, the functional requirement of the test, and a summary of test results.

Table 4: Summary of In vitro (Physical) Testing Performed

In vitro Test	Significance / Relevance Functional Requirement	Summary of Tests / Results
Stent Material		
Material Composition Analysis	Suitability of material for implant	Chemical composition of 316L Stainless steel tubing meets chemical composition requirements of ASTM F138-00.
Ultimate Tensile Strength and Percent Elongation	Stent integrity during deployment and implant life	Percent elongation and tensile strength were measured for all tubing diameters. Percent elongation and tensile strength were within specification for all samples tested.

In vitro Test	Significance / Relevance Functional Requirement	Summary of Tests / Results
Corrosion Resistance	Suitability of material for implant	All stents tested met requirements for corrosion resistance per ASTM F2129-01.
Stent		
Dimensional Verification: Strut Width, Wall Thickness, Stent Length	Stent integrity and suitability of device for implant	Dimensional requirements for strut width, wall thickness and stent length are routinely measured during in-process testing.
Stent Expansion Uniformity	Uniformity of expansion following deployment	All stents, expanded to nominal diameter, met the specification.
Metal to Lumen Ratio	Metal to lumen contact for expanded stent	The metal to lumen ratio for each stent length and each labeled stent diameter met the requirement for metal to lumen surface contact.
Foreshortening	Deployed and expanded stent length	Percent of stent shortening when expanded to labeled diameter met requirements for stent length.
Recoil for Balloon Expandable Stents	Recoil following deployment	Stent diameter measurements with fully expanded delivery system and after delivery system removal met requirements set for recoil.
Stent Integrity / Stent Over-expansion	Integrity and suitability of material for implant when over-expanded	All stents tested were examined and exhibited no structural damage after over expansion.
Compression Resistance / Hoop Strength	Characterization of radial stiffness	Stent demonstrated acceptable compression resistance / hoop strength for all samples tested.
Stent Radial Stiffness and Radial Strength	Characterization of radial stiffness	Stent demonstrated acceptable radial stiffness when subjected to external radial loads.
Stress and Fatigue Analysis / Finite Element Analysis (FEA)	Structural integrity after stent fatigue	Results indicate a safe fatigue design in that the modeled stress of implant conditions will not result in failure of stent due to fatigue.
Accelerated Durability Testing / Pulsatile Fatigue	Failure modes detection over simulated 10-year use	No evidence of fatigue induced surface defects were observed in stents with 10-year simulated use.
Flex Fatigue	Cyclic loading forces during flexure	No stent fractures were seen in stents after flexing.
Magnetic Resonance Imaging (MRI) Safety and Compatibility	MRI compatibility	RF induced heating assessment – maximum temperature rise in testing would not impose a safety risk to the patient. Displacement Force – determined to be less than would be induced by gravitational forces. Magnetically induced torque – no torque interaction was demonstrated at 3.0 Tesla.

In vitro Test	Significance / Relevance Functional Requirement	Summary of Tests / Results
Radiopacity	Stent visibility using angiographic or radiographic imaging	Radiopacity of stents was demonstrated to be clinically acceptable.
Stent Conformability	Ability of the stent to bend to a particular curvature	All stents met the conformability specification of torque required to bend the stent.
Kink Resistance	Ability of the stent to reach a small radius of curvature without kinking	The results of the kink resistance test were considered acceptable for all curvatures tested.
Stent Delivery System		
System Flexibility	Ability to access target vessel	System met the flexibility/tracking specification.
Sheath Insertion	Ability to insert and withdraw the delivery system through the recommended size introducer sheath	Delivery systems were inserted and withdrawn through introducer sheaths with forces below the specified maximum allowed removal forces.
Balloon Rated Burst Pressure	Ability to meet the labeled burst specifications	All catheter models tested; burst pressure data provided in product labeling.
Multiple Inflation (Constrained and Unconstrained)	Balloon is capable of inflation within stent multiple times	All balloon models tested met required number of inflate/deflate cycles while positioned within a stent.
Stent Diameter to Balloon Pressure (Compliance Chart)	Delivery system balloon compliance	Values for balloon compliance included in product labeling.
Stent Deployment Accuracy	To confirm that stent deploys accurately and safely	All stents deployed at pressures below the maximum allowable deployment pressure with stents being deployed accurately in position relative to the delivery catheter markerbands.
Stent Inner Diameter	Stent to reach labeled diameter at nominal balloon pressure.	Balloon expansion to nominal pressures resulted in stents expanding to labeled diameter.
Proximal Balloon Bond Strength	Tensile strength of balloon bond	All bonds tested exceeded requirements of tensile strength.
Crossing Profile	Ability to access target vessel	All stent systems measured below maximum allowable profile specifications.
Balloon Inflation and Deflation Time	Inflate and deflate rate for each delivery system model	All models tested inflated to rated burst pressure (RBP) and deflated at rates below the specification.
Stent Securement Post Conditioning	Force required to displace stent from delivery system	All stent models remained in place on the delivery systems at forces greater than the specified minimum force specified for model.

Sterilization Verification

The Express LD Premounted Stent System is sterilized using an ethylene oxide sterilization process. Validation of the sterilization process was based on ISO 11135:1994, "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}.

Product Shelf Life Verification

Performance testing was conducted following accelerated aging to simulate 2 years of aging to demonstrate that the device performs within product specification for the labeled shelf life of 2 years.

Packaging Verification

Packaging verification testing was performed to demonstrate that the design of the device packaging will withstand the hazards of the distribution environment and that the sterility of the device will be maintained throughout the labeled shelf life of the product per ASTM F-88 (package peel strength) and ASTM F-1929 (packaging seal integrity).

B. **Animal Studies**

The Express LD stent has been evaluated in a preclinical animal study conducted to evaluate the 30-day and 180-day vascular response to the stent, and to assess the safety of the stent via clinical, physiologic, and gross tissue observations in a healthy porcine model under Good Laboratory Practices (GLP) per 21 CFR Part 58. Additionally, the animal study evaluated the acute performance of the Express LD Premounted Stent System in a healthy porcine model. A summary of the study is provided in **Table 5**.

