
SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device generic name:	Iliac stent
Device trade name:	Astron Peripheral Self-Expanding Nitinol Stent System (Astron Stent System)
Product Code (procode)	NIO
Applicant's name and address:	BIOTRONIK, Inc. 6024 Jean Road Lake Oswego, OR 97035
PMA Number	P140030
Date of Panel recommendation	None
Date of notice of approval to the applicant	December 17, 2015

II. INDICATIONS FOR USE

The Astron Stent System is indicated for improving luminal diameter in patients with iliac atherosclerotic lesions in vessel reference diameters between 4.3mm and 9.5mm and lesion lengths up to 105mm.

III. CONTRAINDICATIONS

There are no known contraindications.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Astron stent system Instructions for Use.

V. DEVICE DESCRIPTION

The Astron stent system is a self-expanding stent loaded on an over-the-wire delivery system (see **Figure 1**). The stent (1) is laser-cut from a nitinol tube. It carries four radiopaque extensions at each end (1a, 1b) and is completely coated with amorphous silicon carbide (a-SiC:H). The delivery system consists of two coaxially arranged elements: the inner shaft (2) and the outer sheath (3). The inner shaft is made of a thermoplastic polymer. At the proximal end, it is covered with a stainless steel tube. The safety tab (4) that covers the stainless steel tube prevents accidental stent release. The stainless steel tube incorporates a black release marker (5) that indicates the completion of stent deployment and ends with a Luer port (6) at the proximal guide wire exit.

The central guide wire lumen within the inner shaft continues to the radiopaque tip (7). The stent is mounted between the inner shaft and the outer sheath proximal to the tip, between two radiopaque markers (8), which facilitate fluoroscopic visualization, and positioning of the delivery system towards and across the lesion. The outer sheath begins within the T-connector (9) and extends towards the tip. It covers the stent and keeps it constrained within its distal end. A hydrophobic coating is applied to the inside and outside of the entire outer sheath. The annular space between the inner shaft and the outer sheath can be flushed through the Luer port (10) at the T-connector. The guide wire lumen of the inner shaft is flushed through the Luer port at the proximal guide wire exit. The guide wire lumen permits the use of 0.035” guide wires to facilitate advancement of the delivery system through the lesion to be treated. The stent system is shipped with an “Easy Release”-tube (11) inserted over the proximal outer sheath. The “Easy Release”-tube is intended to be inserted into the hemostatic valve of the introducer to reduce friction between the delivery system and the hemostatic valve during stent release.

The stent system and the “Easy Release” tube are compatible with an appropriately sized introducer sheath according to the indications on the label.

The stent is advanced to the intended implantation location by means of the over-the-wire delivery system and is deployed by pulling back the outer sheath at the T-Connector while immobilizing the inner shaft. The stent remains in the vessel as a permanent implant.

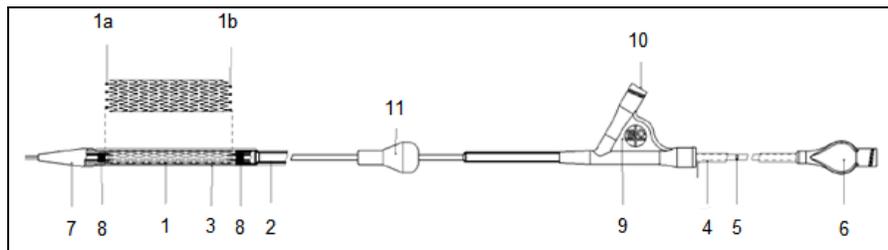


Figure 1: Astron stent system

The Astron stent is available with fully expanded stent diameters of 7, 8, 9 and 10 mm and stent lengths of 30, 40, 60 and 80 mm. A matrix of the available sizes is provided in **Table 1.**

Table 1: Astron Available Sizes

Stent Length (mm)		30		40		60		80	
Usable Length (cm)		72	130	72	130	72	130	72	130
Nominal Stent ø (mm)	7	X	X	X	X	X	X	X	X
	8	X	X	X	X	X	X	X	X
	9	X	X	X	X	X	X	X	X
	10			X		X		X	

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the correction of iliac artery disease:

- Percutaneous transluminal angioplasty (PTA)
- Stenting with another stent for which there is an approved indication
- Bypass surgery
- Lifestyle modifications (exercise and cessation of tobacco use)
- Medical therapy (antiplatelet therapy, lipid control, and medicine to manage claudication symptoms)

Each alternative has its own advantages and disadvantages. A patient should fully discuss those alternatives with his/her physician to select the method that best meets their expectations and lifestyle.

VII. MARKETING HISTORY

Astron self-expanding nitinol stent systems have been market released outside the United States (OUS) since October 2003. The Astron stent system has not been subject to any Field Safety Corrective Action or recall since introduction. A list of countries where the Astron stent system was distributed in 2013 and 2014 is provided in **Table 2**.

Table 2: List of countries where Astron stents were distributed in 2013-2014.

Argentina	Cyprus	Italy	Saudi Arabia
Australia	Czech. Republic	Jordan	Slovakia
Austria	France	Kuwait	Slovenia
Azerbaijan	Georgia	Latvia	Spain
Belgium	Germany	Macedonia	Switzerland
Brazil	Great Britain	Malaysia	Thailand
Bulgaria	Greece	Netherlands	Turkey
Canada	Hungary	Palestine	United Arab Emirates
Chile	India	Poland	Vietnam
China	Iran	Portugal	
Colombia	Iraq	Romania	
Croatia	Israel	Russian Fed.	

