SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Stent, Superficial Femoral
Device Trade Name:	Innova™ Vascular Self-Expanding Stent System
Device Procode:	NIP
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:	P140028
Date of FDA Notice of Approval:	July 21, 2015
Priority Review:	No

II. INDICATIONS FOR USE

The Innova™ Vascular Self-Expanding Stent System is indicated to improve luminal diameter in the treatment of symptomatic de-novo or restenotic lesions in the native superficial femoral artery (SFA) and/or proximal popliteal artery (PPA) with reference vessel diameters from 4.0 mm to 7.0 mm and lesion lengths up to 190 mm.

III. CONTRAINDICATIONS

- Patients with contraindication to antiplatelet and/or anticoagulation therapy.
- Patients who are judged to have a lesion that prevents proper placement or deployment of the stent.
- A lesion that is within an aneurysm or an aneurysm with a proximal or distal segment to the lesion.
- Patients who exhibit angiographic evidence of severe thrombus in the target vessel or lesion site before/after undergoing Percutaneous Transluminal Angioplasty (PTA) procedure.
- A lesion through which a guide wire cannot pass.

IV. WARNINGS AND PRECAUTIONS

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

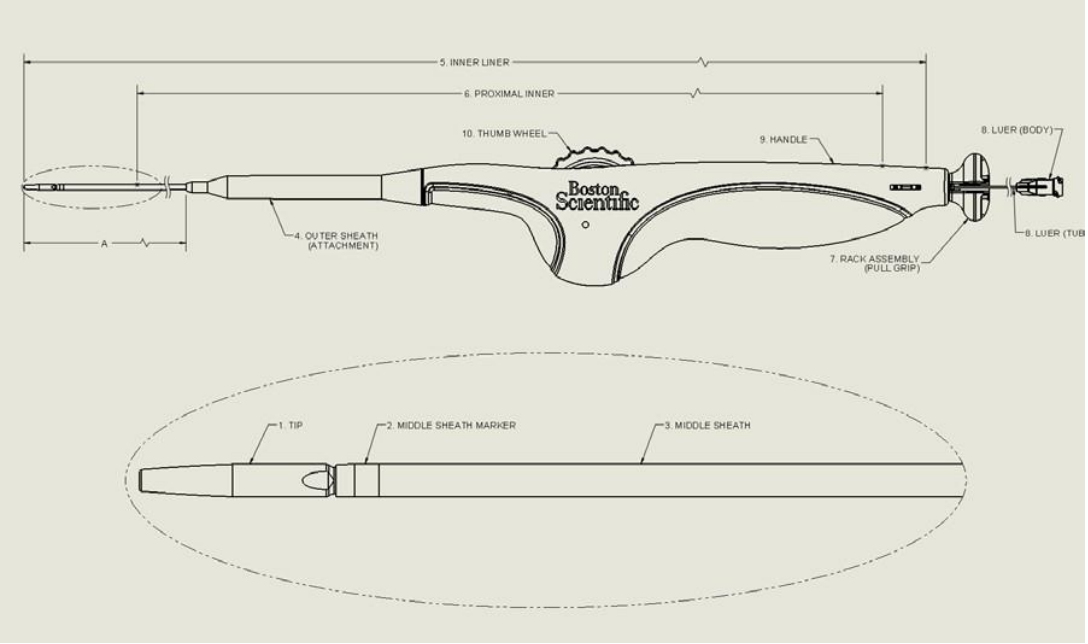
V. DEVICE DESCRIPTION

The Innova Vascular Self-Expanding 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 OD) delivery system. The delivery system is a triaxial design with an outer shaft to stabilize the stent delivery system, a middle shaft to protect and constrain the stent, and an inner shaft to provide a guidewire lumen.

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 Innova Stent System is available in stent diameters ranging from 5-8mm and lengths ranging from 20-200mm. 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 135 cm). The Innova Stent System is illustrated in **Figure 1**.

Figure 1: The Innova Stent system



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

Table 1: Commercial Stent Matrix

Stent Diameter (mm)	Stent Length (mm)	Delivery Catheter Length (mm)
5	20, 40, 60, 80, 100, 120, 150, 180, 200	75, 130
6	20, 40, 60, 80, 100, 120, 150, 180, 200	75, 130
7	20, 40, 60, 80, 100, 120, 150, 180, 200	75, 130
8	20, 40, 60, 80, 100, 120, 150, 180, 200	75, 130

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the correction of peripheral artery disease located in the SFA/PPA arteries, including PTA, PTA accompanied by stenting, stenting alone, conservative medical management, exercise therapy and/or surgical procedures. 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 Innova Stent System has been marketed for a peripheral vascular use in the European Union and other countries since 2011. There was one recall in 2011 due to stent partial deployment, and the delivery system was modified. Since 2012, the modified 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 Innova Stent System is commercially available is provided in **Table 2** below.

Table 2: Countries where the Innova Stent System is Marketed

Australia	Germany	Portugal
Austria	Greece	Russia
Baltics	Hong Kong	Singapore
Bangladesh	Hungary	Slovakia
Belgium	India	South Africa
Brazil	Italy	South Korea
Canada (biliary indication)	Malaysia	Spain
Chile	Middle East / North Africa	Sweden
China	Mexico	Switzerland
Colombia	Netherlands	Taiwan
Czech Republic	New Zealand	Turkey
Denmark	Norway	United Kingdom
Equador	Panama	
Finland	Philippines	
France	Poland	

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of potential adverse effects (e.g., complications) associated with the use of this device:

- Allergic reaction (to drug, contrast, device or other)
- Angina
- Aneurysm
- Arrhythmia
- Arteriovenous fistula
- Bleeding/Hemorrhage
- Bradycardia
- Death
- Drug reactions
- Embolization (air, plaque, thrombus, device, tissue, or other)
- Extremity ischemia/amputation
- Fever
- Hematoma
- Leg pain/claudication
- Myocardial Infarction
- Nausea or vomiting
- Need for urgent intervention or surgery
- Pseudoaneurysm formation
- Renal insufficiency or failure
- Restenosis of stented artery
- Sepsis/infection
- Stent fracture
- Stent migration
- Stent misplacement/jumping
- Stroke
- Target Lesion Revascularization
- Thrombosis/thrombus
- Tissue ischemia/necrosis
- Transient hemodynamic instability (hypotensive/hypertensive episodes)
- Vasospasm
- Vessel injury, including perforation, trauma, rupture and dissection
- Vessel occlusion

IX. SUMMARY OF PRECLINICAL STUDIES

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

A. Biocompatibility Studies

The biocompatibility of the Innova Stent System was evaluated per the requirements of ISO 10993-1. Tests were conducted separately on sterilized product to support the biocompatibility of (1) the Innova Delivery System and (2) the Innova Stent. The delivery system was categorized as an externally communicating device with limited contact duration (<24 hours) with circulating blood. The stent was categorized as an implant device with permanent blood contact (> 30 days).

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)*
- *ISO 10993-1, Biological Evaluation of Medical Devices – Part 1: Evaluation and testing within a risk management framework (2009)*

A summary of the biocompatibility testing conducted can be found in **Table 3** below.