Table 5: GLP Study to Assess the Safety and Vascular Response of Express LD Stents in Iliac Arteries of Domestic Swine

Study Objectives	Number of Animals / Time points / Devices Tested	Relevant Findings
Establish safety of Express LD stents. Determine mortality, morphology, morphometry parameters, device handling characteristics	• 10 animals • 30 and 180 days • 12 devices (6, 7, 8/37 mm)	• No device-related mortality (0/9, 0%) • Percent stenosis low at 30 days, further decreased at 180 days • Luminal thrombi <5% at 30 days, absent at 180 days • Vessels were widely patent at 30 and 180 days • >90% endothelialization at 180 days • Inflammation grades were none to mild at 30 days, increased at 180 days but not severe • Acceptable acute device performance for all parameters

This animal study demonstrated that the Express LD stent can be delivered as specified in the labeling and does not cause any adverse tissue, downstream iliac or systemic responses when placed in non-injured arteries of domestic swine.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study in Europe (the Netherlands, Belgium, the Czech Republic and Poland) and Canada to establish a reasonable assurance of safety and effectiveness of iliac stenting with the Express LD Stent System for the treatment of atherosclerotic lesions found in iliac arteries. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

Subjects were treated between January 7, 2004 and February 4, 2005. The database for this PMA reflected data collected through February 15, 2007 and included 151 subjects. One additional subject was enrolled and received a study stent but was de-registered due to lack of a signed written informed consent form. There were 10 investigational sites.

The study was a prospective, multi-center, single-arm clinical study designed to assess safety and effectiveness of the Express LD stent at 6 months as compared to an objective performance criterion (OPC) representative of the Palmaz® balloon-expandable stent as reported in the literature.

Subjects were enrolled after they had signed the written informed consent form, their eligibility had been established and a guide wire was successfully passed through the target lesion(s). The study was considered complete with regard to the primary endpoint after all enrolled subjects had completed the 6-month follow-up. The study was fully completed after enrolled subjects had completed the 24-month follow-up. All major adverse events, including target lesion revascularization, were adjudicated by an independent clinical events committee.

Subject demographics, clinical history, risk factors, pre- and post-procedure lesion characteristics, procedural characteristics, and outcome variables were summarized using descriptive statistics for continuous variables (mean, standard deviation, n, minimum and maximum) and frequency tables or proportions for discrete variables.

The primary objective of this study was to demonstrate that the mean % loss of luminal diameter at six months was lower than the pre-specified, literature-derived objective performance criterion (OPC) plus delta (15% + 5% = 20%) representative of the Palmaz® balloon-expandable stent. Secondary and tertiary endpoints were summarized using survival analysis for time-to-event endpoints, descriptive statistics for continuous variables and frequency tables or proportions for discrete variables. Analyses were based on subject, limb and/or lesion depending on the variables.

A core laboratory (Bio-Imaging B.V., Leiden, the Netherlands) was employed to review angiographic data (QVA). An independent, multidisciplinary Clinical Events Committee was utilized to categorize agreed upon clinical events according to study endpoints.

1. **Clinical Inclusion and Exclusion Criteria**

Enrollment in the MELODIE study was limited to patients who met the following inclusion criteria:

- Patient ≥ 18 years old
- Patient signed an informed consent form
- Patient with chronic symptomatic (Fontaine class IIa, IIb, and III) atherosclerotic disease in the iliac arteries
- Atherosclerotic de novo or restenotic lesions in the common and/or external iliac artery
- Baseline percent diameter stenosis of ≥ 50% at the target lesion
- Reference Vessel Diameter ≥ 5 mm and ≤ 10 mm
- Patient has at least one sufficient ipsilateral infrapopliteal run-off vessel
- Length of diseased segment(s) ≤ 10 cm and can be treated with a maximum of two overlapping Express LD Iliac stents

Patients were not permitted to enroll in the MELODIE study if they met any of the following exclusion criteria:

- Patients with chronic symptomatic atherosclerotic disease classified as Fontaine class I or IV
- Patients with acute leg ischemia
- Pregnant subjects
- Patients with uncorrected bleeding disorders (platelet count < 150,000/mm^3, or platelet count > 450,000/mm^3) or subjects who could not receive anticoagulant or antiplatelet aggregation therapy (e.g. subjects with active peptic ulcer or gastrointestinal bleeding)
- Patients with a known allergy to stainless steel.
- Patients with known anaphylactoid or other non-anaphylactic allergic reactions to contrast agents that could not be adequately pre-medicated prior to the index procedure
- Patients with a life expectancy of less than 24 months due to other medical co-morbid condition(s) that could limit the subject's ability to take part in the study, the subject's compliance with follow-up requirements or could impact on the scientific integrity of the study
- Patients currently participating in other investigational drug or device studies that had not completed the primary endpoint or that clinically interfered with the endpoints of this study
- Patients who had already participated in this study
- Patients with prior or planned bypass surgery at the target vessel(s)
- Patients with prior stent placement in the target vessel(s)
- Patients with any previous coronary intervention within 30 days of enrollment in this study, or planned coronary intervention within 30 days after enrollment into this study

Angiographic Exclusion Criteria:

- Patients in whom the origin of the profunda femoris and superficial femoral artery was occluded in the limb supplied by the iliac artery to be treated without planned surgical repair
- Patients with heavily calcified and excessive tortuous lesions as determined by angiography at the target site(s)
- Patients with target lesion(s) within or adjacent to the proximal or distal segment of an aneurysm
- Patients with persistent, acute intraluminal thrombus of the proposed target lesion(s) site post thrombolytic therapy
- Patients with perforated vessels evidenced by extravasation of contrast media.
- Patients with multiple lesions in the target vessel(s)

2. **Follow-up Schedule**

All subjects were scheduled to return for follow-up examinations at 30 days and 6 months post-index procedure, with additional follow-up at 12 months and 24 months post-index procedure.

The schedule of observations and assessments that took place during the study is presented in **Table 6** below.

Table 6: Study Events Schedule

	Before implantation stent	Post-Procedure	Hospital Discharge	30 Days (30± 14 days)	6 months (180 ± 30 days)	1 year (365 ± 60 days)	2 years (730 ± 60 days)
Screening							
Written Informed Consent	•						
Demographics and Medical History	•						
Pregnancy test in females of child-bearing potential	•				•	•	•
Platelet count	•						
Eligibility check	•						
Fontaine classification	•						
Baseline angiography	•						
ABI	•						
Angiography		•			•		
CTA						•	•
ABI			•	•	•	•	•
Fontaine classification				•	•	•	•
TLR			•	•	•	•	•
Safety Assessments							
Adverse and Serious Adverse (Device) Events		•	•	•	•	• (Only SA(D)Es)	
Major Adverse Events		•	•	•	•	•	•
Other assessments							
Antiplatelet therapy Anticoagulant therapy	•	•	•	•	•	•	•

3. Clinical Endpoints

With regards to safety, Adverse (Device) Events (AEs) were collected throughout the study with a pre-specified subset of events reviewed and adjudicated by an independent Clinical Events Committee.

With regards to effectiveness, the primary endpoint was angiographic mean percent loss of luminal diameter at 6 months post-procedure defined as ((Post-procedure MLD – Follow-up MLD)/Post-procedure MLD) x100 which was compared against an objective performance criterion (OPC) representative of the Palmaz® balloon-expandable stent as reported in the literature.