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

The following are possible adverse events that may occur relative to the stenting procedure and chronic implant of the Astron stent. These potential adverse events include, but are not limited to, the following:

- Allergic reactions to contrast media, antiplatelet aggregation or anticoagulant medications, amorphous silicon carbide and nitinol and / or its components (e.g. nickel, titanium)
- Bleeding events: Access site bleeding or hemorrhage, hemorrhage requiring transfusion or other treatment

- Death
- Embolization of air, thrombotic or atherosclerotic material
- Emergency surgery to correct vascular complications
- Infection and sepsis
- Stent system events: Failure to deliver stent to intended site, stent misplacement, stent deformation, stent embolization, stent thrombosis or occlusion, stent fracture, stent migration, inadequate apposition or compression of stent/s, withdrawal difficulties, embolization of catheter material
- Tissue necrosis and limb loss due to distal embolization
- Vascular events: Access site hematoma, hypotension/ hypertension, pseudoaneurysm, arteriovenous fistula formation, retroperitoneal hematoma, vessel dissection or perforation, restenosis, thrombosis or occlusion, vasospasm, peripheral ischemia, dissection, distal embolization (air, tissue debris, thrombus)

The BIOFLEX-I clinical trial conducted with the Astron stent system contributed to the analysis of adverse events. The observed serious adverse events of the BIOFLEX-I study are described below in the summary of clinical studies in **Table 17**.

IX. SUMMARY OF PRECLINICAL STUDIES

A. IN VITRO BENCH TESTING

In vitro bench testing was performed to assess the functional characteristics of the Astron stent system. Testing was conducted according to the guidelines provided in *FDA Guidance for Industry and FDA Staff-Non-clinical Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems* (April 18, 2010).

Additionally, testing followed updated guidelines provided in *Select Updates for Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems - Draft Guidance for Industry and Food and Drug Administration Staff* (August 30, 2013).

Error! Reference source not found. below summarizes the bench testing performed on the Astron stent system. The test results are supportive of the device safety and effectiveness.

Table 3: Non-Clinical Engineering Tests of Stent and Delivery System

Test	Test Purpose	Acceptance Criteria	Results
Stent Dimensional and Functional Testing			
Determination of the Austenitic final transformation temperature (A_f)	To evaluate the Austenite finish temperature (A_f) of Astron stent.	Passed test if $A_f = 25 \pm 10^\circ\text{C}$.	Pass

Table 3: Non-Clinical Engineering Tests of Stent and Delivery System

Test	Test Purpose	Acceptance Criteria	Results
Surface Characterization	Characterization of the stent surface and a-SiC:H coating.	Characterization study only.	Elemental components of the coating and stent were detected. Coating was confirmed to be uniform.
Pitting and crevice corrosion resistance – pre-fatigue	To evaluate the susceptibility of the metallic components of the stent to pitting and crevice corrosion pre-fatigue.	Passed test if the range of stable passivity >200 mV, breakdown potential >300 mV vs. Saturated calomel electrode (SCE) and results are comparable or better than post-fatigued samples.	Pass
Corrosion resistance following accelerated durability testing in overlapped configuration	To evaluate the susceptibility of the metallic components of the test article, to corrosion in a simulated physiological environment for the intended implant duration in overlapped configuration.	Passed test if the breakdown potential >200 mV, the breakdown potential >600 mV vs. SCE and results are comparable or better than pre-fatigued samples.	Pass
Galvanic Corrosion	To determine the potential for galvanic corrosion between stents. The susceptibility to galvanic corrosion is determined by corrosion rate in penetration per year.	The stent shall be resistant to corrosion when subjected to physiological conditions at the implantation site. The theoretical calculated corrosion rate in penetration per year must be less than 200 nm/year.	Pass
Dimensional inspection stent	The purpose of this test was to inspect and measure the stent body dimensions before placement onto delivery system.	Passed test if the stent met the design specifications for strut dimensions, stent diameter and stent length. Strut width tolerance (mm): ± 0.015 Strut thickness tolerance (mm): ± 0.020 Stent diameter tolerance (mm): ± 0.3 Stent length tolerance (mm): ± 0.5 (30 mm) or ± 1.0 (40, 60, 80 mm)	Pass
Percent surface area	To determine the surface coverage of the Astron stent in the vessel. Calculation has been performed for all stent sizes.	The test was used for characterization only.	The percent surface area for the stent was characterized.
Foreshortening stent	To determine the foreshortening of the unconstrained Astron stent	Passed test if the foreshortening of the stent was $\leq 7\%$.	Pass
Particle count and visual inspection of stent and coating after expansion into water	To investigate the Astron stent integrity and the coating integrity by particle count and visual inspection of the stent after deployment into water.	Particle count: not more than 6000 particles $\geq 10 \mu\text{m}$ and not more than 600 particles $\geq 25 \mu\text{m}$. Stent coating: No visually detectable coating defects Stent: No cracks or ruptures in the metal stent body up to and including maximum diameter.	Pass