Table 3: Biocompatibility Testing

Test Performed	Test Description	Stent	Delivery System	Results
Cytotoxicity	ISO MEM Elution Assay with L-929 Mouse Fibroblast Cells	X	X	Non-toxic
Sensitization	ISO Guinea Pig Maximization	X	X	Non-sensitizing
Irritation	ISO Intracutaneous Reactivity	X	X	Non-irritating
Pyrogenicity	USP Material-Mediated Pyrogenicity	X	X	Non-pyrogenic
Acute Systemic Toxicity	ISO Systemic Toxicity Study	X	X	Non-toxic
Implantation[1]	ISO Subcutaneous Implantation Study – 8 Week	X	N/A	Non-toxic
	ISO Muscle Implantation Study – 13 Week	X	N/A	Non-toxic
Hemocompatibility	ASTM Hemolysis Study (Direct and Indirect Contact)	X	X	Non-hemolytic
	Complement Activation Assay (C3a and SC5b-9)	X	X	Not a complement activator
	In Vivo Thrombogenicity Study – Jugular Vein	X[a]	X[b]	Non-thrombogenic

Test Performed	Test Description	Stent	Delivery System	Results
Genotoxicity	Bacterial Reverse Mutation (Ames) Assay	X	N/A	Non-mutagenic
	Mouse Lymphoma Assay	X	N/A	Non-genotoxic

[a] Also evaluated as part of the animal studies outlined in Section F, below.
[b] Delivery system tested only in the presence of anticoagulation. Labeling requires procedural anticoagulation, and contraindicates use in patients with uncorrected bleeding disorders, or who cannot receive anticoagulation or antiplatelet aggregation therapy.

Stent thrombogenicity was evaluated as part of other *in vivo* studies conducted to evaluate safety and effectiveness of the device in a vascular implant location, as described in Section F, below. These additional animal studies demonstrated a lack of thrombus formation when stents were implanted in a clinically-relevant vascular implant location.

The omission of chronic toxicity, in vivo genotoxicity, and carcinogenicity testing for the stent was supported by information regarding the starting materials, processing of the finished device and toxicity data from the literature.

The information provided demonstrates that the Innova Stent System is biocompatible.

B. In Vitro Engineering Testing

In vitro engineering testing on the Innova 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 4** below. "Pass" denotes that the test results met product specifications and/or the recommendation in the above-referenced guidance documents.

Table 4: 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 Innova stent exhibited surface composition and passive layer depth consistent with published literature for nitinol surfaces.	Pass

Test	Test Purpose	Acceptance Criteria	Results
Shape Memory and Super Elasticity of Intravascular Stents	To determine the Austenite finish transition temperature (Af) of the stent.	The stent must have an Af temperature 15° to 34°C when tested per ASTM F2082. This ensures the stent will expand to its intended size and shape under normal body temperatures.	Pass
Stent Corrosion Resistance - Post 10-year Pulsatile Fatigue Cycling	To document the potential for fretting, pitting and crevice corrosion of the 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 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 stent was coupled separately with dissimilar material stent. Shall result in "very low" or "negligible" current post testing.	Pass
Stent Dimensional Verification	To characterize the unconstrained diameter of the stent.	The unconstrained expanded diameter must be within -0.25 mm/+0.75 mm of its labeled diameter.	Pass
Percent Surface Area	To characterize the metal to lumen ratio of the stent.	The metal to lumen must be ≤ 30% for all stent sizes.	Pass
Foreshortening	To determine the foreshortening of the stent from the catheter constrained diameter to use diameter.	The change in stent length from catheter constrained diameter to length post deploy shall be ±10% or ±4 mm (whichever is greater).	Pass
Stent Integrity (Stent Over Expansion)	To verify the stent has no clinically significant defects or flaws after deployment	The stent must exhibited no structural damage or factures after deployment and over expansion.	Pass
Radial Stiffness and Radial Strength	To characterize ability of the stent to resist collapse when subject to an external load.	The stent must have a compression resistance ≥ 10.2 g/mm	Pass
Radial Outward Force	To characterize the minimum and maximum outward radial force of the stent within use range.	The outward radial force of each stent diameter must ≥ 2.9 g/mm	Pass

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 < 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 stent using Finite Element Analysis (FEA). The FEA analysis simulated physiological conditions in the SFA.	The FEA analysis must demonstrate that the stent maintains acceptable fatigue safety using the Goodman fatigue analysis with a safety factor > 1.	Pass
Accelerated Durability Testing	To characterize the accelerated durability of overlapping stents after 10-year pulsatile fatigue cycling.	No stent shall have type II or greater fracture occurrence after 400 million cycles (10 year simulation).	Pass
Accelerated Durability Testing	To characterize the accelerated durability of stents after 10-year fatigue cycling with relative SFA physiological motions.	Stents shall demonstrate fatigue integrity after 10 year simulated axial, twist, bend, and compression fatigue testing.	Pass
Magnetic Resonance Imaging (MRI) Safety and Compatibility	To evaluate the 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
Radiopacity	To assess the radiopacity of the stent.	The radiopacity of the stent while loaded in the delivery system and post stent deployment must be clinically acceptable when assessed during animal testing.	Pass

Test	Test Purpose	Acceptance Criteria	Results
Crush Resistance	To verify the ability of the stent to recover to its size and shape after applying an external load.	The recovery of the stent diameter post compression must be 90% or greater for both parallel plate and focal compression testing.	Pass
Kink Resistance	To characterize the smallest radius of curvature the stent can withstand without kinking.	Characterization of what the minimum gage pin diameter is that the stent can be bent around without kinking or experiencing a diameter reduction of at least 50% in the bent condition.	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 delivery system.	The delivery system working length must be ± 1.0cm of the labeled delivery system working length. The delivery system working length profile must be 6F. The delivery system must track and exchange over 0.035" guide wire.	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 delivery system must track through a simulated anatomical model, deliver the stent and be withdrawn remaining fully intact. The delivery system must fully deploy the stent. The delivery system must deploy the stent with an acceptable deployment accuracy and force.	Pass
Catheter Bond Strength	To evaluate the tensile strength of the delivery system bonds.	The delivery system must maintain its integrity during tracking, stent deployment and withdrawal.	Pass
Delivery System Flexibility and Kink Test	To determine the susceptibility of the delivery system to kink.	The delivery system must not kink and maintain guidewire movement when placed in a simulated anatomical model.	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 rotation without catheter failure.	Pass

Test	Test Purpose	Acceptance Criteria	Results
Delivery System Radiopacity	To assess the radiopacity of the delivery system.	The delivery system markers must exhibit clinically acceptable radiopacity.	Pass
Package Integrity	To integrity of the device packaging.	The packaging must withstand the hazards of the distribution and the environment and maintain sterility of the device.	Pass

C. Shelf Life Testing

Performance testing was conducted following 6 months of aging to demonstrate that the device and packaging performs within product specifications for a labeled shelf life of 6 months.

D. Sterilization

The Innova 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*.

E. Animal Studies

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

Preclinical evaluations of the Innova 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. Innova 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 Innova 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 5** below.

Table 5: Summary of Innova GLP Animal Studies

Device	Evaluation Time Points	Target # Stents per Animal & # of Animals	Vessel Location/ Approach	Testing Objective	Results
Porcine Safety					
Innova & Wallstent	30, 90, and 180 days	2 overlap pair/animal 39 animals	Ilio-femoral artery/carotid approach	Compare vascular response of Innova to Wallstent Control in support of safety using mortality, adverse events, morphology, morphometric parameters	Results support safety and vascular compatibility for Innova and Wallstent. No device related mortality or adverse events. No stent thrombosis, no luminal thrombi observed. Complete endothelialization and tissue strut coverage at more than 95% of the Innova stent by 30 days. 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.
Porcine Acute Performance					
Innova	Acute	1 to 2 non-overlapping stents/animal 9 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 performed a clinical study to establish a reasonable assurance of safety and effectiveness of stenting the superficial femoral artery and/or proximal popliteal

artery in the US, Europe, Canada, and Japan under IDE G100291. 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

Patients were treated between April 1, 2011 and June 28, 2013. The database for this PMA reflected data collected through August 14, 2014 and included 299 patients. There were 49 investigational sites.