With regard to success/failure criteria, the objective of the study was to demonstrate non-inferiority of treatment with the Express LD stent compared to an OPC representative of treatment with the Palmaz® stent. The primary efficacy endpoint was the mean percent loss of luminal diameter at 6 months post-procedure as determined by angiography (% Late Loss). The % Late Loss was 16.2%. This value was compared to the OPC of 15% plus a non-inferiority margin (delta) of 5%. The study was deemed successful as a statistically significant primary hypothesis test result (p=0.0061) led to rejection of the null hypothesis of inferiority and a conclusion of non-inferiority.

B. Accountability of PMA Cohort

At the time of database lock, of 151 subjects enrolled in the PMA study, 92% (138/150) of subjects were available for analysis at the completion of the 6 month follow-up, which was the final visit evaluated for safety and effectiveness as the basis for the PMA submission . One hundred, twenty-three subjects (123) completed follow-up through the two year follow-up visit. **Table 7** details the follow-up compliance throughout the entire study.

Table 7: Subject Disposition - Clinical Follow-up Compliance

	Total
All Subjects Enrolled	151
All Treated Subjects	151
No 30-Day Clinical Follow-up	**4**
Prematurely Discontinued	0
Died	0
Device or Procedure Related Death	0
Withdrew Consent	0
Lost to Follow-up	0
Adverse Event	0
Other	0
Missed 30-Day Visit	4
30-Day Clinical Follow-Up Compliance	97.4% (147/151)

	Total
No 6-Month Clinical Follow-up	**13**
Prematurely Discontinued	4
Died	1
Device or Procedure Related Death	0
Withdrew Consent	1
Lost to Follow-up	2
Adverse Event	0
Other	0
Missed 6-Month Visit	9
6-Month Clinical Follow-Up Compliance	92.0% (138/150)
6-Month Angiographic Follow-Up (Subject)	122
6-Month Angiographic Follow-Up (Lesion)	130
No 12-Month Clinical Follow-up	**18**
Prematurely Discontinued	15
Died	3
Device or Procedure Related Death	0
Withdrew Consent	6
Lost to Follow-up	6
Adverse Event	0
Other	0
Missed 12-Month Visit	3
12-Month Clinical Follow-Up Compliance	89.9% (133/148)
12-Month CTA Follow-up (Subject)	123
12-Month CTA Follow-up (Lesion)	132
No 24-Month Clinical Follow-up	**28**
Prematurely Discontinued	26
Died	9
Device or Procedure Related Death	0
Withdrew Consent	8
Lost to Follow-up	8
Adverse Event	0
Other	1
Missed 24-Month Visit	2
24-Month Clinical Follow-Up Compliance	86.6% (123/142)
24-Month CTA Follow-up (Subject)	119
24-Month CTA Follow-up (Lesion)	127

C. **Study Population Demographics and Baseline Parameters**

The patient population in the MELODIE study is representative of the US population with PVD that is eligible to receive an iliac stent. The differences seen between the various iliac stenting study populations reported in the literature compared to MELODIE are minimal and do not affect the clinical interpretation of the study results. Baseline demographics and lesion characteristics of the MELODIE subjects are summarized in **Table 8** through **Table 10** below.

Table 8: Baseline Demographic Characteristics

Characteristic	(N =151 subjects)	[95% CI]
Demographics		
Male	74.8% (113/151)	[67.1%, 81.5%]
Female	25.2% (38/151)	[18.5%, 32.9%]
Age (yr)	60.1±8.4 (151) (43.0, 84.5)	[58.8, 61.5]
Risk factors		
Known Smoking, Ever	87.4% (132/151)	[81.0%, 92.3%]
current	62.1% (82/132)	[53.3%, 70.4%]
previous	37.9% (50/132)	[29.6%, 46.7%]
Known Medically Treated Diabetes	12.6% (19/151)	[7.7%, 19.0%]
Insulin Requiring	6.0% (9/151)	[2.8%, 11.0%]
Non-insulin Requiring	6.6% (10/151)	[3.2%, 11.8%]
Hypertension	60.3% (91/151)	[52.0%, 68.1%]
Hyperlipidemia	54.4% (80/147)	[46.0%, 62.6%]
Comorbidities		
History of Myocardial Infarction	22.0% (33/150)	[15.7%, 29.5%]
Angina Pectoris	14.7% (22/150)	[9.4%, 21.4%]
Stroke or Transient Ischemic Attack	7.3% (11/151)	[3.7%, 12.7%]
Renal Disease	1.3% (2/151)	[0.2%, 4.7%]
Chronic Obstructive Pulmonary Disease	8.7% (13/150)	[4.7%, 14.4%]
Previous treatment of atherosclerotic lesions in the iliac artery	10.7% (16/149)	[6.3%, 16.9%]
Previous vascular surgical intervention in legs	13.9% (21/151)	[8.8%, 20.5%]
Other Disease	28.5% (43/151)	[21.4%, 36.4%]

Table 9: Baseline Clinical Characteristics

Characteristic	(N = 151 subjects)	[95% CI]
Platelet count ($x10^3$)	234.0±59.4 (143) (115.0, 420.0)	[224.3, 243.8]
Claudication		
>1000 meters	1.3% (2/150)	[0.2%, 4.7%]
200 – 1000 meters	15.3% (23/150)	[10.0%, 22.1%]
< 200 meters	83.3% (125/150)	[76.4%, 88.9%]
Tissue Loss		
Right leg	0.0% (0/145)	[0.0%, 2.5%]
Left leg	0.0% (0/145)	[0.0%, 2.5%]

Table 10: Baseline Lesion Characteristics Determined by QVA

Characteristic	(N = 163 lesions)	[95% CI]
Target Lesion Location		
Right Common Iliac Artery	22.1% (36/163)	[16.0%, 29.2%]
Right Common Iliac Artery Extending Into External	3.1% (5/163)	[1.0%, 7.0%]
Right External Iliac Artery	19.0% (31/163)	[13.3%, 25.9%]
Left Common Iliac Artery	19.0% (31/163)	[13.3%, 25.9%]
Left Common Iliac Artery Extending Into External	3.7% (6/163)	[1.4%, 7.8%]
Left External Iliac Artery	33.1% (54/163)	[26.0%, 40.9%]
Minimum Lumen Diameter (MLD, mm)	3.3±1.4 (99) (0.0, 8.2)	[3.0, 3.5]
Reference Vessel Diameter (RVD, mm)	7.9±1.6 (99) (5.0, 13.3)	[7.5, 8.2]
Mean Lumen Diameter (mm)	6.9±1.4 (99) (4.0, 11.9)	[6.7, 7.2]
Percent Diameter Stenosis (%DS)	62.9±19.3 (116) (30.2, 100.0)	[59.4, 66.4]
Target Lesion Length (mm)	32.0±21.7 (99) (3.9, 99.1)	[27.7, 36.3]

D. **Safety and Effectiveness Results**

1. **Safety Results**

The analysis of safety was based on all subjects enrolled in the MELODIE study. **Table 11** and **Table 12** provide the observed adverse event experience reported in the MELODIE Clinical Study.