Table 3: Non-Clinical Engineering Tests of Stent and Delivery System

Test	Test Purpose	Acceptance Criteria	Results
Particle count and visual inspection of stent and coating after expansion in simulated use environment of overlapped stents	To investigate the Astron stent integrity and the coating integrity by particle count and visual inspection of the stent during simulated use within an in-vitro model.	Particle count: not more than 6000 particles $\geq 10 \mu\text{m}$ and not more than 600 particles $\geq 25 \mu\text{m}$. Stent coating: No visually detectable coating defects Stent: No stent body defects.	Pass
Radial force	To measure the force (F_R) exerted by the self-expanding Astron stent on the vessel in the deployed state during expansion.	Passed test if the length normalized radial force of the expanded stent was: $F_R/L (\text{\O}_{\text{nominal}} - 1\text{mm}) > 0.02 \text{ N/mm}$ (at upper recommended vessel diameter) $F_R/L (\text{\O}_{\text{nominal}} - 2\text{mm}) < 0.20 \text{ N/mm}$ (at lower recommended vessel diameter)	Pass
Mechanical properties of the raw materials	To determine the mechanical properties of the raw materials of the Astron stent.	Mechanical properties of the raw materials must meet maximum or minimum criteria for the following parameters: Loading plateau UPS: $> 400 \text{ MPa}$ Tensile Strength TS: $> 1000 \text{ MPa}$ Uniform Elongation: $> 10 \%$ Residual Elongation: $< 0.5 \%$	Pass
Mechanical properties post-processing: tensile testing	To evaluate post processing material properties of nitinol material.	Passed test if the maximum or minimum criteria were met for the following mechanical properties of the post processed materials: Loading plateau UPS: $> 350 \text{ N/mm}^2$ Tensile Strength TS: $> 870 \text{ N/mm}^2$ Uniform Elongation: $> 12 \%$ Residual Elongation: $< 0.5 \%$	Pass
Mechanical properties post-processing: endurance limit	To evaluate 10 million cycles endurance limit data on stent.	Characterization study only: This shall be used to support endurance limit data from literature for the FEA.	The cyclic strain amplitude for material processed in-house for at least 10 million cycles was established.
Mechanical properties post-processing: material model FEA	To evaluate material model parameters for the use in Finite Element Analyses (FEA) of the Astron stent.	Characterization study only: The parameters were defined based on testing conducted on tube-based tensile test specimen that underwent processing steps comparable to Astron stents.	The final material model parameter settings yielded good correspondence between experimental and FEA data.
Mechanical properties post-processing: A_f -temperature	To evaluate the Austenite finish temperature (A_f) of the complete Astron stents.	Passed test if measured $A_f = 25 \pm 10^\circ\text{C}$.	Pass

Table 3: Non-Clinical Engineering Tests of Stent and Delivery System

Test	Test Purpose	Acceptance Criteria	Results
Stress analysis / fatigue analysis	To locate and determine the critical stresses and/or strains within the Astron stent due to manufacture, deployment and worst case <i>in vivo</i> loading by means of a Finite Element Analysis. Calculation of Safety Factor (SF)	Equivalent stress and strain levels and load history shall be documented. Passed test if the following specification was met: SF > 1	Pass
Accelerated durability testing radial overlapped pulsatile load	Determine the fatigue resistance of the expanded Astron stent in overlapped scenario after 380 million physiological load cycles (radial pulsatile load / equivalent to 10 years of service life).	The test was passed if: <ul style="list-style-type: none"> No serious loss in stent integrity No strut fractures of grade IV and V Characterization of coating integrity, particulate evaluation and fretting corrosion by: <ul style="list-style-type: none"> Documentation of all anomalies (e.g. flaps, bare spots) of the stent and stent coating post-testing Documentation of number of visible particulates and sub-visible particulate matter ($\geq 10 \mu\text{m}$ and $\geq 25 \mu\text{m}$) Documentation of size and number of fretting spots 	Pass
MRI safety and compatibility	The Astron stents were evaluated for RF induced heating, image distortion, magnetic force, and magnetic torque for single and overlapping stent up to 200mm. Evaluations were performed in 1.5 T and 3.0 T fields per ASTM 2182-11a, ASTM 2119-07, ASTM 2052-14, and ASTM 2213-06. Labeling recommendations for scanning conditions were also defined.	The test was passed if: <ul style="list-style-type: none"> Displacement and torque results met criteria of ASTM F2052-06 MRI related heating under recommended label conditions was physiological not consequential (i.e. 6.0°C for 15 minutes) Artifacts were characterized 	Pass
X-ray visibility	To determine the X-ray visibility of the Astron stent system and stent.	Passed test if the stent system and the stent were X-ray visible.	Pass
Crush resistance	To determine the crush resistance of the Astron stent.	Passed test if the mean stent diameter per stent section evaluated prior to and after the test did not deviate more than 5 %. Stent straightness: no visible stent deformation	Pass
Flexural rigidity of expanded stent	To determine the flexural rigidity/bending stiffness of the expanded Astron stent.	The bending stiffness of the expanded stent must be $\leq 75 \text{ Nmm}^2$.	Pass
Kink resistance peripheral stents	To characterize the kink resistance of the Astron stent.	The test was for characterization only. This test determines the smallest radius of curvature that the stent can withstand without kinking and recovers its original size and shape.	The smallest radius of curvature was determined.