The SuperNOVA clinical study was a prospective, single arm, controlled, multicenter, global study. The SuperNOVA study was conducted to assess the performance of the Innova™ Self-Expanding Stent System, which is designed to improve luminal diameter in the treatment of symptomatic de-novo or restenotic lesions in the native superficial femoral artery and/or proximal popliteal artery. Subjects whose eligibility was confirmed were enrolled in the study and treated with the Innova™ Self-Expanding Stent System on the day of index procedure. After the index procedure, all subjects were followed to investigate the safety and Effectiveness of the Innova™ Stent System. Subjects were enrolled by 49 centers located in the United States, Europe, Canada and Japan.

The SuperNOVA clinical study was a single arm study. The safety and effectiveness of the Innova™ Self-Expanding Stent System was assessed against performance goals, as described below.

A Clinical Events Committee (CEC) was used to adjudicate any reported death, TLR, TVR, amputation or stent thrombosis that occurred during the SuperNOVA study. The CEC further determined which of these events qualify per protocol definition as a major adverse event (MAE) for the SuperNOVA study.

1. Clinical Inclusion and Exclusion Criteria:

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

- Subjects age 18 and older. Japanese sites only: If age 18 and 19, legal guardian must sign informed consent form prior to initiation of study-related evaluations
- Chronic symptomatic lower limb ischemia defined as Rutherford categories 2, 3 or 4
- Stenotic, restenotic (from angioplasty only) or occlusive lesion(s) located in the native superficial femoral artery or proximal popliteal artery:
    - Degree of stenosis ≤70% by visual angiographic assessment
    - Vessel diameter ≥ 4 and ≤7 mm
    - Total lesion length (or series of lesions) ≥ 30
    - mm and ≤190 mm (note: tandem lesions may be treated, provided that the tandem lesion segment can be covered with only one stent)
    - If lesion was restenotic, percutaneous transluminal angioplasty treatment must be >3 months prior to stent

placement
    - Target lesion located at least 3 cm above the inferior edge of the femur
- Patent infrapopliteal and popliteal artery, i.e., single vessel runoff or better with at least 1 of 3 vessels patent (<50% stenosis) to the ankle or foot
- Subject (or Legal Guardian) was willing and able to provide consent before any study-specific tests or procedures were performed and agreed to attend all required follow-up visits

Patients were <u>not</u> permitted to enroll in the SuperNOVA study if they met any of the following exclusion criteria:

- Previous stent placement in the target vessel
- Subjects who have undergone prior surgery of the SFA/PPA in the target limb to treat atherosclerotic disease
- Subjects who have undergone prior PTA of a non-target lesion in the target SFA/PPA in the past 3 months
- Use of atherectomy devices or other adjunctive treatment in the SFA/PPA during the index procedure
- History of major amputation in the same limb as the target lesion
- Life expectancy less than 12 months due to other medical co-morbid condition(s) that could limit the subject's ability to participate in the clinical study, limit the subject's compliance with the follow-up requirements, or impact the scientific integrity of the clinical study
- 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
- Concomitant renal failure with a serum creatinine >2.0 mg/dL
- Receiving dialysis or immunosuppressant therapy
- Pregnancy
- Current participation in another investigational drug or device clinical study
- Known allergy to Nitinol
- Septicemia at the time of the index procedure
- Presence of other hemodynamically significant outflow lesions requiring intervention within 30 days of the index procedure
- Target lesion is within or near an aneurysm
- Acute ischemia and/or acute thrombosis of the SFA/PPA
- Persistent, intraluminal thrombus of the proposed target lesion post-thrombolytic therapy
- Perforated vessel as evidenced by extravasation of contrast media
- Heavily calcified lesions

2. Follow-up Schedule

All patients were scheduled to return for follow-up examinations at 1 months, 6 months, 12 months, 24 months, and 36 months (48 and 60 months for Japanese patients only) postoperatively.

Preoperatively, an inclusion/exclusion criteria assessment, medication assessment, angiogram, and adverse event assessment were performed. Postoperatively, the objective parameters measured during the study included a Rutherford Classification, Ankle-brachial index (ABI) measurements, a walking impairment questionnaire, 6 minute Hall Walk, SF-36 Health Survey, Medication Assessment, Angiogram, Adverse Event Assessment, Duplex Ultrasound, and X-Ray. Adverse events and complications were recorded at all visits.

The key time points are shown in **Table 6** below:

Table 6: Examination Schedule

	Within 30 days of Procedure	**Index Procedure**	**Pre-Discharge**	**1-month (±7 days)**	**6- month (182±30 days)**	**12-month (365±30 days)**	**2-Year (730±30 days)**	**3-Year[e] (1095±30 days)**	**4-Year (1460 ± 30 days)**	**5-Year (1825 ± 30 days)**
Informed Consent[a]	X									
Confirm Inclusion/Exclusion	X	X								
Demographics and Medical History	X									
Serum Creatinine,	X									
Complete Blood Count	X		X							
Rutherford Categorization	X			X	X	X	X			
ABI Measurements	X		X	X	X	X	X			
Pregnancy Test	X[b]									
Walking Impairment Questionnaire	X			X	X	X				
6 Minute Hall Walk	X			X	X	X				
SF-36V Health Survey	X			X	X	X	X			
Medication Assessment[d]		X	X	X	X	X	X	X		
Angiogram[c]		X								
Adverse Events Assessment		X	X	X	X	X	X	X	X[f]	X[f]
Duplex Ultrasound[c]				X	X	X	X			
X-Ray[c]						X	X	X	X[f]	X[f]

a Subject's consent obtained and informed consent form signed prior to any study-specific tests or procedures
b Performed within 24 hours prior to the index procedure, may be a urine or blood pregnancy test, and is only required for females of childbearing potential
c Angiograms, Ultrasounds and X-rays will be sent to the respective core lab for analysis
d Antiplatelet medications only
e The 3-Year visit must be conducted in the office or hospital for stent integrity assessment via X-ray and adverse event assessment. In Japan, the 4 and 5-year follow up visits must be conducted at the office or hospital for stent integrity assessment via X-ray and adverse event assessment.
f Japan Only

3. Clinical Endpoints

With regards to safety, the primary safety endpoint was a composite MAE rate in order to demonstrate a 12- month MAE-free rate exceeds the performance goal (PG) of 59.6%.

The MAEs to be considered are defined as:

- All causes of death through 1 month post-index procedure
- Target limb major amputation through 12 months post-index procedure
- Target Lesion Revascularization through 12 months post-index procedure

A secondary safety endpoint assessed a composite MAE rate in order to demonstrate a 1- month MAE-free rate exceeds the PG of 88.0%.

The MAEs to be considered are defined as:

- All causes of death through 1 month post-index procedure
- Target limb major amputation through 1 month post-index procedure
- Target Lesion Revascularization through 1 month post-index procedure

With regards to effectiveness, the co-primary effectiveness endpoints assessed vessel primary patency and are tested in a sequential manner, as follows:

- The co-primary effectiveness endpoint (1) assessed stented segments intended to be treated with the core stent matrix (stent lengths from 20 to 150 mm) in order to demonstrate that the 12-month vessel primary patency rate exceeds the PG of 66%.
- The co-primary effectiveness endpoint (2) assessed stented segments intended to be treated with the entire stent matrix (stent lengths from 20 to 200 mm) in order to demonstrate that the 12-month vessel primary patency rate exceeds the PG of 63%. In addition to rejecting the null hypothesis, a non-statistically driven goal needed to be observed, such that the rate of vessel primary patency at 12 months observed with the long stents must be ≥50%.

