Summary of Safety and Effectiveness Data (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Stent, Iliac (NIO)
Device Trade Name:	Epic™ Vascular Self-Expanding Stent System (Epic Stent System)
Applicant's Name and Address:	Boston Scientific Corporation One Scimed Place Maple Grove, MN 55311
Date(s) of Panel Recommendation	None
Premarket Approval Application (PMA) Number:	P110035
Date of FDA Notice of Approval:	April 13, 2012
Expedited:	Not Applicable

II. INDICATIONS FOR USE

The Epic Vascular Self-Expanding Stent System is indicated for the improvement of luminal diameter in patients with de novo or restenotic symptomatic atherosclerotic lesions up to 120 mm in length in the common and/or external iliac arteries, with a reference vessel diameter between 5 and 11 mm.

III. CONTRAINDICATIONS

There are no known contraindications.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Epic Vascular Self-Expanding Stent System Directions for Use (DFU).

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V. DEVICE DESCRIPTION

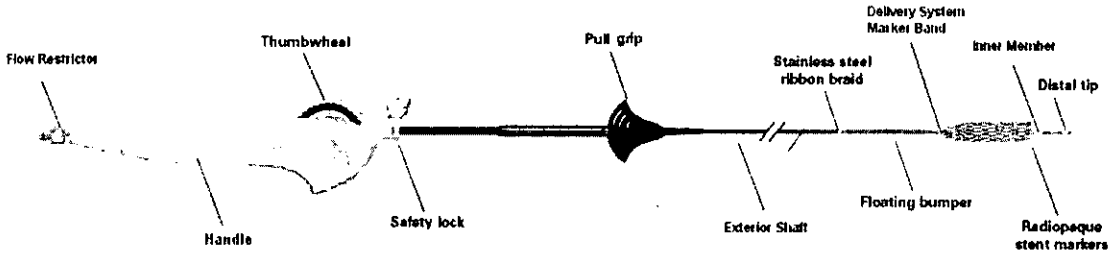
The Epic Stent System is comprised of two components: the implantable endoprosthesis and the stent delivery system. The stent is a laser cut self-expanding stent composed of a nickel titanium alloy (Nitinol). On both the proximal and distal ends of the stent, radiopaque markers made of tantalum increase visibility of the stent to aid in placement. The stent is constrained within a 6F (2.1 mm maximum Outside Diameter) delivery system. The delivery system is a coaxial design with an exterior shaft to protect and constrain the stent prior to deployment.

When ready to be implanted, the stent is deployed by retracting the exterior shaft of the delivery system. A radiopaque marker at the distal end of the delivery system aids in visibility during deployment. As the stent is exposed to body temperature, it expands to appose the vessel wall.

The Epic Stent System is available in stent diameters ranging from 6 – 12 mm and lengths ranging from 20 – 120 mm. The delivery system is an Over-The-Wire system compatible with 0.035" (0.89 mm) guidewires and 6F (2.1 mm) introducer or guide sheaths. The delivery system is offered in two shaft lengths (75 cm and 120 cm).

The Epic Stent System is illustrated in **Figure 1.**

Figure 1: Epic Stent System



The commercial matrix is shown in **Table 1** below:

Table 1: Epic Stent System Product Description

		Target Stent Length									
Stent Diameter	Model	(mm)	20	30	40	50	60	70	80	100	120
	SD	6	X	X	X	X	X	X	X	X	X
		7	X	X	X	X	X	X	X	X	X
	LD	8	X	X	X	X	X	X	X	X	X
		9	X	X	X	X	X	X	X	X	
		10	X	X	X	X	X	X	X	X	
	XLD	12		X	X	X	X				

*Actual labeled stent lengths for each stent diameter may vary slightly.

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VI. ALTERNATIVE PRACTICES AND PROCEDURES

Alternative procedures to treat occlusive disease of the iliac arteries include Percutaneous Transluminal angioplasty (PTA), PTA accompanied by stenting, stenting with another stent for which there is an approved indication, thrombolytic therapy, conservative medical management, exercise therapy, and/or surgical procedures. Atherosclerotic risk factors may be reduced through lifestyle modifications such as cessation of smoking, weight reduction, lipid, control, blood pressure control, and diabetes management.

VII. MARKETING HISTORY

The Epic Stent System has been marketed for a peripheral vascular use in the European Union and other countries since January 2008. There was one recall in April, 2008 due to catheter tip withdrawal issues, and the tip was redesigned. Since January 2009, the new device has been marketed for peripheral vascular use in the European Union and other countries with no market withdrawals. The list of countries where the Epic Stent System is commercially available follows.

Table 2: Countries where the Epic Stent System is Marketed

Albania	Djibouti	Kenya	Philippines
Algeria	Dominican Republic	Kuwait	Poland
Andorra	Dutch Antilles	Latvia	Portugal
Antigua/Barbuda	El Salvador	Lebanon	Qatar
Argentina	Estonia	Libya	Romania
Armenia	Finland	Liechtenstein	Saudi Arabia
Aruba	France	Lithuania	Serbia
Australia	Georgia	Luxembourg	Singapore
Austria	Germany	Macedonia	Slovakia
Bahamas	Great Britain	Malaysia	Slovenia
Bahrain	Greece	Malta	South Africa
Bangladesh	Guatemala	Martinique	Spain
Barbados	Guyana	Mauritania	Sri Lanka
Belgium	Haiti	Moldavia	Surinam
Belize	Honduras	Nepal	Sweden
Bermuda	Hong Kong	Netherlands	Switzerland
Brazil	Hungary	New Zealand	Trinidad & Tobago
Bulgaria	Iceland	Nicaragua	Tunisia
Canada*	India	Norway	Turkey
Chile	Ireland	Oman	United Arab Emirates
Colombia	Israel	Pakistan	Uruguay
Cyprus	Italy and San Marino	Palestinian Territory	Yemen
Czechoslovakia	Jamaica	Panama	
Denmark	Japan*	Paraguay	

*The Epic Stent System is marketed for biliary use in Canada and Japan.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Potential adverse events that may occur following intravascular stent implantation include, but are not limited to:

- Abscess
- Allergic reaction (to drug, contrast, device or other)
- Amputation
- Aneurysm
- Angina/coronary ischemia
- Arrhythmia
- Arteriovenous fistula
- Death
- Drug reactions
- Embolization (air, plaque, thrombus, device, or other)
- Entanglement of delivery system in deployed stent
- Fever
- GI bleeding
- Hemorrhage/hematoma
- Hypotension/hypertension
- Myocardial Infarction (MI)
- Need for urgent intervention or surgery
- Pseudoaneurysm
- Renal insufficiency or failure
- Restenosis of stented artery
- Sepsis/infection
- Stent fracture
- Stent migration
- Stent misplacement/jumping
- Stent thrombosis with possible neurological injury
- Stroke
- Thrombosis/thrombus
- Tissue ischemia/necrosis
- Vasospasm
- Vessel injury, examples include perforation, dissection, intimal tear, rupture
- Vessel occlusion

IX. SUMMARY OF PRECLINICAL STUDIES

A series of non-clinical laboratory studies were performed to evaluate the device.

A. Biocompatibility Studies

A series of Good Laboratory Practice (GLP) biocompatibility tests were conducted to demonstrate that the components of the Epic Stent System are biocompatible.

All biocompatibility testing was conducted in accordance with:

- Guidance for Industry and FDA Staff: Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems Guidance, April 2010
- Good Laboratory Practices Regulations (§21 CFR Part 58)
- EN ISO 10993-1, Biological Evaluation of Medical Devices

The tests summarized in **Table 3** have been conducted in support of the Epic stent component as recommended for a permanent implantable device contacting circulating blood for > 30 days.