Table 3: Non-Clinical Engineering Tests of Stent and Delivery System

Test	Test Purpose	Acceptance Criteria	Results
Delivery System Dimensional and Functional Testing			
Dimensional and visual inspection of the final product	To inspect the physical and dimensional properties of the Astron stent system.	Passed test if the delivery system met the design specifications for length, diameter, etc.	Pass
Crossing profile	To measure the crossing profile of the Astron stent system.	Passed test if the distal part of the Astron stent system could pass through a ring hole gauge of min. Ø: 0.079" and max. Ø: 0.087".	Pass
Compatibility with contrast medium	To evaluate the compatibility of the Astron stent system with contrast medium.	Passed if the following criteria after storage in contrast medium and subsequent stent deployment were met: <ul style="list-style-type: none"> • No visual impairment on the stent • Consistent release behavior of the stent • No deformation of the stent 	Pass
Tensile strength catheter	To determine the bond strength of the joints and/or fixed connections of the Astron stent system after pre-conditioning in a simulated use model.	Passed test if the minimum force at break was as follows: <ul style="list-style-type: none"> • ≥ 10 N for bond between proximal stent stopper and inner sleeve • ≥ 15 N for the bond between the tip and inner sleeve • ≥ 20 N for all other bonds 	Pass
Flexibility - stent system over a guidewire	To demonstrate the flexibility and the resistance to kinking of the stent systems.	Passed test if the stent system did not kink while passed through an anatomically relevant radius curve of 20 mm.	Pass
Adhesive strength of catheter coating	To evaluate the adhesive strength of the hydrophobic surface coating on the distal outer sheath of the Astron stent system after use in a simulated use model.	Passed if there was no visible indication of delaminating of the coating under 20X and 50 X microscopic magnifications.	Pass
Connector test	To ensure that the Luer locks and the T-connectors on the Astron stent system are resistant to overriding torque and stress cracking.	The test was passed if: <ul style="list-style-type: none"> • Overriding torque test: No visually detectable damages after torsional and axial load • Stress cracking: No damages detectable under the microscope after 48h of torsional and axial load 	Pass

Table 3: Non-Clinical Engineering Tests of Stent and Delivery System

Test	Test Purpose	Acceptance Criteria	Results
Simulated Use Testing			
Accuracy of stent placement	To demonstrate that the stent can be accurately placed in a simulated use model.	Passed test if the stent ends were within ± 4 mm of the target deployment area.	Pass
Torque testing	To evaluate the torsional bond/torque strength of the delivery system. Test is performed in a simulated use model.	Passed test if all bonds of the device remained undamaged after ten rotations with the tip clamped in place.	Pass
The following tests were conducted in sequence.			
Environmental conditioning (See also packaging tests)	Ensure that the Astron stent system maintains its integrity after exposure to simulated transport, storage, and handling conditions.	Passed if there are no visual defects or damage to the product	Pass
Trackability	To evaluate the trackability of the Astron stent system by measuring proximal force [N] against the distance tracked [mm] in a simulated use model.	Passed if the force-distance curves are comparable to competitor devices.	Pass
Pushability	To evaluate the pushability of the Astron stent system by measuring distal force [N] to the applied proximal insertion distance [mm] when pushing or positioning the stent system in a simulated use model.	Passed if the force-distance curves are comparable to competitor devices	Pass
Introducer compatibility	To assess the compatibility of the stent system with commercially available introducer sheaths. Test is performed using a simulated use model.	Passed test if the stent system (including easy release) is compatible with pre-determined 6F introducer sheaths.	Pass
Release force	To measure the stent release force during deployment. Test is performed in a simulated use model.	Passed test if the maximum release force was ≤ 15 N.	Pass
Delivery, deployment and retraction	To evaluate if the delivery system can reliably deliver the stent to the intended location in a simulated use model.	Passed test if the delivery system delivers the stent to the intended location without damage to the stent.	Pass

B. STERILIZATION

The Astron stent system is sterilized with ethylene oxide (EO) gas to a sterility assurance level (SAL) of 1×10^{-6} in compliance with ISO 11135-1:2007 – *Sterilization of health care products -- Ethylene oxide -- Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices*. The product has also been shown to meet the endotoxin limit of 20 EU/device in FDA Guideline 1987, LAL endotoxin test.

C. PACKAGING AND PRODUCT SHELF LIFE

Packaging verification testing was performed to demonstrate that the design of the Astron 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 (**Table 4**).