Additional effectiveness endpoints were assessed, but were not powered to make statistically based conclusions, are as follows:

- Technical success: ability to cross and dilate the lesion to achieve residual angiographic stenosis no greater than 30%
- Procedural success: technical success with no MAEs within 24 hours of the procedure
- Primary Patency: target stented segment without a hemodynamically significant stenosis on duplex ultrasound (DUS) and without TLR, bypass of the target lesion, or amputation
- Assisted Primary Patency: target stented segment without a hemodynamically significant stenosis on DUS and without TLR for total occlusion, bypass of the target lesion, or amputation

- Walking Improvement assessed by the Walking Impairment Questionnaire11 and a 6 Minute Hall Walk
- Improved Quality of Life assessed by the SF-36V Health Survey 12, 13
- Target Vessel Revascularization Rate
- Target Lesion Revascularization Rate
- Adverse Event Rates
- Stent Fracture Rate utilizing VIVA definitions:7 Grade 0: No strut fractures, I: single strut fracture, II: multiple strut fractures, III: stent fracture(s) with preserved alignment of the components, IV: stent fracture(s) with mal-alignment of the components, V: stent fracture(s) in a trans-axial spiral configuration
- Rate of Primary Sustained Clinical Improvement: an improvement in Rutherford classification of one or more categories as compared to pre-procedure without the need for repeat TLR
- Rate of Secondary Sustained Clinical Improvement: an improvement in Rutherford classification of one or more categories as compared to pre-procedure including those subjects with repeat TLR
- Rate of Hemodynamic Improvement: Increases in ABI of ≥ 0.10 or to an ABI ≥ 0.90 as compared to pre-procedure without the need for repeat TLR

With regard to success/failure criteria, study success was defined as follows:

- To meet the primary safety endpoint, the one-sided 97.5% lower confidence bound has to be greater than 59.6%.
- To meet the co-primary effectiveness endpoint (1), the one-sided 97.5% lower confidence bound has to be greater than 66%.
- To meet the co-primary effectiveness endpoint (2), the one-sided 97.5% lower confidence bound has to be greater than 63% and the observed 12-month primary patency rate for stented segments treated with the long stents has to be ≥50%.

The primary safety and effectiveness endpoint and other pre-specified endpoints were also summarized and compared in a non-statistically powered manner for the following subgroups: gender (male/female), treated diabetic status (medically-treated diabetics/non-medically treated diabetics) vs. non-diabetics and claudicants (Rutherford 2, 3) vs. critical limb ischemia (Rutherford 4).

B. Accountability of PMA Cohort

At the time of database lock, of 299 patients enrolled in the PMA study, 92% (275) patients are available for analysis at the 12 month post-operative visit. **Table 7** displays subject disposition at each follow-up visit.

Table 7: Subject Disposition

Intent to Treat/Per Protocol (All Enrolled Subjects)	299
Eligible for 1-Month Clinical Follow-up	298
Not Eligible for 1-Month Clinical Follow-up	1
Death ≤ 37 Days with no 1-Month Clinical Follow-up Performed	0
Withdrawal	1
Adverse Event	0
Investigator Discretion	0
Lost to Follow-up	0
Withdrew Consent	1
Other	0
1-Month Clinical Follow-up Performed	295
1-Month Clinical Follow-up or Death (Evaluable)	295
1-Month Clinical Follow-up Compliance[a]	98.7% (295/299)
1-Month Duplex Ultrasound Follow-up Compliance[b]	97.7% (292/299)
Eligible for 6-Month Clinical Follow-up	291
Not Eligible for 6-Month Clinical Follow-up	8
Death ≤ 212 Days with no 6-Month Clinical Follow-up Performed	3
Withdrawal	5
Adverse Event	0
Investigator Discretion	0
Lost to Follow-up	1
Withdrew Consent	4
Other	0
6-Month Clinical Follow-up Performed	276
6-Month Clinical Follow-up or Death (Evaluable)	279
6-Month Clinical Follow-up Compliance[a]	93.2% (276/296)
6-Month Duplex Ultrasound Follow-up Compliance[b]	92.6% (274/296)
Eligible for 12-Month Clinical Follow-up	275
Not Eligible for 12-Month Clinical Follow-up	24
Death ≤ 395 Days with no 12-Month Clinical Follow-up Performed	8
Withdrawal	16
Adverse Event	0
Investigator Discretion	2
Lost to Follow-up	6
Withdrew Consent	8
Other	0
12-Month Clinical Follow-up Performed	266
12-Month Clinical Follow-up or Death (Evaluable)	274
12-Month Clinical Follow-up Compliance[a]	91.4% (266/291)
12-Month Duplex Ultrasound Follow-up Compliance[b]	90.4% (263/291)
12-Month X-ray Follow-up Compliance[b]	85.2% (248/291)

[a]Death prior to the visit window does not contribute to the denominators and numerators of the compliance rate
[b]All duplex ultrasounds and x-ray imaging apply, including anyone without interpretable images

C. Study Population and Baseline Parameters

Table 8 provides a review of baseline demographics and clinical characteristics of the subjects enrolled into the SuperNOVA study. The age of the subjects enrolled spanned from 45 to 93 years. Investigators enrolled 222 (74.2%) male subjects. The demographics of the study population are typical for an interventional peripheral vascular study.

Table 8: Baseline Demographics and Clinical Characteristics (N=299)

Demographics	
Age (Year)	67.4±9.7 (299) (45.0, 93.0)[a]
Male Gender	74.2% (222/299)
Race/Ethnicity	
Hispanic or Latino	1.3% (4/299)
Caucasian	79.6% (238/299)
Asian	14.0% (42/299)
Black, or African heritage	4.3% (13/299)
Native Hawaiian or other Pacific Islander	0.3% (1/299)
American Indian or Alaska Native	0.3% (1/299)
Other	0.0% (0/299)
Not Disclosed	0.0% (0/299)
General Medical History	
History of Smoking	83.9% (251/299)
Current Diabetes Mellitus	40.5% (121/299)
Type 1	2.3% (7/299)
Type 2	36.8% (110/299)
Unknown	1.3% (4/299)
Medically-Treated Diabetes	35.1% (105/299)
History of Hyperlipidemia requiring medication	74.9% (224/299)
History of Hypertension requiring medication	79.9% (239/299)
History of Chronic Obstructive Pulmonary Disease	8.4% (25/299)
Cardiac History	
History of Coronary Artery Disease	43.5% (130/299)
History of Myocardial Infarction (MI)	24.7% (74/299)
History of Congestive Heart Failure	8.4% (25/299)
New York Heart Assoc. (NYHA) Classification	
I	1.3% (4/299)
II	2.7% (8/299)
III	1.3% (4/299)
IV	0.3% (1/299)
Unknown	2.7% (8/299)
History of Percutaneous Coronary Intervention (PCI)	28.4% (85/299)
History of Coronary Artery Bypass Graft (CABG) Surgery	18.1% (54/299)
Current Angina Status	
Stable Angina	14.7% (44/299)
Unstable Angina	0.3% (1/299)
None	81.9% (245/299)
Neurologic/Renal History	

Demographics	
History of Transient Ischemic Attacks (TIA)	7.0% (21/299)
History of Cerebrovascular Accident (CVA)	8.0% (24/299)
History of Renal Insufficiency	10.4% (31/299)
History of Renal Percutaneous Intervention	1.3% (4/299)
Peripheral Vascular History	
History of Peripheral Vascular Surgery	9.0% (27/299)
History of Other Peripheral Endovascular Interventions	41.8% (125/299)
History of Claudication	94.0% (281/299)

[a]Values include the mean plus/minus standard deviation and range

Table 9 and **Table 10** present the site-reported and angiographic core lab assessed lesion characteristics. The majority of Innova stents were implanted in the middle and distal regions of the SFA. The lesion length eligible for participation into the SuperNOVA study was ≥ 30 to ≤190 mm. Results for lesion length are consistent with the differences in methodology, with mean lesion length of 90.8 mm reported by the site investigators and 93.2 mm reported by the core laboratory. The mean percent diameter stenosis was 91.7% and the lesion distribution included 35.6% severely calcified lesions.