Table 11: Major Adverse Events (CEC Adjudicated), All Treated Subjects (N=151)

Events	(N=151 Subjects)		[95% CI]
	# of Events	Subjects with Events	
Procedure through Hospital Discharge			
MAE	1	0.7% (1/151)	[0.0%, 3.6%]
Device/Procedure Related Death	0	0.0% (0/151)	[0.0%, 2.4%]
TLR	1	0.7% (1/151)	[0.0%, 3.6%]
Distal Embolization	0	0.0% (0/151)	[0.0%, 2.4%]
Procedure through 30 Days			
MAE	1	0.7% (1/151)	[0.0%, 3.6%]
Device/Procedure Related Death	0	0.0% (0/151)	[0.0%, 2.4%]
TLR	1	0.7% (1/151)	[0.0%, 3.6%]
Distal Embolization	0	0.0% (0/151)	[0.0%, 2.4%]

Events	(N=151 Subjects)		[95% CI]
	# of Events	Subjects with Events	
Procedure through 6 Months			
MAE	10	6.3% (9/144)	[2.9%, 11.5%]
Device/Procedure Related Death	0	0.0% (0/144)	[0.0%, 2.5%]
TLR	10	6.3% (9/144)	[2.9%, 11.5%]
Distal Embolization	0	0.0% (0/144)	[0.0%, 2.5%]
Procedure through 12 Months			
MAE	13	8.9% (12/135)	[4.7%, 15.0%]
Device/Procedure Related Death	0	0.0% (0/135)	[0.0%, 2.7%]
TLR	13	8.9% (12/135)	[4.7%, 15.0%]
Distal Embolization	0	0.0% (0/135)	[0.0%, 2.7%]
Procedure through 24 Months			
MAE	17	10.2% (13/127)	[5.6%, 16.9%]
Device/Procedure Related Death	0	0.0% (0/127)	[0.0%, 2.9%]
TLR	17	10.2% (13/127)	[5.6%, 16.9%]
Distal Embolization	0	0.0% (0/127)	[0.0%, 2.9%]
Procedure through End of Study			
MAE	17	10.2% (13/127)	[5.6%, 16.9%]
Device/Procedure Related Death	0	0.0% (0/127)	[0.0%, 2.9%]
TLR	17	10.2% (13/127)	[5.6%, 16.9%]
Distal Embolization	0	0.0% (0/127)	[0.0%, 2.9%]

For each event type, rates are based on the number of subjects with at least one event.
"Events" numbers are total episodes of each type of event among all subjects.
"Subjects with Event" numbers are counts of subjects who experienced one or more episodes of the event.
"Events" numbers for "Any MAE" are the sum of the individual MAE component totals.
"Subjects with Event" numbers for "Any MAE" may be less than the sum of the individual "Subjects with Event" totals since a subject could have experienced multiple events of different types.

Table 12: Principal Safety Results; All Treated Subjects (N=151)

Safety Measures	(N=151 subjects) (N=163 lesions) (N=159 limbs)	[95% CI]
Lesion Based		
Target Lesion Revascularization		
In-Hospital	0.6% (1/163)	[0.0%, 3.4%]
30 Days	0.6% (1/163)	[0.0%, 3.4%]
6 Months	6.5% (10/154)	[3.2%, 11.6%]
12 Months	9.0% (13/145)	[4.9%, 14.8%]
24 Months	10.3% (14/136)	[5.7%, 16.7%]
End of Study	10.3% (14/136)	[5.7%, 16.7%]
Subject Based		
In-Hospital Major Adverse Events (MAE)	0.7% (1/151)	[0.0%, 3.6%]
Device/Procedure Related Death	0.0% (0/151)	[0.0%, 2.4%]
TLR	0.7% (1/151)	[0.0%, 3.6%]
Distal Embolization	0.0% (0/151)	[0.0%, 2.4%]
Major Adverse Events (MAE) through 30 Days	0.7% (1/151)	[0.0%, 3.6%]
Device/Procedure Related Death	0.0% (0/151)	[0.0%, 2.4%]
TLR	0.7% (1/151)	[0.0%, 3.6%]
Distal Embolization	0.0% (0/151)	[0.0%, 2.4%]
Major Adverse Events (MAE) through 6 Months	6.3% (9/144)	[2.9%, 11.5%]
Device/Procedure Related Death	0.0% (0/144)	[0.0%, 2.5%]
TLR	6.3% (9/144)	[2.9%, 11.5%]
Distal Embolization	0.0% (0/144)	[0.0%, 2.5%]
Major Adverse Events (MAE) through 12 Months	8.9% (12/135)	[4.7%, 15.0%]
Device/Procedure Related Death	0.0% (0/135)	[0.0%, 2.7%]
TLR	8.9% (12/135)	[4.7%, 15.0%]
Distal Embolization	0.0% (0/135)	[0.0%, 2.7%]
Major Adverse Events (MAE) between 24 Months	10.2% (13/127)	[5.6%, 16.9%]
Device/Procedure Related Death	0.0% (0/127)	[0.0%, 2.9%]
TLR	10.2% (13/127)	[5.6%, 16.9%]
Distal Embolization	0.0% (0/127)	[0.0%, 2.9%]
Major Adverse Events (MAE) through End of Study	10.2% (13/127)	[5.6%, 16.9%]
Device/Procedure Related Death	0.0% (0/127)	[0.0%, 2.9%]
TLR	10.2% (13/127)	[5.6%, 16.9%]
Distal Embolization	0.0% (0/127)	[0.0%, 2.9%]
Non-MAE Death		
Through 210 days	1.4% (2/144)	[0.2%, 4.9%]
Through 365 days	2.2% (3/137)	[0.5%, 6.3%]
Through 730 days	5.3% (7/131)	[2.2%, 10.7%]
Through End of Study	6.9% (9/131)	[3.2%, 12.6%]

2. **Effectiveness Results**

Primary, secondary, and tertiary safety and effectiveness results and major adverse event rates are summarized in **Table 13**, **Table 14**, **Table 15**, and **Figure 3**.