Table 3: Packaging Tests

Test	Test Purpose	Acceptance Criteria	Results
Environmental testing	To evaluate packaging integrity after sterilization and exposure to conditions experienced during normal transport and storage.	The test was passed if: <ul style="list-style-type: none"> • Shipping container integrity: The shipping container must be closed and its content must remain inside. • Box integrity: The box must be closed and its content must remain inside. The quality seal must be closed. • Pouch (sterile barrier) integrity: Any damage to the pouch that could compromise the sterility of the product is not permissible. The pouch must be closed and free of holes, cracks, tears, or creases. The seals must be at least 6 mm wide and passing canals or passing enclosures must be absent. • Labeling integrity: All labels must stay attached to the packaging. All labeling elements must be legible. • Fixation of device: The device must remain fixed inside the packaging in its intended position. 	Pass
Compression testing (packaging)	To evaluate packaging integrity after compression conditioning.	No damage to the product or sterile barrier system	Pass
Peel-open characteristics/ Visual inspection packaging seals	To evaluate the integrity of the sealing seams of the sterile barrier system after sterilization and environmental conditioning.	Peel-open characteristics must be continuous and homogeneous, without delamination or tearing of the materials. Fibers must be absent. The peel transfer of the seals must be at least 6 mm wide and passing canals or passing enclosures must be absent.	Pass
Seal strength	To determine the peel strength of the sealing seams of the sterile barrier system after sterilization and environmental conditioning.	The peel strength of the pouch must be ≥ 2.0 N.	Pass
Dye penetration	To evaluate the integrity of the sealing seams of the sterile barrier system after sterilization and environmental conditioning.	No seal leaks (i.e., no dye penetration through the seal).	Pass

Table 3: Packaging Tests

Test	Test Purpose	Acceptance Criteria	Results
Bubble emission	To evaluate integrity of the sterile barrier system after sterilization and environmental conditioning.	No seal and package leakage (i.e., no bubble emission).	Pass

A three-year shelf life was verified for the Astron stent and delivery system by conducting performance testing on samples that had been real-time aged for three years (**Table 5**). Packaging shelf life was verified by testing performance on samples subjected to accelerated aging simulating three years of shelf life.

Table 4: Shelf life Tests

Test	Test Purpose	Acceptance Criteria	Results
Stent Dimensional and Functional Testing			
Stent dimensions & foreshortening after 3 years real-time aging	To determine the foreshortening as well as diameter and length after expansion of the Astron stent after 3 years real-time aging.	Passed test if the stent met the following specifications stent diameter, stent length, and stent foreshortening. Stent diameter tolerance (mm): ± 0.3 Stent length tolerance (mm): ± 1.0 (stent length 80 mm) Foreshortening of the stent: $\leq 7\%$.	Pass
Radial force after 3 years real-time aging	To measure the force exerted by the self-expanding Astron stent on the vessel in the deployed state during expansion after 3 years real-time aging.	Passed test if the length normalized radial force of the expanded stent was: $F_R/L (\text{Ø}_{\text{nominal}} - 1\text{mm}) > 0.02 \text{ N/mm}$ (at upper recommended vessel diameter) $F_R/L (\text{Ø}_{\text{nominal}} - 2\text{mm}) < 0.20 \text{ N/mm}$ (at lower recommended vessel diameter)	Pass
Particle count and visual inspection of stent and coating after delivery, deployment and retraction into water after 3 years real-time aging	To investigate the Astron stent integrity and the coating integrity by particle count and visual inspection of the stent during simulated use within an in-vitro model after 3 years real time aging.	Particle count: not more than 6000 particles $\geq 10 \mu\text{m}$ and not more than 600 particles $\geq 25 \mu\text{m}$. Stent coating: No visually detectable coating defects Stent: No stent body defects.	Pass
Delivery System Dimensional and Functional Testing			
Functional tests after 3 years real-time aging	To evaluate functionality of the Astron stent system after real time aging of 3 years including visual and dimensional investigation.	The test was passed when the specifications were met according to the un-aged device design requirements.	Pass

Table 4: Shelf life Tests

Test	Test Purpose	Acceptance Criteria	Results
Torque testing after 3 years real-time aging	To evaluate the torsional bond / torque strength of the delivery system after 3 years real time aging. Test is performed in a simulated use model.	Passed test if all bonds of the device remained undamaged after ten rotations with the tip clamped in place.	Pass
Adhesive strength of catheter coating after 3 years real-time aging	To evaluate the adhesive strength of the hydrophobic surface coating on the distal outer sheath of the Astron stent system after 3 years real time aging and after use in a simulated use model.	Passed if there was no visible indication of delaminating of the coating under 20X and 50X microscopic magnifications.	Pass
Packaging Testing			
Peel-open characteristics / Visual Inspection packaging seals and seal strength after accelerated aging representing 3 years	To evaluate the integrity of the sealing seams of the sterile barrier after sterilization, environmental conditioning and accelerated aging.	Peel-open characteristics must be continuous and homogeneous, without delamination or tearing of the materials. Fibers must be absent. The peel transfer of the seals must be at least 6 mm wide and passing canals or passing enclosures must be absent. The peel strength of the pouch must be ≥ 2.0 N.	Pass
Dye penetration after accelerated aging representing 3 years	To evaluate the integrity of the sealing seams of the sterile barrier system after sterilization, environmental conditioning and accelerated aging.	No seal leaks (i.e., no dye penetration through the seal).	Pass
Bubble emission after accelerated aging representing 3 years	To evaluate integrity of the sterile barrier system after sterilization, environmental conditioning and accelerated aging.	No seal and package leakage (i.e., no bubble emission).	Pass

D. ANIMAL STUDIES

The purpose of the animal studies was to evaluate *in vivo* safety of the Astron stent system. This was done by examination of the vascular response (i.e., patency, degree of inflammation, thrombosis) and mechanical integrity (evaluation of strut fractures) of overlapped stents in comparison to control devices. A marketed iliac stent was used as control. The two safety studies (28-day and 90-day) were conducted using healthy swine model and were performed in accordance with the Good Laboratory Practice (GLP) for Non-clinical Laboratory Studies requirements outlined in 21 CFR Part 58. The results of the animal studies support the safety and performance of the device. A description of the studies and results is provided in **Table 6**.