Table 3: Biological Evaluation Tests Performed on Stent

Test Performed / Applicable EN ISO 10993 Part Number	Test Purpose	Acceptance Criteria	Results
Cytotoxicity MEM Elution / Part 5	To determine the potential for cytotoxicity	The test article meets test requirements if none of the cultures treated with the test article show greater than Mild reactivity (Grade 2).	Pass
Sensitization Guinea Pig Max / Part 10	To evaluate the allergenic potential or sensitizing capacity of a test article.	Skin reaction scores received by the test group must be equal or less than the scores received by the negative control group.	Pass
Irritation Intracutaneous Reactivity / Part 10	To screen test article extracts for potential irritation effects.	The requirements of the test are met if the difference between the test article and the control mean score is 1.0 or less (negligible or slight).	Pass
Acute Systemic Toxicity / Part 11	To screen test article extracts for potential systemic toxic effects.	Test is considered negative if none of the animals injected with the test article show a significantly greater biological reaction than the animals treated with the vehicle control.	Pass
Material-Mediated Rabbit Pyrogenicity / Part 11	To determine the presence of chemical pyrogens in extracts of a test article causing a febrile response in rabbits.	If no rabbit shows an individual rise in temperature of 0.5°C or more above baseline, the test article meets the requirements of the test.	Pass

Test Performed / Applicable EN ISO 10993 Part Number	Test Purpose	Acceptance Criteria	Results
Hemolysis Direct Contact / Part 4	To assess the hemolytic activity of the test article when in direct contact with blood.	Results are considered "pass" if the hemolytic index of test article is 5% or less.	Pass
Hemolysis Indirect Contact / Part 4	To assess the hemolytic activity of a test article extract in contact with blood.	Results are considered "pass" if the hemolytic index of test article extract is 5% or less.	Pass
Complement Activation / Part 4	Measurement of complement activation indicates whether a test article is capable of inducing a complement-induced inflammatory immune response in humans.	The concentration of C3a and SC5b-9 in serum exposed to the positive control should be significantly greater than those in the corresponding untreated serum. The test article will be considered positive or negative based upon a statistical comparison to the positive control.	Pass
In Vitro Hemocompatibility Assay / Part 4	To determine if the test article would adversely affect the various cellular and non-cellular components of the blood.	Test article results should be comparable to the results of the negative blood control or the reference material controls.	Pass
Partial Thromboplastin Time / Part 4	To determine the time citrated plasma exposed to a test material takes to form a clot when exposed to a suspension of phospholipid particles and calcium chloride.	Results are considered "pass" if the average clotting time of the test article is at least 50% compared to that of the negative control.	Pass
Genotoxicity Ames Assay / Part 3	To evaluate the mutagenic potential of leachables from the test article.	The test article is considered negative if it does not cause increase in 2-fold the mean revertant in all test strains of bacteria.	Pass
Genotoxicity Mouse Lymphoma / Part 3	To evaluate mutagenicity of the test agents.	The test article is considered negative if the test article-dosed cultures have a mutation frequency (MF) of less than 1.8 fold higher than that of the concurrent negative control plates.	Pass
Sub-chronic Toxicity, Implantation/ Part 6 & 11	To evaluate the potential for local and systemic toxicity of a test article implanted subcutaneously in rats for 13 weeks.	Test is considered negative if the test article did not induce a significantly greater biological reaction than the control article.	Pass
Implantation - In Vivo Thrombogenicity / Part 4 & 6	This test is to confirm there is no abnormal thrombosis related to the stent.	No significant differences in vascular response between test article and control stents in stent-related mortality or luminal thrombus.	Pass
Implantation / Part 6	To evaluate the potential for a local irritant or toxic response to material(s) implanted in direct contact with subcutaneous tissue of the rabbit.	Test is considered negative if the test article did not induce a significantly greater biological reaction than the control article.	Pass

Test Performed / Applicable EN ISO 10993 Part Number	Test Purpose	Acceptance Criteria	Results
USP Physicochemical Test for Plastics / Part 18	To determine the physical and chemical properties of an extract of a test material.	Non-volatile residue <15mg, residue on ignition <5mg (only performed when Non-volatile residue is > 15 mg), heavy metals <1ppm and buffering capacity <10ml.	Pass

The tests summarized in **Table 4** have been performed in support of the Epic delivery system catheter as recommended for externally communicating device contacting the circulating blood with limited exposure of < 24 hours.

Table 4: Biological Evaluation Tests Performed on Epic Delivery System Catheter

Test Performed / Applicable EN ISO 10993 Part Number	Test Purpose	Acceptance Criteria	Results
Cytotoxicity MEM Elution / Part 5	To determine the potential for cytotoxicity	The test article meets test requirements if none of the cultures treated with the test article show greater than Mild reactivity (Grade 2).	Pass
Sensitization Guinea Pig Maximization / Part 10	To evaluate the allergenic potential or sensitizing capacity of a test article.	Skin reaction scores received by the test group must be equal or less than the scores received by the negative control group.	Pass
Irritation Intracutaneous Reactivity / Part 10	To screen test article extracts for potential irritation effects.	The requirements of the test are met if the difference between the test article and the control mean score is 1.0 or less (negligible or slight).	Pass
Acute Systemic Toxicity / Part 11	To screen test article extracts for potential systemic toxic effects.	Test is considered negative if none of the animals injected with the test article show a significantly greater biological reaction than the animals treated with the vehicle control.	Pass
Material-Mediated Rabbit Pyrogenicity / Part 11	To determine the presence of chemical pyrogens in extracts of a test article causing a febrile response in rabbits.	If no rabbit shows an individual rise in temperature of 0.5°C or more above baseline, the test article meets the requirements of the test.	Pass
Hemolysis Direct Contact / Part 4	To assess the hemolytic activity of the test article when in direct contact with blood.	Results are considered "pass" if the hemolytic index of test article is 5% or less.	Pass
Hemolysis Indirect Contact / Part 4	To assess the hemolytic activity of a test article extract in contact with blood.	Results are considered "pass" if the hemolytic index of test article extract is 5% or less.	Pass

Test Performed / Applicable EN ISO 10993 Part Number	Test Purpose	Acceptance Criteria	Results
Complement Activation / Part 4	Measurement of complement activation indicates whether a test article is capable of inducing a complement-induced inflammatory immune response in humans.	The concentration of C3a and SC5b-9 in serum exposed to the positive control should be significantly greater than those in the corresponding untreated serum. The test article will be considered positive or negative based upon a statistical comparison to the positive control.	Pass
In Vitro Hemocompatibility Assay / Part 4	To determine if the test article would adversely affect the various cellular and non-cellular components of the blood.	Test article results should be comparable to the results of the negative blood control or the reference material controls.	Pass
Partial Thromboplastin Time / Part 4	To determine the time citrated plasma exposed to a test material takes to form a clot when exposed to a suspension of phospholipid particles and calcium chloride.	Results are considered "pass" if the average clotting time of the test article is at least 50% compared to that of the negative control.	Pass
USP Physicochemical Test for Plastics <661> / Part 18	To determine the physical and chemical properties of an extract of a test material.	Non-volatile residue <15mg, residue on ignition <5mg (only performed when Non-volatile residue is > 15 mg), heavy metals <1ppm and buffering capacity <10ml.	Pass

B. In Vitro Engineering Testing

In vitro engineering testing on the Epic Stent System was conducted, as applicable, in accordance with:

- *FDA Guidance for Industry and Staff: Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems*, April 18, 2010
- *FDA Guidance for Industry and Staff: Establishing Safety and Compatibility of Passive Implants in the Magnetic Resonance (MR) Environment,* August 2008

The in vitro engineering studies are summarized in **Table 5**. "Pass" denotes that the test results met product specifications and/or the recommendation in the above-referenced guidance documents.