Table 9: Baseline Site-Reported Lesion Characteristics (N=299 Lesions)

	Overall
Treated Limb	
Right leg	46.2% (138/299)
Left leg	53.8% (161/299)
Arterial Segments[a]	
Proximal	11.0% (33/299)
Mid	58.2% (174/299)
Distal	58.2% (174/299)
Ostial	0.3% (1/299)
Proximal Popliteal Artery	15.7% (47/299)
Target Lesion Reference Vessel Diameter (RVD, mm)	5.6±0.7 (299) (4.0, 7.0) [1]
Target Lesion % Diameter Stenosis	91.7±9.2 (299) (70.0, 100.0) [1]
Target Lesion Length (mm)	90.8±44.4 (299) (30.0, 190.0) [1]
Thrombus Seen	2.3% (7/299)
TASC II Lesion Classification	
A	40.5% (121/299)
B	42.1% (126/299)
C	13.7% (41/299)
D	3.7% (11/299)
Predilation	
Predilation Performed	81.9% (245/299)
If Yes, Number of Predilation Balloons Used	1.1±0.4 (245) (1.0, 5.0) [b]
Post-Deployment Dilation	
Post-Deployment dilation Performed	96.7% (289/299)
If Yes, Number of post-deployment Balloons Used	1.1±0.4 (289) (1.0, 3.0) [b]
Target Lesion Final Outcome	
Final % Stenosis	4.2±8.2 (299) (0.0, 50.0) [b]
Thrombus seen in treated vessel at the end of the procedure	0.7% (2/299)

[a] Subjects under "Arterial Segments" may have checked more than one location present
[b]Values include the mean plus/minus standard deviation and range

Table 10: Angiographic Core Lab Baseline Measurements

	N= 299 Lesions
Treated Limb	
Right leg	45.6% (136/298)
Left leg	54.4% (162/298)
Arterial Segments[a]	
Proximal	10.4% (31/298)
Mid	57.0% (170/298)
Distal	67.4% (201/298)
Ostial	1.7% (5/298)
Proximal Popliteal Artery	15.1% (45/298)
mm from Ostium (mm)	100.1±54.2 (75) (0.0, 233.1)[b]
Length (mm)	93.2±49.1 (293) (10.2, 284.7)[b]
Target Lesion Reference Vessel Diameter (RVD, mm)	5.0±0.9 (295) (2.9, 7.6)[b]
Lesion Type	
Eccentric Lesion	46.6% (139/298)
Concentric Lesion	52.3% (156/298)
Bend (degrees)	
>45 degrees	0.0% (0/298)
>90 degrees	0.0% (0/298)
Thrombus	
Grade 0	97.7% (291/298)
Grade 1	0.7% (2/298)
Grade 2	0.3% (1/298)
Grade 3	0.3% (1/298)
Grade 4	0.0% (0/298)
Grade 5	0.0% (0/298)
Calcification	
None/Mild	29.5% (88/298)
Moderate	34.6% (103/298)
Severe	35.6% (106/298)
Ulceration (Present)	13.4% (40/298)
Aneurysm (Present)	3.4% (10/298)
Patency to Foot	
No Infrapopliteal Vessel Patent	9.2% (23/250)
1 Infrapopliteal Vessel Patent	30.0% (75/250)
2 Infrapopliteal Vessels Patent	37.6% (94/250)
3 Infrapopliteal Vessels Patent	23.2% (58/250)
Anterior Tibial Artery (Patent)	37.6% (112/298)
Posterior Tibial Artery	54.0% (161/298)
Peroneal Artery	56.7% (169/298)
Profunda Femoris Artery	66.1% (197/298)

Core lab reported "Treated Limb" may differ from the site reported "Treated Limb".
[a]Subjects under "Arterial Segments" may have checked more than one location present
Thrombus could have subjects with "N/A" response as allowed by CRF so percentages may not add up to 100%.
[b] Values include the mean plus/minus standard deviation and range

D. Safety and Effectiveness Results

1. Safety Results

Primary Safety Endpoint Results

Table 11 summarizes the primary safety endpoint results for the SuperNOVA study. The 12 month MAE free rate was 85.8% with the lower 95% Confidence interval exceeding the established PG of 59.6%**.**

Table 11: Primary Safety Endpoint (N=299 Subjects)

Primary Safety Endpoint	Overall Subjects	95% CI	Lower 1-Sided[b] 97.5% CI	PG
12-Month freedom from MAE[a]	85.8% (230/268)	[81.1%, 89.8%]	81.1%	59.6% (Met)
12-Month MAE[a] (Composite Endpoint)	14.2% (38/268)			
All Causes of Deaths at 1 Month	0.0% (0/268)			
Target Limb Major Amputation	0.4% (1/268)			
Target Lesion Revascularization (TLR)	14.2% (38/268)			

[a]Twelve-Month Major Adverse Events (MAEs) defined as all causes of death through 1 month, target limb major amputation through 12 months and/or target lesion revascularization through 12 months.
[b]Binomial Exact Method
Abbreviation: PG, Performance Goal

Secondary Safety Endpoint Results

Table 12 summarizes the secondary safety endpoint results for the SuperNOVA study. The 1 month MAE free rate was 99.7%.

Table 12: Secondary Safety Endpoint (N=299 Subjects)

Secondary Safety Endpoint	Overall Subjects	95% CI	Lower 1-Sided[b] 97.5% CI	PG
1-Month freedom from MAE[a]	99.7% (296/297)	[98.1%, 100.0%]	98.1%	88.0% (Met)
1-Month MAE[a] (Composite Endpoint)	0.3% (1/297)			
All Causes of Deaths	0.0% (0/297)			
Target Limb Major Amputation	0.0% (0/297)			
Target Lesion Revascularization (TLR)	0.3% (1/297)			

[a]One-month Major Adverse Events (MAEs) defined as all causes of death, target limb major amputation and/or target lesion revascularization through 1 month.
[b]Binomial Exact Method
Abbreviation: PG, Performance Goal

The evaluation of adverse events consists of review of the following categories:

- Unanticipated Adverse Device Effects
- Major Adverse events
- Serious site reported adverse events
- Non-serious site reported adverse events

Regular internal Safety Monitoring reviews were conducted to monitor the occurrence and type of safety events. Additionally, external review was conducted by a Clinical Events Committee which adjudicated all deaths, stent thrombosis and suspected MAEs. Adjudicated decisions of the CEC supersede those of the investigational center(s) in the event of disparity. The Independent Data Reviewer (IDR) reviews all aggregate serious adverse data at time points determined by the charter.

Deaths

Table 13 lists the deaths and causes of death that have occurred among subjects while participating in the SuperNOVA study. Ten deaths have been reported to date, which spans to 464 days post index procedure. The CEC adjudicated 6 deaths as cardiac-related, including any deaths with an unknown cause. Two deaths were due to vascular issues and include a stroke and post-PTA bleeding. One death was adjudicated as non-cardiac and non-vascular. According to the reporting investigators, neither the study procedure nor study device was related to any of the ten deaths.