Table 13: Principal Effectiveness and Safety Results, All Treated Subjects (N=151)

Effectiveness and Safety Measures	**(N=151 subjects) (N=163 lesions) (N=159 limbs)**	**[95% CI]**
Effectiveness Measures		
Lesion Based		
Angiographic Mean Percent Loss of Lumen Diameter at 6 Months	16.2±18.4 (112) (-18.5, 100.0)	[12.8, 19.6]
Angiographic Binary Restenosis at 6 Months	5.6% (7/124)	[2.3%, 11.3%]
Angiographic Percent Diameter Stenosis at 6 Months	24.3±16.0 (124) (-9.5, 100.0)	[21.5, 27.1]
CTA Target Lesion Patency at 12 Months	97.2% (103/106)	[92.0%, 99.4%]
CTA Target Lesion Patency at 24 Months	94.1% (95/101)	[87.5%, 97.8%]
Technical Success	98.0% (147/150)	[94.3%, 99.6%]
Subject Based		
Procedural Success	97.1% (136/140)	[92.8%, 99.2%]
Clinical Success		
30 Days	88.2% (127/144)	[81.8%, 93.0%]
6 Months	83.1% (108/130)	[75.5%, 89.1%]
12 Months	82.5% (99/120)	[74.5%, 88.8%]
24 Months	78.8% (89/113)	[70.1%, 85.9%]
Limb Based		
Hemodynamic Success		
In-Hospital	75.3% (116/154)	[67.7%, 81.9%]
30 Days	79.3% (119/150)	[72.0%, 85.5%]
6 Months	71.2% (94/132)	[62.7%, 78.8%]
12 Months	60.2% (71/118)	[50.7%, 69.1%]
24 Months	57.9% (66/114)	[48.3%, 67.1%]
Safety Measures		
Lesion Based		
Target Lesion Revascularization		
In-Hospital	0.6% (1/163)	[0.0%, 3.4%]
30 Days	0.6% (1/163)	[0.0%, 3.4%]
6 Months	6.5% (10/154)	[3.2%, 11.6%]
12 Months	9.0% (13/145)	[4.9%, 14.8%]
24 Months	10.3% (14/136)	[5.7%, 16.7%]
End of Study	10.3% (14/136)	[5.7%, 16.7%]

Effectiveness and Safety Measures	(N=151 subjects) (N=163 lesions) (N=159 limbs)	[95% CI]
Subject Based		
In-Hospital Major Adverse Events (MAE)	0.7% (1/151)	[0.0%, 3.6%]
Device/Procedure Related Death	0.0% (0/151)	[0.0%, 2.4%]
TLR	0.7% (1/151)	[0.0%, 3.6%]
Distal Embolization	0.0% (0/151)	[0.0%, 2.4%]
Major Adverse Events (MAE) through 30 Days	0.7% (1/151)	[0.0%, 3.6%]
Device/Procedure Related Death	0.0% (0/151)	[0.0%, 2.4%]
TLR	0.7% (1/151)	[0.0%, 3.6%]
Distal Embolization	0.0% (0/151)	[0.0%, 2.4%]
Major Adverse Events (MAE) through 6 Months	6.3% (9/144)	[2.9%, 11.5%]
Device/Procedure Related Death	0.0% (0/144)	[0.0%, 2.5%]
TLR	6.3% (9/144)	[2.9%, 11.5%]
Distal Embolization	0.0% (0/144)	[0.0%, 2.5%]
Major Adverse Events (MAE) through 12 Months	8.9% (12/135)	[4.7%, 15.0%]
Device/Procedure Related Death	0.0% (0/135)	[0.0%, 2.7%]
TLR	8.9% (12/135)	[4.7%, 15.0%]
Distal Embolization	0.0% (0/135)	[0.0%, 2.7%]
Major Adverse Events (MAE) between 24 Months	10.2% (13/127)	[5.6%, 16.9%]
Device/Procedure Related Death	0.0% (0/127)	[0.0%, 2.9%]
TLR	10.2% (13/127)	[5.6%, 16.9%]
Distal Embolization	0.0% (0/127)	[0.0%, 2.9%]
Major Adverse Events (MAE) through End of Study	10.2% (13/127)	[5.6%, 16.9%]
Device/Procedure Related Death	0.0% (0/127)	[0.0%, 2.9%]
TLR	10.2% (13/127)	[5.6%, 16.9%]
Distal Embolization	0.0% (0/127)	[0.0%, 2.9%]
Non-MAE Death		
Through 210 days	1.4% (2/144)	[0.2%, 4.9%]
Through 365 days	2.2% (3/137)	[0.5%, 6.3%]
Through 730 days	5.3% (7/131)	[2.2%, 10.7%]
Through End of Study	6.9% (9/131)	[3.2%, 12.6%]

* All measurements taken after a confirmed TLR are excluded from this table.

"Technical Success" defined as successful delivery and deployment of the study stent to the target lesion with ≤ 30% residual stenosis as determined by angiography.

"Procedural Success" defined as Technical Success without the occurrence of Major Adverse Events during the procedure and immediately post-procedure until discharge.

"Clinical Success" defined as an improvement of the Fontaine classification by at least one class compared to the pre-procedure classification.

"Hemodynamic Success" defined as improved ankle brachial index (ABI) by ≥ 0.1 above pre-procedure value and not deteriorated by > 0.15 from the maximum post-procedure value.

Table 14: Primary Endpoint: Angiographic Mean % Loss of Luminal Diameter, All Treated Lesions (N=163) in All Treated Subjects (N=151)

	(N=112 paired lesions)	Literature OPC	Delta	p-value
Angiographic Mean % Loss of Luminal Diameter	16.21±18.42	15.0±16.0	5.0	0.0061

* All measurements taken after a confirmed TLR are excluded from this table.