Table 5: Stent and Delivery Catheter Engineering Testing

Test	Test Purpose	Acceptance Criteria	Results
Material Composition	To verify the composition of nitinol and tantalum stent materials and to measure the composition and thickness of the surface passivation layer	The stent material must conform to ASTM F2063-00 for the nitinol material and to ASTTM F560-04 for the tantalum material. The Epic stent exhibited surface composition and passive layer depth consistent with published literature for nitinol surfaces.	Pass
Shape Memory and Superelasticity of Intravascular Stents	To determine the Austenite finish transition temperature (Af) of the stent.	The Epic stent must have an Af temperature ≤ 30°C.	Pass The stent demonstrated an Af temperature between 17.5 °C and 27.2°C when tested per ASTM F2082.
Stent Corrosion Resistance - Post 10-year Pulsatile Fatigue Cycling	To document the potential for fretting, pitting and crevice corrosion of the Epic stent.	Both fretting corrosion and crevice and pitting corrosion are evaluated on stents after 10-year pulsatile fatigue cycling (400 million cycles). The stents must have no fretting corrosion greater than 75% of any cross section. Pitting and crevice corrosion was characterized and found no evidence of pitting or material loss when tested per ASTM F2129.	Pass
Stent Corrosion Resistance – Galvanic Corrosion	To document the potential for galvanic corrosion when coupled with stents of dissimilar materials.	The resistance to galvanic corrosion was characterized when the Epic stent was coupled separately with the Boston Scientific's Elgiloy Wallstent and tantalum material in an electrolyte solution. No significant stent mass loss was detected indicating that testing did not cause the Epic stents to lose material	Pass

<table>
<tr><th>Test</th><th>Test Purpose</th><th>Acceptance Criteria</th><th>Results</th></tr>
<tr><td>Stent Dimensional Verification</td><td>To characterize the unconstrained diameter of the Epic stent.</td><td>The unconstrained expanded diameter must be within -0.5 mm/+1 mm of its labeled diameter.</td><td>Pass</td></tr>
<tr><td>Percent Surface Area</td><td>To characterize the metal to lumen ratio of the stent.</td><td>The metal to lumen must be ≤ 30% for all stent sizes.</td><td>Pass</td></tr>
<tr><td>Foreshortening</td><td>To determine the foreshortening of the stent from the catheter constrained diameter to use diameter.</td><td>The Epic stent percent change in length must be < 10% for stent diameters 6-10mm and < 21% for the 12mm stent diameter.</td><td>Pass</td></tr>
<tr><td>Stent Integrity (Stent Over Expansion)</td><td>To verify the stent has no clinically significant defects or flaws after deployment</td><td>The stent must exhibited no structural damage or factures after deployment and over expansion. In addition overlapping Epic stents were inspected post 10-year pulsatile fatigue at 200x magnification and exhibited no cracks.</td><td>Pass</td></tr>
<tr><td>Radial Stiffness and Radial Strength</td><td>To characterize ability of the stent to resist collapse when subject to an external load.</td><td>The Epic stent must have a compression resistance > 8.5 g/mm for the 6-10 mm stent diameters and > 5.3 g/mm for the 12 mm stent diameter.</td><td>Pass</td></tr>
<tr><td>Radial Outward Force</td><td>To characterize the minimum and maximum outward radial force of the stent within use range.</td><td>The outward radial force of each stent diameter must meet the specifications shown below.

Outward Radial Force Specifications
<table>
<tr><th>Stent Size (mm)</th><th>Min Force (g/mm)</th><th>Max Force (g/mm)</th></tr>
<tr><td>6</td><td>≥ 1.9</td><td>≤ 17.8</td></tr>
<tr><td>7</td><td>≥ 1.9</td><td>≤ 16.5</td></tr>
<tr><td>8</td><td>≥ 1.9</td><td>≤ 15.2</td></tr>
<tr><td>9</td><td>≥ 1.9</td><td>≤ 13.9</td></tr>
<tr><td>10</td><td>≥ 1.9</td><td>≤ 12.6</td></tr>
<tr><td>12</td><td>≥ 1.5</td><td>≤ 11.4</td></tr>
</table></td><td>Pass</td></tr>
</table>

Test	Test Purpose	Acceptance Criteria	Results
Mechanical Properties - Pre processing	To evaluate nitinol material prior to processing.	The mechanical properties of the nitinol material must meet the following specifications. • Loading Plateau > 60ksi • Unloading Plateau > 17ksi • Ultimate Tensile Strength > 150ksi • Strain at Peak Load > 10% • Unrecovered Strain (permanent set after 8% strain) < 0.5%	Pass
Mechanical Properties - Post Processing	To verify the permanent set of the nitinol material post-thermal processing.	The permanent set of the nitinol material post-thermal processing must be <1.5%.	Pass
Stress/Strain Analysis/Fatigue Analysis (Finite Element Analysis)	To evaluate the durability and integrity of the Epic stent using Finite Element Analysis (FEA). The FEA analysis simulated the concentric expansion and compression of the Epic stent in vivo	The FEA analysis must demonstrate that the Epic stent maintains acceptable fatigue safety using the Goodman fatigue analysis.	Pass
Accelerated Durability Testing	To characterize the accelerated durability of overlapping Epic stents after 10-year pulsatile fatigue cycling.	No stent shall have type II or greater fracture occurrence after 400 million cycles (10 year simulation). No stent fractures were observed in any of the stent pairs after fatigue testing.	Pass
Magnetic Resonance Imaging (MRI) Safety and Compatibility	To evaluate the Epic stent for magnetically induced forced, magnetically induced torque, image artifact, and radio frequency (RF) induced heating when placed in field strengths of 1.5 and 3.0 Tesla.	The stent must meet the requirements of *Guidance for Industry and FDA Staff: Establishing Safety and Compatibility of Passive Implants in the MR (Magnetic Resonance) Environment*, ASTM F2052, ASTM F2213, ASTM F2182, and ASTM 2119 standards for MR Conditional. The conditions under which the device can be safety scanned are reflected in the Directions for Use (DFU).	Pass

Test	Test Purpose	Acceptance Criteria	Results
Radiopacity	To assess the radiopacity of the stent.	The radiopacity of the Epic stent while loaded in the delivery system and post stent deployment must be clinically acceptable when assessed During animal testing.	Pass
Crush Resistance	To verify the ability of the stent to recover to its size and shape after applying an external load.	The unconstrained expanded diameter of the Epic stent must be +1mm to -0.5mm of the labeled diameter post-crush.	Pass
Kink Resistance	To characterize the smallest radius of curvature the stent can withstand without kinking.	All stents tested recovered to the original shape and size; neither permanent deformation nor full collapse occurred during testing of the Epic stent.	Pass
Stent Marker Securement	To characterize the force required to dislodge a tantalum marker from the stent.	The force to dislodge the marker from the stent must be ≥0.7lbs.	Pass
Delivery System Dimensional Verification	To document dimensional characteristics of the Epic delivery system.	The catheter effective length must be within ± 1.0cm of the labeled catheter length. The delivery system working length profile must be 6F. The delivery system minimum inner diameter (ID) must allow a 0.036" mandrel or equivalent to pass through the lumen.	Pass
Delivery, Deployment and Retraction	To assess the ability of the delivery system to deliver the stent to the intended location and deploy the stent.	The force required to advance and withdraw the delivery system in a simulated clinical model must be < 690g (1.52lbs.). The Epic device must fully deploy the stent and the delivery system must remain fully intact.	Pass
Catheter Bond Strength	To evaluate the tensile strength of the delivery system bonds.	The tensile strength of the Epic delivery system bonds must meet product specifications (specification ranged from ≥ 1.57 lbs to ≥ 7.65 lbs depending on bond being tested).	Pass