Table 13: List of Deaths Reported (N=299 Subjects)

Site-Reported Cause of Death	CEC Adjudication	Days from Index Procedure
Death of unknown cause	Cardiac Death	169
NSTEMI	Cardiac Death	194
Worsening of general health status post clostridial enterocolitis after lung cancer	Non- cardiovascular Death	162
Cardiopulmonary arrest	Cardiac Death	296
Death cause unknown	Cardiac Death	427
Cardiogenic Shock	Not Yet Adjudicated	443
CVA	Vascular Death	119
Geromarasmus	Cardiac Death	256
Cardiac arrest	Cardiac Death	259
Arterial bleeding after PTCA	Vascular Death	121

Abbreviations: NSTEMI- Non-ST elevated Myocardial Infarction PTCA: percutaneous transluminal coronary angioplasty CVA: cerebrovascular accident.

Unanticipated Adverse Device Effects (UADEs)

No UADEs have been reported.

Serious Adverse Events

Table 14 displays the rates of Serious Adverse Events (SAE) by MedDRA System/Organ Class that were reported as of the data snapshot date of August 14, 2014.

Table 14: Serious Adverse Events by MedDRA System/Organ Class

Serious Adverse Event by SOC and PT[a]	Events	Rate of Subjects With Event
Any serious adverse event	309	49.2% (147/299)
Not Coded	4	0.7% (2/299)
Cardiac disorders	36	8.4% (25/299)
Congenital, familial and genetic disorders	1	0.3% (1/299)
Gastrointestinal disorders	18	4.3% (13/299)
Retroperitoneal hematoma	2	0.7% (2/299)
General disorders and administration site conditions	14	4.3% (13/299)
Catheter site hemorrhage	2	0.7% (2/299)
Impaired healing	1	0.3% (1/299)
Immune system disorders	2	0.7% (2/299)
Infections and infestations	18	5.7% (17/299)
Catheter site infection	1	0.3% (1/299)
Localized infection	1	0.3% (1/299)
Injury, poisoning and procedural complications	21	5.7% (17/299)
Arterial injury	1	0.3% (1/299)
Metabolism and nutrition disorders	3	1.0% (3/299)
Musculoskeletal and connective tissue disorders	14	4.0% (12/299)
Pain in extremity	2	0.7% (2/299)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	9	2.7% (8/299)
Nervous system disorders	9	2.3% (7/299)
Renal and urinary disorders	5	1.7% (5/299)
Reproductive system and breast disorders	1	0.3% (1/299)
Respiratory, thoracic and mediastinal disorders	3	1.0% (3/299)
Skin and subcutaneous tissue disorders	2	0.7% (2/299)
Surgical and medical procedures	1	0.3% (1/299)
Vascular disorders	148	28.1% (84/299)
Arterial thrombosis limb	5	1.3% (4/299)
Femoral arterial stenosis	38	10.7% (32/299)
Femoral artery dissection	1	0.3% (1/299)
Femoral artery occlusion	8	1.7% (5/299)
Intermittent claudication	7	2.0% (6/299)
Peripheral arterial occlusive disease	1	0.3% (1/299)

[a]All PTs that were experienced are not listed. The PTs that are listed are physician-reported to be either device and/or procedure-related.

Stent Fractures

X-rays were performed at 12 months post-implantation and analyzed by the angiographic core lab to assess stent integrity. This analysis yielded a fracture rate of 1.9% (6/324). Four of the 6 stents remained patent at 12 months.

2. Effectiveness Results

Co-Primary Effectiveness Endpoints

Table 15 presents primary patency results for the co-primary effectiveness endpoints incorporated into the SuperNOVA study. The performance goal of 66% was not met. These lower patency rates may have been influenced by a number of factors, including the lesion length, lesion location, degree of calcification, and challenging outflow conditions. As presented in **Figure 2** and **Table 16**, the freedom from loss of primary patency at 12 months for the core stent matrix was 76.7%.

Table 15: Co-Primary Effectiveness Endpoints (N=299)

	Overall	**95% CI**	**Lower 1-Sided[e] 97.5% CI**	**PG**
12-Month Primary Patency in Core Matrix Stents[a]	69.5% (157/226)	[63.0%, 75.4%]	63.0%	66.0% (Not Met)
12-Month Primary Patency in Entire Stent Matrix[b]	66.4% (174/262)			
12-Month Primary Patency in Long Stents[c,d]	47.2% (17/36)			

[a]Core Matrix Stents (20-150 mm) , [b]Entire Stent Matrix (20-200 mm), [c]Long Stents (180 200 mm),
[d]The observed rate must be ≥ 50.0%, [e]Binomial Exact Method, Abbreviation: PG, Performance Goal

Figure 2: Primary Patency in Core Stents through 12 Months

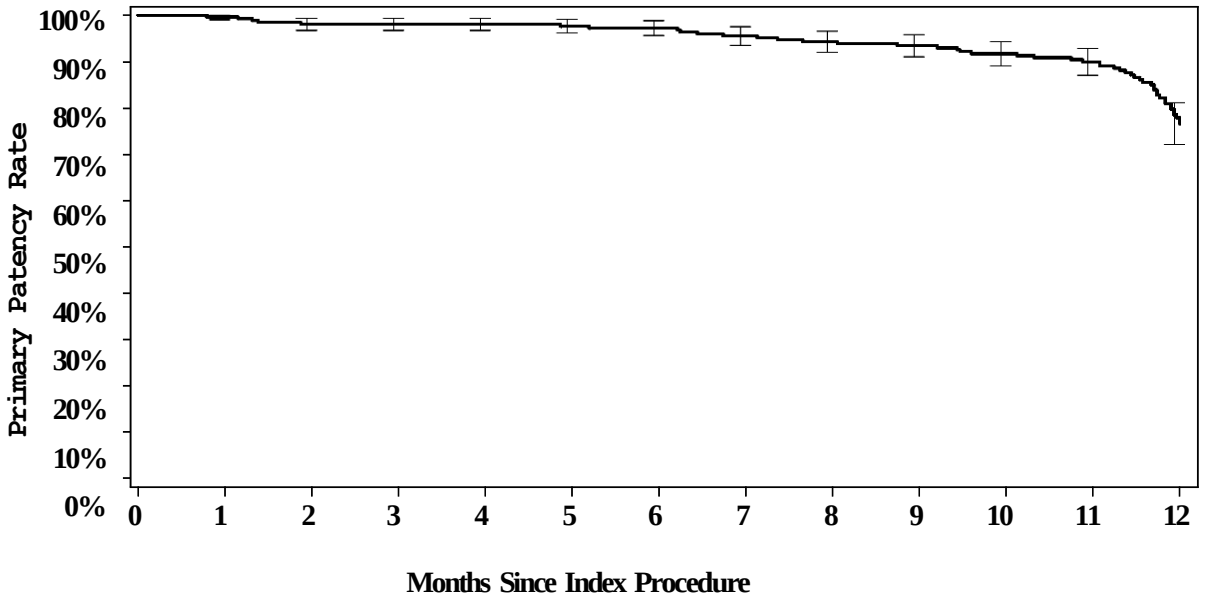


Table 16: Primary Patency in Core Stents Subjects through 12 Months

	Time from Index Procedure (months)							
Number of Subjects	**0**	**1**	**2**	**3**	**4**	**6**	**9**	**12**
Entered	260	259	254	244	243	243	236	220
Censored	1	4	6	1	0	5	7	78
At Risk*	259.5	257	251	243.5	243	240.5	232.5	181
Events	0	1	4	0	0	2	9	32
Events/Month	0.0	1.0	4.0	0.0	0.0	1.0	3.1	10.1
Event Rate	0%	0.4%	2.0%	2.0%	2.0%	2.8%	6.6%	23.3%
Event Free	100%	99.6%	98.0%	98.0%	98.0%	97.2%	93.4%	76.7%
Std Error	0%	0.4%	0.9%	0.9%	0.9%	1.0%	1.6%	3.0%
SVS SE	0%	0.4%	0.9%	0.9%	0.9%	1%	1.6%	2.8%

Subjects event-free at 12 months or later are censored at greater than 12 months. Intervals are end inclusive, e.g. interval 6 is defined as 4-6 months, inclusive. Event rate and standard error estimates are for interval end. Standard errors by Greenwood formula. *At Risk = entered – 0.5*censored.