Table 6: Summary of animal studies conducted on Astron stent system

Study Type	Number of Animals	Implant location	# Stents	Testing summary
28-day safety study	5 swine	Femoral arteries / carotid approach	<p>10 Astron 5 overlapping stent pairs stent diameter: 7mm stent lengths: 80mm + 40mm</p> <p>10 control 5 overlapping stent pairs stent diameter: 7mm stent lengths: 80mm + 40mm</p>	<p>All devices were easy to position and deploy in the femoral arteries and all device performance parameters were rated as good or excellent.</p> <p>No evidence of dissection, thrombosis or aneurysms was observed by angiography.</p> <p>All angiographic parameters indicating lumen patency were similar to the results of the control device.</p> <p>Evaluation of vascular morphometry and inflammation showed no significant differences between Astron and the control.</p> <p>Endothelialization scores were not significantly different between both groups.</p> <p>Strut fractures: No statistical difference was observed among the groups.</p>
90-day safety study	5 swine	Iliac arteries / carotid approach	<p>8 Astron 4 overlapping stent pairs stent diameter: 7 or 8mm stent length: 40mm + 40mm</p> <p>8 control 4 overlapping stent pairs stent diameter: 7 or 8mm stent length: 40mm + 40mm</p>	<p>All device performance parameters were rated as good.</p> <p>No evidence of dissection, thrombosis or aneurysms was observed angiographically. Angiographic parameters indicating lumen patency did not show significant differences between Astron and the control.</p> <p>Histomorphometry demonstrated similar results for all parameters for both groups.</p> <p>Inflammation scores were significantly lower for the Astron group than for the control group. Low fibrin scores and complete endothelialization in both groups at 90 days demonstrate that the healing process was completed.</p> <p>No strut fracture was observed in any of the groups.</p>

E. BIOCOMPATIBILITY

Biocompatibility testing for the Astron stent and delivery system was conducted separately on (1) coupons representative of the stent, and (2) the delivery system. In addition, chemical characterization testing was conducted on the test articles and the final sterilized devices to confirm that the test articles were representative of the final sterilized device. The stent was categorized as an implant device with permanent contact (> 30 days) with circulating blood and cardiovascular tissue, and the delivery system was categorized as an externally communicating device with limited contact duration (< 24 hours) with circulating blood and cardiovascular tissue. Tests were conducted on ethylene oxide sterilized samples.

All biocompatibility testing was conducted in accordance with:

- Guidance for Industry and FDA Staff: Non-Clinical Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems (April 18, 2010)
- Good Laboratory Practices Regulations (21 CFR § 58)

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

A summary of the biocompatibility information provided to support this PMA can be found in **Table 7**, below.

The results from the biocompatibility evaluation support the overall conclusion that the Astron stent system is biocompatible for its intended use and duration.

Table 7: Summary Biocompatibility Testing

Test Performed	Test Description	Delivery System	Stent (coupon)	Results
Cytotoxicity	ISO Neutral Red Uptake Cytotoxicity	X	X	Non-cytotoxic
Sensitization	ISO Guinea Pig Maximization	X	X	Non-sensitizing
Irritation	ISO Intracutaneous Reactivity	X	X	Non-irritant
Acute Systemic Toxicity	ISO Systemic Toxicity	X	X	Non-toxic
Pyrogenicity	USP Material-Mediated Pyrogenicity	X	X	Non-pyrogenic
Implantation	14 day ISO Intramuscular Implantation	n/a	X	Non-toxic
	90 day ISO Intramuscular Implantation	n/a	X	Non-toxic
Hemocompatibility	ASTM Hemolysis (Direct and Indirect Contact)	X	X	Non-hemolytic
	Direct Contact Complement Activation (C3a & SC5b-9)	X	X	Not a complement activator
Supportive Analytical Chemistry Tests				
Chemical characterization	Gas Chromatography - Mass Spectroscopy (GC/MS) for volatile and semi-volatile, organic compounds	X	X	Data from test article and final, sterilized device confirm that test articles are representative of final, sterilized device
	Inductively Coupled Plasma (ICP) Spectroscopy for metallic compounds	n/a	X	Data from test article and final, sterilized device confirm that test articles are representative of final, sterilized device
	Ultra-Performance Liquid Chromatography - Mass Spectroscopy (LC/MS) for semi-volatile and non-volatile organic compounds	X	X	Data from test article and final, sterilized device confirm that test articles are representative of final, sterilized device
Ion-release	Immersion up to 63 days in Phosphate Buffered Saline (PBS) at 37°C. Extract analyzed by ICP-MS.	n/a	X	Data from test article and final, sterilized device confirm that test articles are representative of final, sterilized device

The potential for thrombogenicity, sub-chronic toxicity, and chronic toxicity were evaluated as part of other *in vivo* studies to evaluate the safety and effectiveness of the product in a vascular location, as described in Section D below. These additional animal studies demonstrated a lack of thrombus formation, inflammation and toxicity when the stent and delivery system were used in a clinically-relevant vascular location.