Test	Test Purpose	Acceptance Criteria	Results
Delivery System Flexibility and Kink Test	To determine the susceptibility of the delivery system to kink.	The Epic delivery system must not kink and must maintain guidewire movement when placed on minimum radius of curvature of 1.5" (38.1 cm).	Pass
Torque Strength	To assess the ability of the delivery system to withstand torsional forces.	The delivery system must be able to be subjected to 2 handle rotations without catheter failure.	Pass
Delivery System Radiopacity	To assess the radiopacity of the stent.	The Epic delivery system markers must exhibited clinically acceptable radiopacity.	Pass

C. Packaging Testing

Packaging verification testing was performed to demonstrate that the design of the Epic Stent System packaging can withstand the hazards of the distribution environment and that the sterility of the device is maintained throughout the labeled shelf life.

D. Shelf Life Testing

Performance testing was conducted following 3 years of aging to demonstrate that the device and packaging performs within product specifications for a labeled shelf life of 3 years.

E. Sterilization

The Epic Stent System is sterilized using ethylene oxide (EO) gas and has been validated per AAMI / ANSI / ISO 11135:2007, *Sterilization of health care products - Ethylene oxide - Part 1: Requirements for the development, validation, and routine control of a sterilization process for medical devices.* Results from the sterilization studies show that the product satisfies a minimum Sterility Assurance Level (SAL) of 10^{-6} and residual levels were within acceptable ranges in accordance with EN ISO 10993-7:2008, *Biological Evaluation of Medical Devices - Part 7: Ethylene Oxide Sterilization Residuals.*

F. Animal Studies

The objective of the nonclinical study program for the Epic Stent System was to evaluate the safety, vascular compatibility, stent integrity, and device and delivery system performance of the Epic stent as compared to the commercially available Boston Scientific Wallstent® Endoprosthesis (Wallstent).

Preclinical evaluations of the Epic stent using the overlapping porcine external iliac artery stent model supported safety and vascular compatibility, with comparable results to Wallstent in key safety parameters including early and late in-stent healing. Epic stent and delivery system acute performance as assessed in the same porcine model demonstrated acceptable clinical performance. Studies were conducted in accordance with §21 CFR 58 (Good Laboratory Practices).

The results support the conclusion that the Epic Stent System is safe based on comparison to a commercially approved product, and is appropriate for commercial release. Summaries of the study designs and results are included in **Table 6**.

Table 6: Summary of Epic GLP Animal Studies

Device	Evaluation Time Points	Target # Stents/Animal & # of Animals	Vessel Location/ Approach	Testing Objective	Results
Porcine Safety Study 1					
Epic	30, 90, 180 days	2 overlap pair/ animal 45 animals	Ilio-femoral artery/ carotid approach	Compare vascular response of Epic to Wallstent Control in support of safety using mortality, adverse events, morphology, morphometry parameters	Results support safety and vascular compatibility for Epic and Wallstent: No device related mortality or adverse events. No stent thrombosis, no luminal thrombi observed. Complete endothelialization and tissue strut coverage at all time points. Inflammation, para-strut fibrin, and medial smooth muscle cell loss graded predominantly absent or mild. Neointimal area, medial area, and vascular wall stable over time.
Wallstent					
Porcine Safety Study 2					
Epic	Acute, 30, 180 days	2 overlap pair/animal 13 animals	Iliac artery/ carotid approach	Compare vascular response of Epic to Wallstent Control in support of safety using mortality, adverse events, morphology, morphometry parameters Evaluate device and delivery system handling characteristics	Results support safety and vascular compatibility for Epic and Wallstent: No device related mortality or adverse events. No stent thrombosis, no luminal thrombi observed. Complete endothelialization and tissue strut coverage at all time points. Para-strut fibrin and inflammation graded absent or mild. Neointimal area, medial area, and vascular wall stable over time. Acceptable acute device performance for all parameters.
Wallstent	30, 180 days	2 overlap pair/animal 8 animals			

Device	Evaluation Time Points	Target # Stents/Animal & # of Animals	Vessel Location/ Approach	Testing Objective	Results
Porcine Acute Performance Study					
Epic	Acute	2 non-overlapping stents/animal 6 animals	Iliac and femoral artery/ contralateral femoral approach	Evaluate device and delivery system handling characteristics using a contralateral approach model	Acceptable acute device performance for all parameters.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant collected clinical data through the ORION clinical trial to establish a reasonable assurance of safety and effectiveness of iliac stenting with the Epic Stent System for the treatment of atherosclerotic lesions found in iliac arteries. The trial was evaluated under IDE G080045. Data from this clinical trial were the basis for the PMA approval decision. A summary of the clinical trial is presented below. Additional data from a clinical study (SUMMIT) conducted in Germany was used to support a reasonable assurance of safety and effectiveness of iliac artery stenting using the 6.0 mm diameter and 120 mm length Epic Stent System for the treatment of subjects with atherosclerotic *de novo* and restenotic iliac artery disease (Section E – Additional Clinical Data).

A. STUDY DESIGN

The ORION clinical study was a prospective, single-arm, non-randomized clinical trial which was designed to determine whether the Epic Stent System showed acceptable performance at 9 months for primary stenting of iliac atherosclerotic lesions. The primary endpoint was the 9-month device- and/or procedure-related major adverse event (MAE) rate, adjudicated by an independent Clinical Events Committee (CEC). MAE was defined as death within 30 days, myocardial infarction (MI) that occurs during index hospitalization, target vessel revascularization (TVR) through 9 months, and/or amputation of index limb through 9 months. For the primary endpoint of 9-month MAE, an exact, one-sided 95% upper confidence bound was calculated and compared to the prespecified performance goal. The expected 9-month MAE rate of 8.0% for the Epic Stent System and for iliac artery stenting with self-expanding stents was based on published literature. The performance goal (17.0%) included this expected rate of 8.0% plus a margin of 9.0%.

There were 125 subjects enrolled at 28 investigational centers in the US. Subjects were enrolled from May 14, 2009, to December 14, 2010. The study was considered complete with regard to the primary endpoint when subjects completed 9-month follow-up evaluations. Additional follow-up is ongoing to 3 years.

Subjects were enrolled after they signed the written informed consent form, their eligibility had been established and the Epic Stent System had entered the body. All MAEs were adjudicated by an independent CEC.

Core laboratories were utilized to review angiographic (CardioVascular Institute at Beth Israel Deaconess Medical Center) and ultrasound data (VasCore). An independent, multidisciplinary CEC was utilized to adjudicate clinical events according to the study protocol.