As presented in **Figure 3** and **Table 17**, the freedom from loss of primary patency at 12 months for the entire stent matrix was 73.7%.

Figure 3: Primary Patency in All Stents through 12 Months

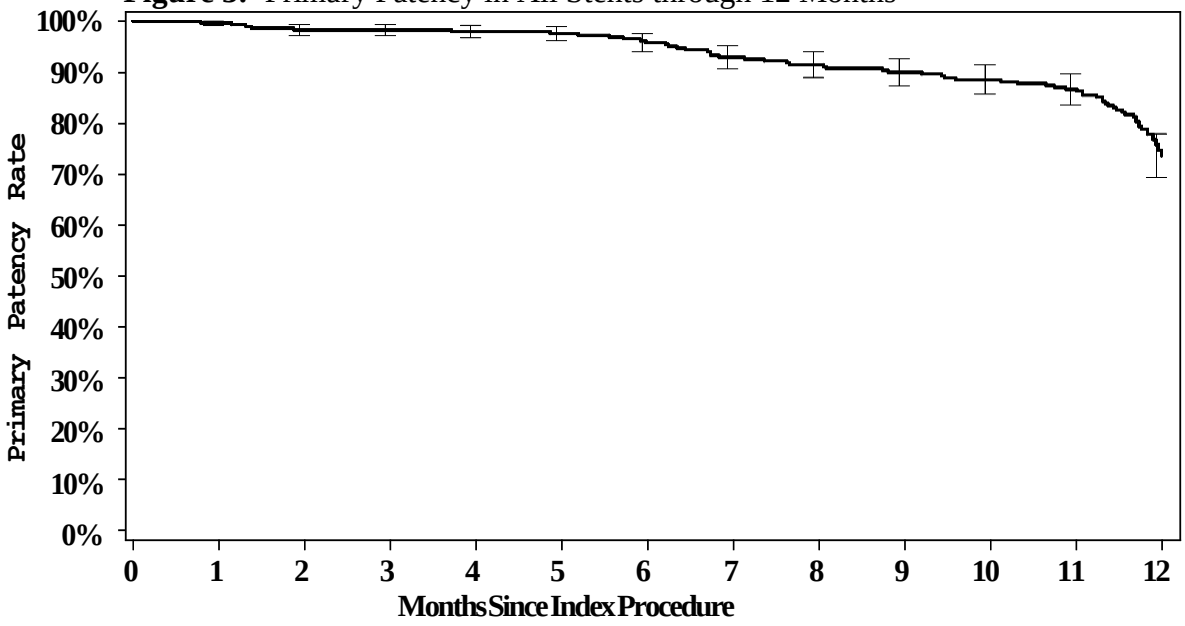


Table 17: Primary Patency in All Stents through 12 Months

	Time from Index Procedure (months)							
Number of Subjects	**0**	**1**	**2**	**3**	**4**	**6**	**9**	**12**
Entered	299	298	293	283	282	280	269	246
Censored	1	4	6	1	1	5	7	82
At Risk*	298.5	296	290	282.5	281.5	277.5	265.5	205
Events	0	1	4	0	1	6	16	37
Events/Month	0.0	1.0	4.0	0.0	1.0	2.9	5.5	11.7
Event Rate	0%	0.3%	1.7%	1.7%	2.1%	4.2%	10.0%	26.3%
Event Free	100%	99.7%	98.3%	98.3%	97.9%	95.8%	90.0%	73.7%
Std Error	0%	0.3%	0.8%	0.8%	0.8%	1.2%	1.8%	2.9%
SVS SE	0%	0.3%	0.8%	0.8%	0.8%	1.2%	1.7%	2.6%

Subjects event-free at 12 months or later are censored at greater than 12 months. Intervals are end inclusive, e.g. interval 6 is defined as 4-6 months, inclusive. Event rate and standard error estimates are for interval end. Standard errors by Greenwood formula. *At Risk = entered – 0.5*censored.

Secondary Effectiveness Endpoints

The secondary effectiveness endpoints are summarized in **Table 18** and **Table 19** below.

Table 18: Technical and Procedural Success (N=299)

	Overall	**95% CI**
Technical Success	99.0% (296/299)	[97.1%, 99.8%]
Procedure Success	99.0% (296/299)	[97.1%, 99.8%]

Technical success was defined as the ability to cross and dilate the lesion to achieve residual angiographic stenosis no greater than 30%.

Procedural success is defined as technical success with no MAEs within 24 hours of the index procedure.

Table 19: Analysis of Secondary Effectiveness Endpoints **(N= 299)**

Secondary Effectiveness Endpoint	**Overall**
Primary Patency at 12 Months	66.4% (174/262)
Primary Patency for Core Stent Matrix at 12 Months	69.5% (157/226)
Assisted Primary Patency at 12 Months	83.8% (207/247)
Assisted Primary Patency for Core Stent Matrix at 12 Months	85.5% (183/214)
Target Vessel Revascularization (TVR) Rate at 12 Months	13.8% (38/275)
Target Lesion Revascularization (TLR) Rate at 12 Months	13.8% (38/275)
Improvement in the Rutherford Clinical Improvement Scale of ≥ one at 12 months without the need for repeat TLR	79.5% (209/263)
Improvement in the Rutherford Clinical Improvement Scale of ≥ one at 12 months including subjects with repeat TLR	90.1% (237/263)
Increase in ABI of ≥ 0.10 or to an ABI ≥ 0.90 as compared to pre-procedure without the need for repeat TLR	59.0% (164/278)
Walking Improvement – Change in Walking Impairment Questionnaire Score from Baseline to 12 Months	34.03±37.22 (263) (-50.00, 100.00)
Walking Improvement – Change in Total Distance Walked over 6 Minutes from Baseline to 12 Months	69.3±130.1 (235) (-294.0, 1033.0)
Stent Fracture Rate at 12 Months	1.9% (6/318)

3. Subgroup Analyses

Gender: The female population had a higher overall TLR rate (22.4% vs. 11.4%) and a lower 12 month primary patency rate in the core stents matrix (55.6% vs 73.8%) than the male population. The female subgroup was slightly older with a greater prevalence of Rutherford classification 3 and 4 as well as hypertension compared to the male subgroup. The male subgroup had a higher prevalence of diabetes and coronary artery disease than the female subgroup. Despite these differences and the differences observed for patency in the core stent matrix, both female and male subgroups behaved similarly with respect to patency in the long stent matrix (44.4% and 48.1%, respectively). This subgroup analysis was not statistically powered.

Medically-Treated Diabetic Status: There was a slight trend towards higher patency in the non-diabetic population for shorter lesions (<150mm) and no differences seen in the MAE rate, but the findings were not statistically significant as the analysis was not sufficiently powered.