Chemical characterization data from coated and uncoated stents were used in lieu of traditional biocompatibility testing on the uncoated Astron stent. The chemical characterization testing demonstrated there were no volatile, semi-volatile or non-volatile organics or metallic ions that can be extracted from either the coated or uncoated stents. In addition, they provided data from coating integrity and fatigue testing to demonstrate the durability of the coating, as described in Section IX above.

The omission of genotoxicity and carcinogenicity testing were supported by information regarding the starting materials and processing of the finished stent in conjunction with chemical characterization data and toxicity information from the literature.

X. SUMMARY OF CLINICAL STUDIES

BIOTRONIK collected clinical data through the BIOFLEX-I clinical trial to establish a reasonable assurance of safety and effectiveness of iliac stenting with the Astron stent system for the treatment of atherosclerotic lesions found in iliac arteries. The trial was conducted under Investigational Device Exemption (IDE) #G100002. Data from this clinical trial were the basis for the PMA approval decision. A summary of the clinical trial is presented below.

A. STUDY DESIGN

BIOFLEX-I was a prospective, non-randomized, multi-center, study focusing separately on lesion treatment in the superficial femoral or proximal popliteal arteries, and the iliac artery. Only the iliac artery lesion treatment cohort is applicable to the Astron stent. Overall, the BIOFLEX-I study provisionally enrolled 474 subjects in order to achieve 161 evaluable Astron stent group subjects at 30 sites located in the United States, Canada and Austria.

The Astron stent was used for the treatment of common or external iliac artery lesions in 161 subjects in all 30 study sites. The primary endpoint for the Astron stent was a composite safety and effectiveness endpoint of the of procedure- or stent-related Major Adverse Events (MAE) rate at 12 months post-index procedure. The MAE rate includes 30-day mortality, along with 12-month rates of target lesion revascularization (TLR) and index limb amputation.

Subjects were considered eligible for Astron stent implantation if they had de novo or restenotic, atherosclerotic (≤ 140 mm long) or occlusive (≤ 100 mm long) lesions in either the common or external iliac arteries, with reference vessel diameters ranging from 6 to 9 mm. Evaluable subjects are subjects that underwent an investigational stent implant procedure where the stent system entered the introducer sheath.

Following enrollment/baseline and the index procedure, all evaluable subjects were assessed at 1, 6 and 12 months post-index procedure.

1. Clinical Inclusion and Exclusion Criteria

Subjects enrolled in the BIOFLEX-I Iliac study were required to meet the general and angiographic inclusion criteria. Potential study subjects who met any of the general and angiographic exclusion criteria were not eligible for enrollment in the study. Error! Reference source not found.8 lists all of the Inclusion and Exclusion Criteria.

Table 8: Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
<p>To support the objectives of this study, the following initial inclusion criteria must be met for a subject to be enrolled and considered for the index procedure:</p> <ul style="list-style-type: none"> • Age ≥ 18 years • Willingness to comply with study follow-up requirements • Candidate for PTA • Life-style limiting claudication or rest pain with an ABI ≤ 0.9 (resting or exercise). Thigh brachial index (TBI) may be used / performed if ABI is inadequate. • Written informed consent 	<p>To support the objectives of this study, the following initial exclusion criteria must not be present for a subject to be enrolled:</p> <ul style="list-style-type: none"> • Subjects pregnant or planning to become pregnant during the course of the study • Life expectancy of less than one year • Subject has major or minor tissue loss in the target limb(s); minor tissue loss defined as non-healing ulcer or focal gangrene with diffuse pedal ischemia; major tissue loss defined as tissue loss extending above transmetatarsal level where functional foot is no longer salvageable. • Previously stented lesion(s) in the target vessel • Target lesion(s) received previous treatment within six months prior to enrollment • Prior peripheral vascular bypass surgery involving the target limb(s) • Thrombophlebitis or deep vein thrombosis within the past 30 days • Known allergy to nitinol (nickel and/or titanium) • Participation in any other clinical investigational device or drug study. Subjects may be concurrently enrolled in a post-market study, as long as the post-market study device, drug or protocol does not interfere with the investigational treatment or protocol of this study. • Previous stroke or transient ischemic attack within the last six months prior to enrollment • Previous coronary or peripheral bypass surgery (non-target limb) within 30 days prior to enrollment • Intolerance to contrast agents that cannot be medically managed and/or intolerance to anti-platelet, anti-coagulant or thrombolytic medications • Refuses blood transfusions • Any medical condition, that in the opinion of the investigator, poses an unacceptable risk for implant of a stent according to the study indications