1. **Clinical Inclusion and Exclusion Criteria**

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

   General:

   - Signed informed consent
   - At least 18 years old
   - Documented chronic, symptomatic iliac artery atherosclerotic disease (Rutherford/Becker category 1, 2, 3 or 4)
   - Lifestyle-limiting claudication or rest pain

   Angiographic:

   - De novo or restenotic lesions in the common and/or external iliac artery (applies to all target lesions if multiple)
   - Subjects with bilateral disease may have only one target lesion treated per side
   - Two target lesions may be treated with a maximum of two stents (if two target lesions are treated, each lesion must be covered with a maximum of one stent)
   - Length of diseased segment(s) $\leq$ 13 cm and treatment is planned with no more than 2 overlapped Epic stents
   - Baseline diameter stenosis $\geq$ 50% (operator visual assessment)
   - Reference vessel diameter $\geq$ 5 mm and $\leq$ 11 mm
   - At least one sufficient ipsilateral infrapopliteal run-off vessel
   - Origin of profunda femoris artery is patent

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

   General:

   - Target vessel with in-stent restenosis
   - Acute critical limb ischemia
   - Tissue loss (Rutherford/Becker category 5 or 6)
   - Any major amputations to the target limb

- Any minor amputation of the target limb in the last 12 months. If a minor amputation occurred greater than 12 months, stump needs to be completely healed.
- Life expectancy less than 24 months due to other medical co-morbid condition(s) that could limit the subject's ability to participate in the trial, limit the subject's compliance with the follow-up requirements, or impact the scientific integrity of the trial
- Known hypersensitivity or contraindication to contrast dye that, in the opinion of the investigator, cannot be adequately pre-medicated.
- Intolerance to antiplatelet, anticoagulant, or thrombolytic medications
- Platelet count < 150,000 mm^3 or > 600,000 mm^3
- Serum creatinine > 2.0 mg/dL
- Dialysis-dependent end stage renal disease
- Pregnancy
- Current participation in another drug or device trial that has not completed the primary endpoint or that may potentially confound the results of this trial
- Known allergy to Nitinol

Angiographic:

- Presence of arterial lesions (with the exception of renal, carotid or short, focal SFA lesions) requiring intervention within 30 days of the index procedure
- Superficial femoral artery occlusion in the limb supplied by target vessel
- Heavily calcified and/or excessively tortuous lesions in the target vessel as determined by angiography
- Target lesion is within or near an aneurysm
- Persistent, intraluminal thrombus of the proposed target lesion post-thrombolytic therapy
- Perforated vessel as evidenced by extravasation of contrast media
- Vascular graft, aneurysm or postsurgical stenosis of the target vessel
- Multiple lesions in the same target vessel unable to be treated with a maximum of two stents

2. Follow-up Schedule

The schedule of visits and assessments were required for the study is presented in **Table 7.** Office follow-up examinations were required at 30 days, 9 months and 1 year post index procedure, with additional phone follow-up at 2 and 3 years post index procedure.

Table 7: Examination Schedule

	Baseline		Index Procedure	Postprocedure/ Pre-Hospital Discharge	1-Month (30 days) ± 7 days	9-month (270 days) ± 30 days	1-year (365 days) ± 30 days	2-year (730 days) ± 30 days	3-year (1,095 days) ± 30 days
	≤ 7 days Before Index Procedure	≤ 24 hours Before Index Procedure							
Informed Consent	X								
Inclusion/Exclusion	X	X	X						
Demographics and Medical History	X								
Physical Examination[1]	X								
Rutherford Categorization	X			X	X	X	X		
ABI	X			X	X	X	X		
TASC Classification			X						
Pregnancy Test[2]		X							
Serum Creatinine	X								
Platelets	X								
Recommended Anti-Coagulant Therapy[3] Assessment	X								
Required Anti-Platelet Therapy[3] Assessment		X	X	X	X	X	X	X	X
Walking Impairment Questionnaire (WIQ)	X					X	X		
Duplex Ultrasound (DUS)					X	X	X		
Angiography			X						
AE Assessment[4]			X	X	X	X	X	X	X

[1] Physical examination includes gross assessment of standard organ systems (e.g., cardiac, pulmonary, etc).

[2] Pregnancy test (via urine or blood) required only for females of childbearing potential.

[3] Anti-platelet therapy preprocedure and required to be continued throughout participation in the trial, and procedural anti-coagulant medication consistent with current clinical practice.

[4] AE assessment and reporting includes AEs, SAEs and MAEs.

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3. Clinical Endpoints

Adverse events were collected throughout the study with a prespecified subset of events adjudicated by an independent Clinical Events Committee.

The Primary Endpoint was the 9-month device- and/or procedure-related major adverse event (MAE) rate (subject-based), adjudicated by an independent CEC. MAE was defined as death within 30 days, myocardial infarction (MI) that occurs during index hospitalization, target vessel revascularization (TVR) through 9 months, and/or amputation of index limb through 9 months.

Secondary Endpoints through 30 days included:

- Technical success (residual stenosis ≤30% based on visual assessment immediately post-procedure)
- Procedural success (technical success and no in-hospital major adverse events)
- Early clinical success at hospital discharge and 30 days post-procedure: improvement in Rutherford classification by ≥1 class as compared to baseline
- Early hemodynamic success at hospital discharge and 30 days post-procedure: improvement in Ankle-Brachial Index (ABI) by ≥0.1 as compared to baseline
- Frequency distribution of Rutherford classification preprocedure and at 30 days postprocedure
- Target vessel revascularization (TVR)
- Target lesion revascularization (TLR)
- Amputation of index limb
- Myocardial infarction (MI) that occurs during index hospitalization
- Death
- Stent thrombosis

Secondary Endpoints through 9 months included:

- Late clinical success at 9 months post-procedure: improvement in Rutherford classification by ≥1 class as compared to baseline
- Frequency distribution of Rutherford classification at 9 months
- Primary, primary-assisted, and secondary patencies at 9 months as assessed by duplex ultrasound
- Restenosis at 9 months as assessed by duplex ultrasound
- Late hemodynamic success at 9 months postprocedure: improvement in ABI by ≥0.1 as compared to baseline
- Change in Walking Impairment Questionnaire scores at 9 months postprocedure
- Target vessel revascularization (TVR)
- Target lesion revascularization (TLR)
- Amputation of index limb
- Death
- Stent thrombosis
- Incidence of unanticipated adverse device effects
- Incidence of all serious adverse events (SAE) reported within the trial
- Incidence of all non-serious adverse events reported within the trial

B. Accountability of PMA Cohort

Of the 125 patients enrolled, 91.1% (113/124) completed 9-month follow-up evaluations. Details of 1-month and 9-month follow-up compliance are provided in **Table 8**.

Table 8: Subject Disposition, Clinical Follow-up Compliance Intent-to-Treat, All Subjects (N=125)

	Total (Subject)	Total (Lesion)
Intent to Treat (All Enrolled Subjects)	125	166
Per Protocol (Received Study Stent)	125	166
Not Eligible for 1-Month Clinical Follow-up	0	0
Death ≤ 37 Days with no 1-Month Clinical Follow-up Performed	0	0
Eligible for 1-Month Clinical Follow-up	125	166
No 1-Month Clinical Follow-up	5	6
Missed Follow-up	1	1
Alive, Unable to Contact	1	1
Terminated	4	5
Died	0	0
Withdrawal	1	1
Loss to Follow-up	3	4
1-Month Visit Clinical Follow-up Performed	120	160
1-Month Visit Clinical Follow-up Compliance[1]	96.0% (120/125)	96.4% (160/166)
Not Eligible for 9-Month Clinical Follow-up	1	1
Death ≤ 300 Days with no 9-Month Clinical Follow-up Performed	1	1
Eligible for 9-Month Clinical Follow-up	124	165
No 9-Month Clinical Follow-up	11	14
Missed Follow-up	4	5
Alive, Unable to Contact	1	1
Alive, Refused to Return for Visit	3	4
Terminated	7	9
Died	0	0
Withdrawal	3	4
Loss to Follow-up	4	5
9-Month Visit Clinical Follow-up Performed	113	151
9-Month Visit Clinical Follow-up Compliance[1]	91.1% (113/124)	91.5% (151/165)

[1] Death prior to the 9-Month (1-Month) window does not contribute to the denominators and numerators of the compliance rates.