Rutherford Classification: The subgroup analysis based on Rutherford classification (claudication vs. critical limb ischemia [CLI]) was not conclusive given the very small proportion of subjects with CLI (n=14). This analysis was not statistically powered.

Stent Matrix: The last subgroup analysis was based on stent matrix (core vs. long vs. entire matrix) and was not statistically powered. The findings showed similar patency rates between the entire matrix and the core matrix, both showing an advantage over the long matrix as it should be expected.

Applicability to Pediatric Population

Peripheral artery disease is typically not found in pediatric populations. The Innova Stent System is not indicated for use in pediatric patients. The SuperNOVA clinical study did not evaluate safety and effectiveness in the pediatric population.

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 185 investigators (49 Principal Investigators). None of the clinical investigators had disclosable financial interests/arrangements as defined in sections 54.2(a), (b), (c), and (f). The information provided does not raise any questions about the reliability of the data.

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

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory 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.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The co-primary effectiveness endpoint was defined as stent patency at 12 months as evidences by a peak systolic velocity ratio (PSVR) of ≤2.4 determined from DUS and freedom from target lesion revascularization (TLR).. The intent-to-treat (ITT) cohort included all 299 subjects. In the core matrix of the ITT analysis, 69.5% (157/226) of subjects met the primary effectiveness endpoint . In the entire stent matrix of the ITT analysis, 66.4% (174/262) of subjects met the primary effectiveness endpoint. The long stent matrix (180-200 mm stents) did not have an established performance goal. Primary patency in the long stent matrix was 47.2% (17/36) of subjects enrolled. The lower bound of the two-sided 95% confidence interval (CI) for the core stent matrix was 63.0%. Therefore, the primary effectiveness objective of 66% was not met. The lower bound of the two-sided 95% confidence interval (CI) for the entire stent matrix was 60.3%. Therefore, the primary effectiveness objective of 63% was not met.

The primary effectiveness analysis used a conservative approach that was subject to bias in estimates of the 12 month patency since failure of patency was recorded regardless of whether 12-month data were available (such as cases of TLR prior to 12 months). A supporting analysis conforming to FDA guidance using Kaplan-Meier methods avoided this issue by evaluating all available data in a time-to-event format and censoring subjects with missing data at the appropriate times. Kaplan-Meier freedom from loss of patency had a 12-month estimate of 73.7%.

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory and animal studies as well as data collected in a clinical study conducted to support PMA approval as described above. The primary safety endpoint for this study was freedom from major adverse events. MAEs are defined as all causes of death through 1 month, target limb major amputation through 12 months and/or target lesion revascularization through 12 months.

Study success was based on the proportion of patients with freedom from 12 month MAE, including all causes of death through 1 month post-index procedure, target limb major amputation through 12 months post-index procedure, and target lesion revascularization (TLR) through 12 months post-index procedure when tested against the performance goal of 59.6% using the lower bound of the 95% CI. The ITT cohort, 85.8% (230/268), met the primary safety endpoint.

C. Benefit-Risk Conclusion

The probable benefits of the device are based on data collected in a clinical study conducted to support PMA approval as described above. The probable benefits of the INNOVA Vascular Self-expanding Stent System of improving the patient symptoms and quality of life outweigh the probable risks associated with use of the device.

Additional factors that were considered in determining probable risks and benefits for the INNOVA Vascular Stent Self-expanding Stent System included:

- Patient follow-up was satisfactory and with limited missing data. Follow-up for the PMA was 12 months but follow-up will continue for 3 years (5 years for Japan) to evaluate the longer term device performance, such as the duration of the benefit and long term adverse event rates.

- The pivotal study was a multi-center study conducted in the United States, Europe, Japan and Canada centers. The results obtained should not differ from the post-market performance.

- Most patients with the disease have symptoms only, but some patients may have more extensive disease involvement. The device treats the hemodynamic consequences of the disease to improve perfusion and function. The disease is chronic and affects the mobility of the patient and the quality of life. It is treatable but not curable.

- There are alternative treatments available, but this treatment is highly valued by patients because it improves their quality of life with lesser need for repeat procedures compared to a performance goal based upon angioplasty results without stenting.

- Patient risk is minimized by limiting use to operators who have the necessary training to use the device safely and effectively and by adherence to recommended periprocedural medications regimens.

In conclusion, given the available information above, the data support that the probable benefits outweigh the probable risks for using the device to improve luminal diameter in symptomatic patients with de novo or restenotic native lesions or occlusions of the superficial femoral artery and/or proximal popliteal artery with reference vessel diameters ranging from 4.0 mm to 7.0 mm and lesion length up to 190 mm.

D. Overall Conclusions

The clinical and non-clinical data in this application provide a reasonable assurance that the device is safe and effective. The SuperNOVA clinical study met its primary and secondary safety endpoints supporting the Innova™ Self-Expanding Stent System. Although the observed patency for the co-primary effectiveness endpoints in the core matrix and the entire matrix surpassed the established PG in absolute

numbers, the lower confidence bounds did not, thus the primary effectiveness objective was not met. Patency in the long stent matrix was 47.2%, which failed to meet the PG of 50% (note that this was a non-statistically driven goal). The lower patency rates may have been influenced by a number of factors, including the lesion length, lesion location, degree of calcification, and challenging outflow conditions. Treatment with the Innova Stent System provided improvement in the symptoms and quality of life of the subjects enrolled in the SuperNOVA study. Generally, the therapy showed a good safety profile and favorable clinical outcomes. The benefits of the INNOVA Vascular Stent Self-expanding Stent System outweigh the risks when the device is used as indicated in accordance with the labeling and Directions for Use.

XIII. CDRH DECISION

CDRH issued an approval order on July 21, 2015. The final conditions of approval cited in the approval order are described below.

1. *SuperNOVA Continued Follow-Up Study:* This study must be conducted per Protocol 90875294, Version AE, dated July 12, 2013, and Statistical Analysis Plan 90875301, Version AB, dated July 2, 2014. This study is a multi-center, single arm, prospective continued follow-up of the SuperNOVA global pivotal study. It will evaluate the long-term safety and effectiveness of the Innova stent. All 256 remaining patients (10 patients exited due to death) of the 299 SuperNOVA global pivotal study enrolled from 49 investigational sites will be followed annually through 36 months post-procedure (60 months for subjects enrolled in Japan) with expected no more than 20% attrition, not including attrition due to death.

   The safety and effectiveness endpoints to be assessed through 36 months (60 months for subjects enrolled in Japan) post-procedure are: (1) the composite Major Adverse (MAE) Rate and its individual components; (2) primary and assisted primary patency; (3) stent fracture rate; and (4) other effectiveness rates as defined in the protocol.

   A. Primary Safety Endpoint –

      - The safety endpoint assesses a composite MAE rate and will be reported at 2 and 3 years post-procedure. The MAEs considered and adjudicated by the Clinical Events committee are defined as:
        - Death
        - Target limb major amputation
        - Target Lesion Revascularization
        - Target Vessel Revascularization
        - Stent Thrombosis

   B. Co-Primary Effectiveness Endpoints -

      - The effectiveness endpoints assess vessel primary patency as determined by Duplex Ultrasound (DUS). Primary patency will be reported at 2

years post-procedure for the core stent matrix, the long stents and the entire matrix.

- Vessel primary patency is defined as freedom from more than 50% stenosis based on DUS peak systolic velocity ratio comparing data within the target segment to the proximal normal arterial segment in the absence of Target Lesion Revascularization or bypass.
- The DUS will be conducted at each site per protocol requirements and sent to an independent core laboratory for analysis.
- A systolic velocity ratio >2.4 suggests >50% stenosis.

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

XIV. 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.

XV. REFERENCES

None.