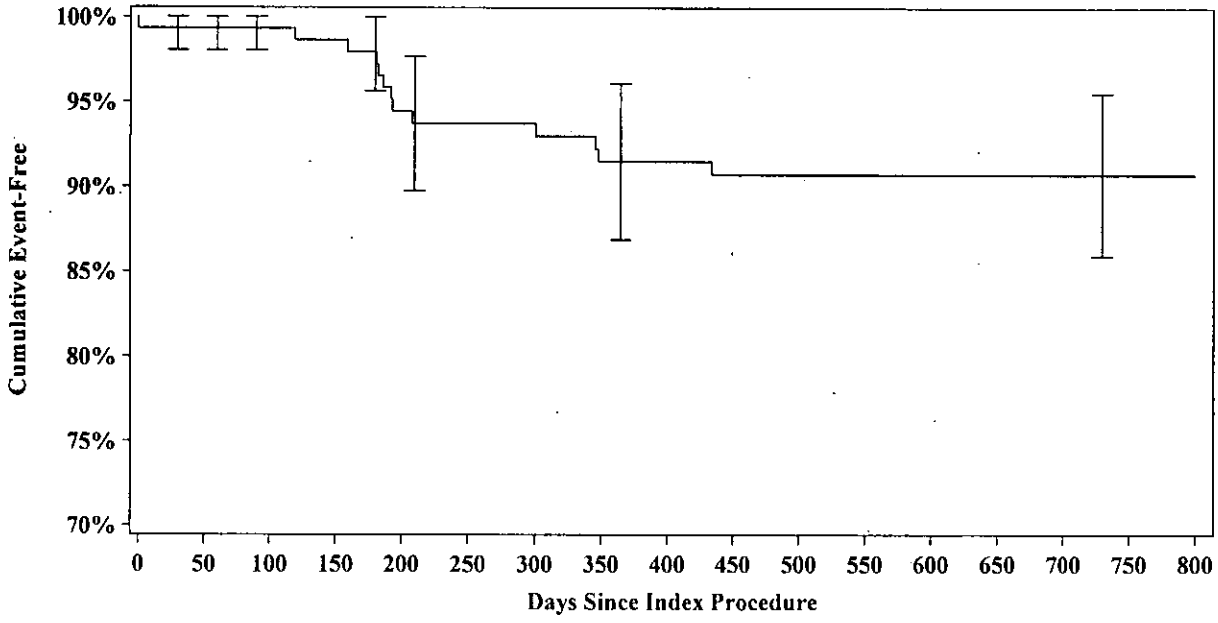
Table 15: Summary of Secondary and Tertiary Endpoints, All Treated Subjects (N=151)

Effectiveness and Safety Measures	(N=151 subjects) (N=163 lesions) (N=159 limbs)	[95% CI]
Effectiveness Measures		
Lesion Based		
Angiographic Binary Restenosis at 6 Months	5.6% (7/124)	[2.3%, 11.3%]
Angiographic Percent Diameter Stenosis at 6 Months	24.3±16.0 (124) (-9.5, 100.0)	[21.5, 27.1]
CTA Target Lesion Patency at 12 Months	97.2% (103/106)	[92.0%, 99.4%]
CTA Target Lesion Patency at 24 Months	94.1% (95/101)	[87.5%, 97.8%]
Technical Success	98.0% (147/150)	[94.3%, 99.6%]
Subject Based		
Procedural Success	97.1% (136/140)	[92.8%, 99.2%]
Clinical Success		
30 Days	88.2% (127/144)	[81.8%, 93.0%]
6 Months	83.1% (108/130)	[75.5%, 89.1%]
12 Months	82.5% (99/120)	[74.5%, 88.8%]
24 Months	78.8% (89/113)	[70.1%, 85.9%]
Limb Based		
Hemodynamic Success		
In-Hospital	75.3% (116/154)	[67.7%, 81.9%]
30 Days	79.3% (119/150)	[72.0%, 85.5%]
6 Months	71.2% (94/132)	[62.7%, 78.8%]
12 Months	60.2% (71/118)	[50.7%, 69.1%]
24 Months	57.9% (66/114)	[48.3%, 67.1%]
Safety Measures		
Lesion Based		
Target Lesion Revascularization		
In-Hospital	0.6% (1/163)	[0.0%, 3.4%]
30 Days	0.6% (1/163)	[0.0%, 3.4%]
6 Months	6.5% (10/154)	[3.2%, 11.6%]
12 Months	9.0% (13/145)	[4.9%, 14.8%]
24 Months	10.3% (14/136)	[5.7%, 16.7%]

Subject Based		
Major Adverse Events (MAE)		
In-Hospital	0.7% (1/151)	[0.0%, 3.6%]
30 Days	0.7% (1/151)	[0.0%, 3.6%]
6 Months	6.3% (9/144)	[2.9%, 11.5%]
12 Months	8.9% (12/135)	[4.7%, 15.0%]
24 Months	10.2% (13/127)	[5.6%, 16.9%]

All measurements taken after a confirmed TLR are excluded from this table.

The Kaplan-Meier curve for all pivotal subjects is presented in **Figure 3.** As can be seen, major adverse events occur with acceptable rates throughout the study.



(N = 151 Subjects)	0	30	60	90	180	210	365	730	End of Study
Entered	151	150	149	145	144	141	129	123	71
Censored	0	1	4	1	1	6	3	51	71
At Risk	151	149.5	147	144.5	143.5	138	127.5	97.5	35.5
Events	1	0	0	0	2	6	3	1	0
Events/Month	30.0	0.0	0.0	0.0	0.7	6.0	0.6	0.1	0.0
Event Free	99.3%	99.3%	99.3%	99.3%	98.0%	93.7%	91.5%	90.7%	--
Std Error	0.7%	0.7%	0.7%	0.7%	1.2%	2.0%	2.3%	2.4%	--

Intervals are inclusive, e.g., interval 180 is defined as 91-180 days, inclusive.
Entered: # subjects eligible at the start of the interval.
Censored: # subjects censored during the interval.
At risk is # entered – half of # censored in the time interval.
Events: # subjects with events in the interval.
Survival rate estimates are from the Kaplan-Meier method, reported at each interval's end.
The standard error was calculated using Greenwood's formula.

Figure 3: Freedom from Major Adverse Events (CEC Adjudicated) to End of Study, Event-Free Survival ±1.96 SE, All Enrolled Subjects (N=151)

XI. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

A. Retrospective Performance Goal

To assess further the safety and effectiveness of the Express LD stent in the treatment of stenosed or occlusive atherosclerotic iliac artery disease, a composite safety and effectiveness performance goal was developed from contemporary literature, and retrospectively applied to the MELODIE data.

The endpoint for this retrospective performance goal is a composite of the following safety and effectiveness endpoints:

- procedure/device-related death to 30 days
- in-hospital MI
- TLR through 12 months (365 days)
- amputation of the target limb through 12 months (365 days)

Based on a review of the literature, the expected rate for this endpoint at 12 months was estimated to be 10%. Using a delta of 9%, the performance goal for this endpoint was 19%.

The observed rate of this endpoint in the MELODIE study was 11.1% with a one-sided 95% upper confidence limit of 16.7% (see **Table 16**). This is lower than the performance goal of 19%, further supporting the safety and effectiveness of iliac stenting with the Express LD stent.

Table 16: Analysis of 12-month Composite Safety and Effectiveness Endpoint for the MELODIE study, All Treated Subjects (N=151)

Endpoint	(N = 151 Subjects)	One-sided 95% upper CI to test the performance goal*
12-Month MAE	11.1% (15/135)	16.7%
Procedure/device-related death to 30 days	0.0% (0/135)	
In-hospital MI	0.7% (1/135)	
TLR to 12 months	8.9% (12/135)	
Amputation to 12 months	2.2% (3/135)	

* The hypotheses for testing the performance goal of 19% are: H_0: $\pi \geq 19\%$ and H_1: $\pi < 19\%$, where π is the rate of 12-month MAE for the MELODIE study. To conclude the Express LD stent is significantly less than the performance goal, the one-sided 95% upper confidence interval under H_0 from the MELODIE study must be less than 19%.