C. Study Population and Baseline Parameters

Table 9 presents baseline demographic and clinical characteristics. The ORION population was predominantly male (64.8%) with a history of smoking (96.0%), claudication (92.8%), hyperlipidemia (78.4%), and hypertension (76.0%). **Table 10** summarizes baseline lesion characteristics. Among the 160 evaluable baseline lesions, mean RVD was 7.69±1.79 mm, mean lesion length was 31.04±22.13 mm, and mean percent diameter stenosis was 71.51±16.27%.

Table 9: Baseline Demographics and Clinical Characteristics All Subjects (N=125)

Variable	(N=125 Subjects)
Demographics	
Age, Mean±SD (N), .(min,max)	61.09±9.25 (125) (39.00, 83.00)
Male Gender	64.8% (81/125)
Race/Ethnicity	
Hispanic or Latino	2.4% (3/125)
Caucasian	89.6% (112/125)
Asian	0.0% (0/125)
Black, or African heritage	6.4% (8/125)
Native Hawaiian or other Pacific Islander	0.0% (0/125)
American Indian or Alaska Native	0.8% (1/125)
Other	0.8% (1/125)
General Medical History	
History of Smoking	96.0% (120/125)
Current Diabetes Mellitus	36.8% (46/125)
History of Hyperlipidemia	78.4% (98/125)
History of Hypertension	76.0% (95/125)
History of COPD	24.8% (31/125)
Cardiac History	
History of CAD	58.4% (73/125)
History of MI	28.0% (35/125)
History of PCI	36.8% (46/125)
History of CABG	17.6% (22/125)
Neurologic/Renal History	
History of Transient Ischemic Attacks	4.0% (5/125)
History of Cerebrovascular Accident	5.6% (7/125)
History of Renal Insufficiency	7.2% (9/125)
Peripheral Vascular History	
History of Peripheral Vascular Surgery	8.0% (10/125)
History of Other Peripheral Endovascular Interventions	20.0% (25/125)
History of Claudication	92.8% (116/125)

Table 10: Baseline Lesion Characteristics – Core Lab All Lesions (N=166)

Lesion Characteristic	(N=166 Lesions)
Iliac Artery Segment	
Left Common Iliac Artery	36.3% (58/160)
Left External Iliac Artery	10.0% (16/160)
Right Common Iliac Artery	36.3% (58/160)
Right External Iliac Artery	17.5% (28/160)
Reference Vessel Diameter (RVD, mm)	7.69±1.79 (160) (4.61, 12.79)
Stent Size to RVD Ratio	1.19±0.25 (160) (0.68, 1.87)
Minimum Lumen Diameter (MLD, mm)	2.20±1.34 (160) (0.00, 5.44)
Percent Diameter Stenosis (% DS)	71.51±16.27 (160) (39.78, 100.00)
Lesion Length (mm)	31.04±22.13 (160) (4.08, 130.10)
Calcification	
None/Mild	23.1% (37/160)
Moderate	28.1% (45/160)
Severe	48.8% (78/160)

D. Safety and Effectiveness Results

1. Safety Results

For the primary endpoint of 9-month MAE, an exact, one-sided 95% upper confidence bound was calculated and compared to the prespecified performance goal. The expected 9-month MAE rate of 8.0% for the Epic Stent System and for iliac artery stenting with self-expanding stents was based on published literature. The performance goal (17.0%) included this expected rate of 8.0% plus a margin of 9.0%. All enrolled subjects were assessed for adverse events at the 9-month follow-up visit. Assuming a maximum of 15% attrition due to non-compliance with follow-up or other reasons, a minimum of 104 subjects was required to be evaluable for the primary endpoint.

Mathematical representations of the null and alternative hypotheses for the primary endpoint are:

H_0: $\theta_{Test} \geq PG$ (Unacceptable Performance)

H_1: $\theta_{Test} < PG$ (Acceptable Performance)

where θ_{Test} is the expected 9-month MAE rate for Epic™ and PG is the prespecified Performance Goal (17%).

The primary endpoint of the ORION Clinical Study is detailed in **Table 11**. The 9-month MAE rate (primary endpoint) was 3.4% (4/117) with a one-sided upper confidence bound of 7.7%, significantly less than the performance goal of 17.0% ($P < 0.0001$). The individual components of the composite MAE experienced are presented in **Table 12**. There were 4 subjects with TVR

through 9 months, no deaths within 30 days, no index hospitalization MI and no amputations of the index limb through 9 months.

Table 11: Primary Endpoint- Performance Goal Assessment, All Subjects (N=125)

Measure	(N=125 Subjects)	One-sided 95% Upper Confidence Bound	Performance Goal	p-Value*
9-Month MAE	3.4% (4/117)	7.7%	17.0	<0.0001

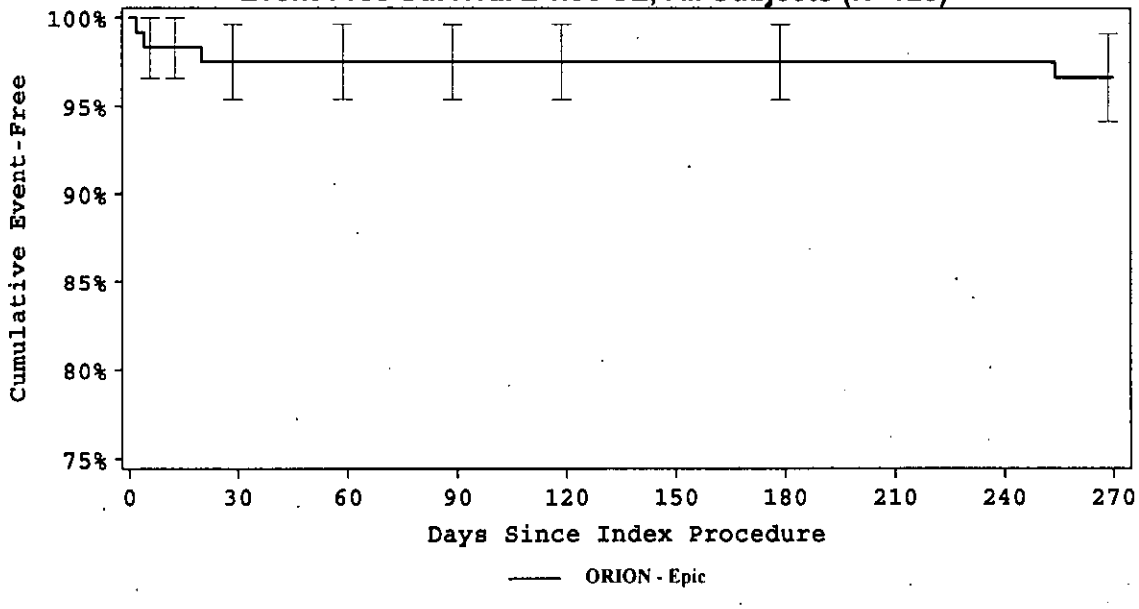
*P-value is from the one-sided exact-test

Table 12: Primary Safety Results All Subjects (N=125)

	(N=125 Subjects)	[95% CI]
9-Month MAE (per subject)	3.4% (4/117)	[0.9%, 8.5%]
Device- or index procedure-related Death within 30 days	0.0% (0/117)	[0.0%, 3.1%]
Myocardial Infarction (MI) during index hospitalization	0.0% (0/117)	[0.0%, 3.1%]
Target Vessel Revascularization (TVR) through 9 months	3.4% (4/117)	[0.9%, 8.5%]
Amputation of index limb through 9 months	0.0% (0/117)	[0.0%, 3.1%]

The Kaplan-Meier curve for all evaluable subjects is presented in **Figure 2**. The MAE rate is acceptable through the 9-month follow-up time point (270 days).