B. **Overlapping Stent Analysis**

An analysis was completed comparing outcomes in subjects with overlapping stents to those subjects without overlapping stents. Twenty-seven subjects in the MELODIE study had overlapping stents placed. **Table 17** shows the number of subjects that had overlapping stents by overlap configuration.

Table 17: Quantity of Overlapping Stent Configurations

Stent Size	27 mm	37 mm	57 mm
25 mm	0	1	0
27 mm	1	2	1
37 mm	[redacted]	8	7
57 mm	[redacted]	[redacted]	7

Table 18 displays outcomes in MELODIE subjects treated with overlapping stents compared to those without overlapping stents. In general, outcomes in patients treated with overlapping stents are similar to outcomes in patients not treated with overlapping stents. Technical, procedural and hemodynamic success endpoints were very similar between the two groups. There were no device or procedure related deaths and no instances of distal embolization in either group. Any conclusions drawn from **Table 18** must be interpreted with caution as the MELODIE study was not designed or powered to compare outcomes in patients with and without overlapping stents. It is generally known that there is a trend for more MAEs, particularly TVR, in patients with overlapped stents and longer lesions in the peripheral arteries, just as is seen in the coronary arteries.

Table 18: Principal Effectiveness and Safety Results, Patients with overlapping stents versus patients with no overlapping stents

	Subjects with overlapping stents		Subjects with no overlapping stents	
Effectiveness and Safety Measures	**(N=27 subjects) (N=34 lesions) (N=32 limbs)**	**[95% CI]**	**(N=124 subjects) (N=129 lesions) (N=127 limbs)**	**[95% CI]**
Effectiveness Measures				
Lesion Based				
Angiographic Mean Percent Loss of Lumen Diameter at 6 Months	18.3±22.4 (26) (-18.5, 100.0)	[9.7, 26.9]	15.6±17.1 (86) (-18.3, 100.0)	[12.0, 19.2]
Angiographic Binary Restenosis at 6 Months	11.1% (3/27)	[2.4%, 29.2%]	4.1% (4/97)	[1.1%, 10.2%]
Angiographic Percent Diameter Stenosis at 6 Months	28.2±19.3 (27) (8.8, 100.0)	[20.9, 35.5]	23.2±14.8 (97) (-9.5, 100.0)	[20.2, 26.1]
CTA Target Lesion Patency at 12 Months	90.9% (20/22)	[70.8%, 98.9%]	98.8% (83/84)	[93.5%, 100.0%]
CTA Target Lesion Patency at 24 Months	90.5% (19/21)	[69.6%, 98.8%]	95.0% (76/80)	[87.7%, 98.6%]
Technical Success	96.9% (31/32)	[83.8%, 99.9%]	98.3% (116/118)	[94.0%, 99.8%]

Effectiveness and Safety Measures	Subjects with overlapping stents (N=27 subjects) (N=34 lesions) (N=32 limbs)	[95% CI]	Subjects with no overlapping stents (N=124 subjects) (N=129 lesions) (N=127 limbs)	[95% CI]
Subject Based				
Procedural Success	96.2% (25/26)	[80.4%, 99.9%]	97.4% (111/114)	[92.5%, 99.5%]
Clinical Success				
30 Days	92.0% (23/25)	[74.0%, 99.0%]	87.4% (104/119)	[80.1%, 92.8%]
6 Months	91.3% (21/23)	[72.0%, 98.9%]	81.3% (87/107)	[72.6%, 88.2%]
12 Months	90.5% (19/21)	[69.6%, 98.8%]	80.8% (80/99)	[71.7%, 88.0%]
24 Months	95.0% (19/20)	[75.1%, 99.9%]	75.3% (70/93)	[65.2%, 83.6%]
Limb Based				
Hemodynamic Success				
In-Hospital	81.3% (26/32)	[63.6%, 92.8%]	73.8% (90/122)	[65.0%, 81.3%]
30 Days	80.6% (25/31)	[62.5%, 92.5%]	79.0% (94/119)	[70.6%, 85.9%]
6 Months	89.3% (25/28)	[71.8%, 97.7%]	66.3% (69/104)	[56.4%, 75.3%]
12 Months	73.9% (17/23)	[51.6%, 89.8%]	56.8% (54/95)	[46.3%, 67.0%]
24 Months	69.6% (16/23)	[47.1%, 86.8%]	54.9% (50/91)	[44.2%, 65.4%]
Safety Measures				
Lesion Based				
Target Lesion Revascularization				
In-Hospital	0.0% (0/34)	[0.0%, 10.3%]	0.8% (1/129)	[0.0%, 4.2%]
30 Days	0.0% (0/34)	[0.0%, 10.3%]	0.8% (1/129)	[0.0%, 4.2%]
6 Months	12.9% (4/31)	[3.6%, 29.8%]	4.9% (6/123)	[1.8%, 10.3%]
12 Months	16.1% (5/31)	[5.5%, 33.7%]	7.0% (8/114)	[3.1%, 13.4%]
24 Months	16.7% (5/30)	[5.6%, 34.7%]	8.5% (9/106)	[4.0%, 15.5%]
End of Study	16.7% (5/30)	[5.6%, 34.7%]	8.5% (9/106)	[4.0%, 15.5%]
Subject Based				
In-Hospital Major Adverse Events (MAE)	0.0% (0/27)	[0.0%, 12.8%]	0.8% (1/124)	[0.0%, 4.4%]
Device/Procedure Related Death	0.0% (0/27)	[0.0%, 12.8%]	0.0% (0/124)	[0.0%, 2.9%]
TLR	0.0% (0/27)	[0.0%, 12.8%]	0.8% (1/124)	[0.0%, 4.4%]