Figure 2: Freedom from 9 month MAE Event-Free Survival ± 1.96 SE, All Subjects (N=125)



2. Effectiveness Results

Secondary endpoints were summarized at the specified time points using the descriptive statistics, individually or in comparison to their values at baseline.

Primary and secondary effectiveness results are summarized in **Table 13** and **14**.

Table 13: Primary and Secondary Effectiveness Results, (N=125 Subjects; N=162 Limbs; N=166 Vessels; N=166 Lesions)

Parameter	Epic[a]
9-Month Clinical Outcomes	
Subject based	
Late clinical success[a]	89.9% (98/109)
Lesion based	
Primary patency	95.9% (117/122)
Primary-assisted patency	98.4% (120/122)
Secondary patency	100% (120/120)
Restenosis	2.5% (3/122)
Target lesion revascularization (TLR)	3.2% (5/156)
Limb based	
Early hemodynamic success[b]	
Hospital discharge	61.2% (93/152)
30 days	66.2% (100/151)
Late hemodynamic success[c]	66.7% (94/141)
Vessel based	
TVR	3.2% (5/156)
Peri-procedural Endpoints	
Technical success (per lesion)[d]	100% (166/166)
Procedure success (per subject)[e]	99.2% (124/125)

Numbers are % (counts/sample size) or mean±SD (n); outcomes are based on protocol definitions.

a Improvement in Rutherford classification at 9 months by ≥ 1 class as compared to baseline

b: Improvement in ankle-brachial index at hospital discharge and 30 days by ≥ 0.1 as compared to baseline

c: Improvement in ankle-brachial index at 9 months by ≥ 0.1 as compared to baseline

d: Residual stenosis ≤ 30% based on visual assessment immediately post-procedure

e: Residual stenosis ≤ 30% based on visual assessment immediately post-procedure and no in-hospital MAE

Table 14: Summary of Patency and Restenosis Results at 9 Months due to Alternate Analysis, (All Lesions (N=166) in all Subjects (N=125))

	Epic*
Lesion Based	
Primary-assisted patency	96.7% (118/122)
Secondary patency	98.3% (118/120)
Restenosis	4.1% (5/122)

*Two cases of restenosis and TLR occurred in subject (Left Common and Right Common Iliac Arteries) at the most proximal part of the stents (located at the ostium of both iliac arteries). In this case, conventional method of deriving Systolic Velocity Ratio (SVR) is invalid and the Proximal PSV (Peak Systolic Velocity) was analyzed to assess restenosis at 9 months. These are the results after the alternate analysis has been applied.

The rates of center-reported serious adverse events (SAEs) are summarized by MedDRA System / Organ Class and MedDRA Preferred Term in Tables 15. The rates include all reported serious events, regardless of study device or procedure relatedness.

Table 15. Rates of Center-Reported Serious Adverse Events to 300 Days Intent-to-Treat, All Subjects (N=125)

Serious Adverse Event		(N=125 Subjects)	
MedDRA System/Organ Class	**MedDRA Preferred Term**	**Events**	**Rate of Subjects with Event**
Total	Total	88	32.0% (40/125)
Not Coded	Not Coded	1	0.8% (1/125)
Blood And Lymphatic System Disorders	Total	4	1.6% (2/125)
	Anaemia	2	0.8% (1/125)
	Febrile Neutropenia	1	0.8% (1/125)
	Haemorrhagic Anaemia	1	0.8% (1/125)
Cardiac Disorders	Total	23	12.8% (16/125)
	Acute Coronary Syndrome	1	0.8% (1/125)
	Angina Pectoris	3	2.4% (3/125)
	Angina Unstable	1	0.8% (1/125)
	Atrial Fibrillation	7	3.2% (4/125)
	Cardiac Arrest	1	0.8% (1/125)
	Coronary Artery Disease	4	2.4% (3/125)
	Coronary Artery Stenosis	1	0.8% (1/125)
	Ischaemic Cardiomyopathy	2	1.6% (2/125)
	Mitral Valve Stenosis	1	0.8% (1/125)
	Myocardial Infarction	2	1.6% (2/125)
Eye Disorders	Total	1	0.8% (1/125)
	Blindness	1	0.8% (1/125)
Gastrointestinal Disorders	Total	6	2.4% (3/125)
	Abdominal Pain	2	0.8% (1/125)
	Constipation	1	0.8% (1/125)
	Gastrointestinal Haemorrhage	1	0.8% (1/125)
	Ileus	1	0.8% (1/125)
	Upper Gastrointestinal Haemorrhage	1	0.8% (1/125)
General Disorders And Administration Site Conditions	Total	5	4.0% (5/125)
	Catheter Site Haematoma	1	0.8% (1/125)
	Catheter Site Haemorrhage	1	0.8% (1/125)
	Chest Discomfort	1	0.8% (1/125)
	Non-cardiac Chest Pain	1	0.8% (1/125)
	Oedema Peripheral	1	0.8% (1/125)
Hepatobiliary Disorders	Total	3	1.6% (2/125)

Serious Adverse Event		(N=125 Subjects)	
MedDRA System/Organ Class	MedDRA Preferred Term	Events	Rate of Subjects with Event
Hepatobiliary Disorders	Bile Duct Stenosis	1	0.8% (1/125)
	Cholecystitis Acute	1	0.8% (1/125)
	Cholecystitis Chronic	1	0.8% (1/125)
Infections And Infestations	Total	8	4.0% (5/125)
	Abdominal Abscess	1	0.8% (1/125)
	Clostridial Infection	1	0.8% (1/125)
	Diverticulitis	2	0.8% (1/125)
	Pneumonia	3	2.4% (3/125)
	Wound Infection	1	0.8% (1/125)
Injury, Poisoning And Procedural Complications	Total	6	4.0% (5/125)
	Drug Toxicity	1	0.8% (1/125)
	Stent-graft Malfunction	2	1.6% (2/125)
	Vascular Pseudoaneurysm	2	1.6% (2/125)
	Wound Dehiscence	1	0.8% (1/125)
Investigations	Total	1	0.8% (1/125)
	Blood Creatinine Increased	1	0.8% (1/125)
Musculoskeletal And Connective Tissue Disorders	Total	2	1.6% (2/125)
	Lumbar Spinal Stenosis	1	0.8% (1/125)
	Pain In Extremity	1	0.8% (1/125)
Neoplasms Benign, Malignant And Unspecified (incl Cysts And Polyps)	Total	3	2.4% (3/125)
	Breast Cancer	1	0.8% (1/125)
	Lung Neoplasm Malignant	1	0.8% (1/125)
	Recurrent Cancer	1	0.8% (1/125)
Nervous System Disorders	Total	4	3.2% (4/125)
	Carotid Artery Stenosis	1	0.8% (1/125)
	Diplegia	1	0.8% (1/125)
	Headache	1	0.8% (1/125)
	Hypoaesthesia	1	0.8% (1/125)
Psychiatric Disorders	Total	1	0.8% (1/125)
	Mental Status Changes	1	0.8% (1/125)
Respiratory, Thoracic And Mediastinal Disorders	Total	7	3.2% (4/125)
	Acute Pulmonary Oedema	1	0.8% (1/125)
	Acute Respiratory Failure	1	0.8% (1/125)
	Chronic Obstructive Pulmonary Disease	4	1.6% (2/125)
	Pneumonia Aspiration	1	0.8% (1/125)
Vascular Disorders	Total	13	8.8% (11/125)
	Angiodysplasia	1	0.8% (1/125)
	Arterial Stenosis	1	0.8% (1/125)
	Iliac Artery Thrombosis	1	0.8% (1/125)