	Subjects with overlapping stents		Subjects with no overlapping stents	
Effectiveness and Safety Measures	**(N=27 subjects) (N=34 lesions) (N=32 limbs)**	**[95% CI]**	**(N=124 subjects) (N=129 lesions) (N=127 limbs)**	**[95% CI]**
Distal Embolization	0.0% (0/27)	[0.0%, 12.8%]	0.0% (0/124)	[0.0%, 2.9%]
Major Adverse Events (MAE) through 30 Days	0.0% (0/27)	[0.0%, 12.8%]	0.8% (1/124)	[0.0%, 4.4%]
Device/Procedure Related Death	0.0% (0/27)	[0.0%, 12.8%]	0.0% (0/124)	[0.0%, 2.9%]
TLR	0.0% (0/27)	[0.0%, 12.8%]	0.8% (1/124)	[0.0%, 4.4%]
Distal Embolization	0.0% (0/27)	[0.0%, 12.8%]	0.0% (0/124)	[0.0%, 2.9%]
Major Adverse Events (MAE) through 6 Months	12.0% (3/25)	[2.5%, 31.2%]	5.0% (6/119)	[1.9%, 10.7%]
Device/Procedure Related Death	0.0% (0/25)	[0.0%, 13.7%]	0.0% (0/119)	[0.0%, 3.1%]
TLR	12.0% (3/25)	[2.5%, 31.2%]	5.0% (6/119)	[1.9%, 10.7%]
Distal Embolization	0.0% (0/25)	[0.0%, 13.7%]	0.0% (0/119)	[0.0%, 3.1%]
Major Adverse Events (MAE) through 12 Months	16.0% (4/25)	[4.5%, 36.1%]	7.3% (8/110)	[3.2%, 13.8%]
Device/Procedure Related Death	0.0% (0/25)	[0.0%, 13.7%]	0.0% (0/110)	[0.0%, 3.3%]
TLR	16.0% (4/25)	[4.5%, 36.1%]	7.3% (8/110)	[3.2%, 13.8%]
Distal Embolization	0.0% (0/25)	[0.0%, 13.7%]	0.0% (0/110)	[0.0%, 3.3%]
Major Adverse Events (MAE) between 24 Months	16.7% (4/24)	[4.7%, 37.4%]	8.7% (9/103)	[4.1%, 15.9%]
Device/Procedure Related Death	0.0% (0/24)	[0.0%, 14.2%]	0.0% (0/103)	[0.0%, 3.5%]
TLR	16.7% (4/24)	[4.7%, 37.4%]	8.7% (9/103)	[4.1%, 15.9%]
Distal Embolization	0.0% (0/24)	[0.0%, 14.2%]	0.0% (0/103)	[0.0%, 3.5%]
Major Adverse Events (MAE) through End of Study	16.7% (4/24)	[4.7%, 37.4%]	8.7% (9/103)	[4.1%, 15.9%]
Device/Procedure Related Death	0.0% (0/24)	[0.0%, 14.2%]	0.0% (0/103)	[0.0%, 3.5%]
TLR	16.7% (4/24)	[4.7%, 37.4%]	8.7% (9/103)	[4.1%, 15.9%]
Distal Embolization	0.0% (0/24)	[0.0%, 14.2%]	0.0% (0/103)	[0.0%, 3.5%]
Non-MAE Death				
Through 210 days	0.0% (0/25)	[0.0%, 13.7%]	1.7% (2/119)	[0.2%, 5.9%]
Through 365 days	0.0% (0/25)	[0.0%, 13.7%]	2.7% (3/112)	[0.6%, 7.6%]

	Subjects with overlapping stents		Subjects with no overlapping stents	
Effectiveness and Safety Measures	**(N=27 subjects) (N=34 lesions) (N=32 limbs)**	**[95% CI]**	**(N=124 subjects) (N=129 lesions) (N=127 limbs)**	**[95% CI]**
Through 730 days	4.2% (1/24)	[0.1%, 21.1%]	5.6% (6/107)	[2.1%, 11.8%]
Through End of Study	4.2% (1/24)	[0.1%, 21.1%]	7.5% (8/107)	[3.3%, 14.2%]

* All measurements taken after a confirmed TLR are excluded from this table.

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

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

The data in this application support the reasonable assurance of safety and effectiveness of the Express LD Iliac Premounted Stent System when used in accordance with the indications for use.

Non-clinical studies, including biocompatibility testing, in vitro testing, sterilization testing, shelf life testing, packaging testing, and animal studies demonstrate that the stent will perform as intended. Specifically, the biocompatibility and in vivo animal testing that were conducted demonstrated that the acute and chronic in vivo performance characteristics of the product provide reasonable assurance of safety and are acceptable for clinical use. The in vitro engineering testing conducted on the stent and delivery system(s) demonstrated that the performance characteristics met the product specifications. The test results obtained from the sterilization testing demonstrated that the product can be adequately sterilized and is acceptable for clinical use. The shelf-life testing demonstrated that the product can be labeled with a shelf life of 2 years.

The MELODIE study demonstrated that the Express LD stent is safe and effective in the treatment of stenosed or occlusive atherosclerotic iliac artery disease. Specifically, the primary efficacy endpoint was met. At six months post-implantation, the angiographic mean percent loss of luminal diameter for the Express LD stent was 16.2%±18.4% with an upper 95% confidence bound of 18.7%, which was lower than the OPC plus delta value of 20.0% (15% plus 5% delta) representative of the Palmaz® balloon-expandable stent (p=0.0061). Angiographic binary restenosis at 6 months was 5.6%. Computer tomographic angiography (CTA) performed at the 12-month and 24-month follow-up visits demonstrated maintained target lesion patency (%DS<50%) of 97.2% and 94.1%, respectively. Clinical and hemodynamic effectiveness were also demonstrated. Eighty-eight percent of MELODIE subjects improved by at least one Fontaine class 30 days after the procedure, with improvement maintained through the 24-month conclusion of the study for 79% of subjects. The percent of subjects with Fontaine Stage IIb symptoms or

worse improved from 84.1% pre-procedure to 16.8% at 24 months ($p<0.0001$). Ankle-brachial index improved from 0.68 at baseline to 0.87 at 24 months ($p <0.0001$). The MELODIE study demonstrated an acceptable safety profile for Express LD Iliac Premounted Stent System. The incidence of MAE at 24 months was low (10.2%), consisting only of TLR. There was no distal embolization or device/procedure-related death. Of the nine deaths occurring in the 24-month study period, three were from cardiovascular causes, five were from cancer, and one from respiratory insufficiency.

Outcomes in patients treated with overlapping stents are similar to outcomes in patients not treated with overlapping stents. Technical, procedural and hemodynamic success endpoints were similar between the two groups. There were no device or procedure related deaths and no instances of distal embolization in either group.

Additionally, retrospective assessment of the MELODIE data using a contemporary literature-derived composite performance goal further supports the safety and effectiveness of the Express LD stent in the treatment of stenosed or occlusive atherosclerotic iliac artery disease. The 12-month composite safety and effectiveness rate in the MELODIE study was 11.1% with a one-sided 95% upper confidence limit of 16.7%, as compared to the performance goal of 19%.

XIV. CDRH DECISION

CDRH issued an approval order on March 05, 2010.

The applicant's manufacturing facilities were inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

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

Post-approval Requirements and Restrictions: See approval order.