Serious Adverse Event		(N=125 Subjects)	
MedDRA System/Organ Class	MedDRA Preferred Term	Events	Rate of Subjects with Event
Vascular Disorders	Intermittent Claudication	2	1.6% (2/125)
	Peripheral Artery Dissection	3	2.4% (3/125)
	Peripheral Ischaemia	1	0.8% (1/125)
	Peripheral Vascular Disorder	1	0.8% (1/125)
	Thrombosis	1	0.8% (1/125)
	Vascular Occlusion	1	0.8% (1/125)
	Vessel Perforation	1	0.8% (1/125)

Conclusions: The ORION trial demonstrated the Epic Stent System to be safe and effective in the treatment of atherosclerotic iliac artery disease.

3. Subgroup Analysis

ORION Study Results by Gender/Sex

The ORION clinical study enrolled a total of 81 (64.8%) male subject and 44 (35.2%) female subjects. As shown in **Table 16**, there were 3 TVR events among the female subjects and 1 TVR among the male subjects. Lesion based primary patency was reported as 98.7% (75/76) and 91.3% (42/46) for the male and female subgroups respectively. These data support similar safety and efficacy outcomes for males and females.

Table 16: Primary Effectiveness and Safety Endpoints by Gender
All Lesions (N=166) in (N=125) Subjects

Measures	Male Event Rate	Female Event Rate
9-Month MAE (per subject)	1.3% (1/76)	7.3% (3/41)
Device- or index procedure-related Death within 30 days	0.0% (0/76)	0.0% (0/41)
Myocardial Infarction (MI) during index hospitalization	0.0% (0/76)	0.0% (0/41)
Target Vessel Revascularization (TVR) through 9 months	1.3% (1/76)	7.3% (3/41)
Amputation of index limb through 9 months	0.0% (0/76)	0.0% (0/41)
Lesion Based		
9-Month Primary patency	98.7% (75/76)	91.3% (42/46)
9-Month Primary-assisted patency	98.7% (75/76)	97.8% (45/46)
9-Month Secondary patency	100.0% (75/75)	100.0% (45/45)
Subject Based		
9-Month Primary patency	98.4% (62/63)	90.6% (29/32)
9-Month Primary-assisted patency	98.4% (62/63)	96.9% (31/32)
9-Month Secondary patency	100.0% (63/63)	100.0% (31/31)

Applicability to Pediatric Population
Peripheral artery disease is not typically found in pediatric populations. The Epic Stent System is not indicated for use in pediatric patients. The BSC ORION clinical study did not evaluate safety and effectiveness in the pediatric population.

XI. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

1. Study Design

The SUMMIT Registry is an investigator-sponsored, multicenter study in Germany designed to assess the performance of the Epic stent system in symptomatic subjects with superficial femoral artery (SFA)/popliteal artery disease. The study includes follow-up visits at 6 months and 12 months. One hundred subjects were enrolled in the study. To date, baseline data for all subjects and interim clinical and Duplex Ultrasound (DUS) data from the first 35 subjects have been analyzed.

2. Study Endpoints

The primary effectiveness endpoint of the study is duplex ultrasound (DUS) peak systolic velocity ratio (PSVR) comparing data within the treated segment to the proximal normal arterial segment at 6 months and 12 months. A PSVR > 2.5 suggests >50% restenosis.

The primary safety endpoint of the study is a composite outcome measure defined as freedom from all cause death, index limb amputation and target lesion revascularization through 30 days.

Key secondary endpoints include technical success, ankle-brachial index assessments, and rate of clinically driven target lesion revascularization.

3. Conclusion

Of the 35 patients evaluated in this interim analysis of the SUMMIT Registry, there were 16 patients treated with 6 mm-diameter Epic stents and 13 patients treated with the 120 mm-length Epic stents that support the safety and effectiveness of the Epic Stent System in treatment of iliac artery lesions. All lesions were treated successfully. All subjects assessed by DUS at discharge had a PSVR below 2.5. Of the 35 subjects assessed at 6 months, there was one target lesion revascularization at 6 months in a 6 x 120 mm stent. There were 4 subjects (11.4%) that experienced binary restenosis (PSVR ≥2.5). One subject underwent a pre-determined amputation of the 5th toe on the target limb; this subject was classified as Rutherford 5 at baseline. There were no stent-related serious adverse events and no stent thromboses among these 35 subjects.

While the ORION study provided sufficient data to demonstrate safety and effectiveness in vessel diameters 5 - 11 mm and lesion lengths up to 120 mm, there were only a few patients who received the 6 mm diameter stent or the 120 mm stent length. Therefore, the sponsor submitted supplemental clinical data from the SUMMIT study to support the safety and effectiveness

of the 6 mm diameter and 120 mm length stent sizes. Given that SFA disease is typically more difficult to treat than iliac disease, and that the ORION study already demonstrated safety and effectiveness in the appropriate iliac vessel diameters and lesion lengths the SUMMIT data were considered appropriate to be used to supplement the safety and effectiveness data from the ORION study.

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

A. Safety and Effectiveness Conclusions

The biocompatibility and *in vivo* animal testing demonstrated that the acute and chronic *in vivo* performance characteristics of the Epic Stent System provide reasonable assurance of safety and acceptability for clinical use.

The *in vitro* engineering testing conducted on the stent and delivery system 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 has established acceptable performance for a labeled shelf life up to 3 years.

The ORION clinical study evaluated the safety and efficacy of the Epic Stent System in the treatment of iliac artery stenosis in de novo or restenotic (from prior PTA) lesions ≤ 13 cm in length in arteries with diameter ≥ 5 mm to ≤ 11 mm. The primary endpoint was met as the rate of 9-month MAE with the intent-to-treat analysis set was 3.4% (4/117) with a one-sided upper confidence bound of 7.7%, significantly less ($P < 0.0001$) than the prespecified performance goal of 17.0%. Target vessel revascularization was 3.4% (4/117) and accounted for the observed MAE rate. There were 3 stent thrombosis events in the first 30 days, possibly related to placement technique and/or patient comorbidities, resulting in revascularization of the target lesions, and one additional subject with a revascularization at 9 months. There were no device- and/or procedure-related deaths or amputations through 9 months. All lesions were patent at 9 months (also accounting for those which were revascularized).

In summary, the results of the ORION study met the prespecified performance criterion for MAE and demonstrated safety and effectiveness measures that compare favorably with those of other iliac stents.

B. Overall Conclusions
The clinical testing conducted demonstrated that the Epic Stent System provides a reasonable assurance of safety and effectiveness when used as indicated in accordance with the Directions for Use.

XIV. CDRH DECISION

CDRH issued an approval order on April 13, 2012. The final conditions of approval cited in the approval order are described below.

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.