Inclusion Criteria	Exclusion Criteria
<p>For a subject to receive an investigational stent, the following procedure-related criteria must be met:</p> <ul style="list-style-type: none"> • One <i>de novo</i>, restenotic or occluded lesion representing an iliac indication • OR • Two <i>de novo</i>, restenotic or occluded lesions representing one femoro-popliteal indication and one iliac indication on contralateral limbs - (i.e. one lesion per limb) • Lesions may be one solid lesion or a series of multiple, smaller lesions to be treated as one lesion • Subjects with bilateral, iliac disease (i.e. one iliac lesion per limb) are eligible for enrollment into the study. The target lesion will be selected at the investigator's discretion based on study eligibility criteria. The contralateral iliac intervention may be performed at the time of the index procedure; however, the use of an investigational treatment is prohibited. If the contralateral iliac intervention is not performed at the time of the index procedure, the intervention must be performed at least 30 days after the index procedure. The use of an investigational treatment for the subsequent contralateral intervention is also prohibited. • Iliac lesions must be located only in either the common or external iliac artery • Lesions must be treatable with a maximum of two stents • Angiographic evidence of $\geq 70\%$ stenosis or occlusion (operator visual assessment) • Lesion length ≤ 140 mm (if <i>de novo</i> or restenotic) or ≤ 100 mm (if occluded) • Target vessel reference diameter: 6 to 9 mm (iliac arteries) by visual estimate • Angiographic evidence of patent SFA and PPA and angiographic evidence of at least one distal vessel runoff to the foot. Patent is defined as $< 50\%$ stenosis. 	<p>For a subject to receive an investigational stent, the following procedure-related criteria must not be present:</p> <ul style="list-style-type: none"> • $INR \geq 1.6$ • Concomitant renal failure with serum creatinine level > 2.5 mg/dL • Unresolved neutropenia (white blood cell count $< 3,000/\mu\text{L}$) or thrombocytopenia (platelet count $< 80,000/\mu\text{L}$) at the time of the index procedure • Unresolved bleeding disorder ($INR \geq 1.6$) at the time of the index procedure • Presence of other ipsilateral, arterial lesions distal to the target lesion requiring treatment within 30 days of the index procedure (either before or after) or at the time of the index procedure • Additional percutaneous interventional procedures (cardiac and/or peripheral) planned within 30 days after the index procedure (either before or after) • Treatment that requires access via upper extremity, popliteal or pedal arteries. • Presence of a complication following pre-dilation of target lesion • Presence of a target vessel/lesion that is excessively tortuous or calcified or is adjacent to an acute thrombus that is unresponsive to anti-thrombotic therapies • Target lesion is located within an aneurysm or associated with an aneurysm in the vessel segment either proximal or distal to the target lesion • Target lesion requires the use of cutting balloons, atherectomy or ablative devices • Subjects with less than single vessel runoff to the foot

2. Follow up Schedule

The required schedule of visits and assessments for the iliac cohort of the BIOFLEX-I study are provided in **Error! Reference source not found.9**. These visits included baseline evaluation (including subject screening and enrollment), index procedure, and office follow up exams at 1-, 6- and 12- month post-index procedure.

Table 9: Study Visit Assessment Schedule

	Baseline	Index Proc	1-Mo Visit ± 7 days	6-Mo Visit ± 30 days	12-Mo Visit ± 30 days	Unsch Visit
Informed consent (enrollment)	X					
Subject demographics / risk factors	X					
Blood pressure	X					
ABI measurement	X			X	X	
Subjective claudication status	X			X	X	X
Six-minute walk test	X			X	X	

	Baseline	Index Proc	1-Mo Visit ±7 days	6-Mo Visit ±30 days	12-Mo Visit ±30 days	Unsch Visit
WIQ	X			X	X	
Concomitant medications	X	X	X	X	X	X
Creatinine measurement		X				
INR measurement		X				
Complete blood count		X				
Angios to assess pre- and post-procedure lesion characteristics		X				
Arterial access information		X				
Highest/lowest ACT (heparin only)		X				
Procedure length		X				
Duplex ultrasound			X		X	
Adverse event assessment		X	X	X	X	X

3. Clinical Endpoints

The primary endpoint for the Astron stent is a composite safety and effectiveness endpoint of the rate of procedure- or stent-related MAEs at 12 months post-index procedure. The MAE rate includes 30-day mortality, along with 12-month rates of clinically-driven TLR and index limb amputation.

Secondary effectiveness endpoints for the Astron stent were as follows:

- Determination of the contribution of each individual MAE to the primary, composite endpoint
- Primary patency at 12 months
- Primary assisted patency
- Secondary patency
- Acute procedural success
- 30-day clinical success
- Ankle-brachial indices (ABI) at pre-treatment and 12 months
- Walking Impairment Questionnaire (WIQ) scores at pre-treatment and 12 months
- Six-minute walk distance at pre-treatment (baseline) and 12 months
- Rates of all adverse events not included in the evaluation of the primary endpoints
- Comparison of all primary and secondary endpoints between occlusive lesions (100% stenosis) and non-occlusive lesions (70% - 99% stenosis)

The definition for MAEs follows the recommendations given in the FDA guidance issued April 18, 2010, “Guidance for Industry and FDA Staff - Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems”.

The study success/failure criteria were established by comparing the primary endpoint to a performance goal of < 15% percent, which was based on a literature review. As such, the study evaluated whether the observed rate of MAEs at 12 months could statistically meet a performance goal of <15%, given a 7.5% expected 12-month MAE rate, with an assumed delta value of 7.5%. The primary composite endpoint hypothesis was evaluated using an exact binomial test of the observed MAE rate against the pre-specified performance goal of 15%.

The primary endpoint to evaluate the safety and effectiveness of the Astron stent is designed based on the primary assessment used in prior IDE clinical trials for currently approved iliac stents.

The study included several additional, secondary endpoints, but no formal hypotheses were associated with the evaluation of the secondary endpoints.

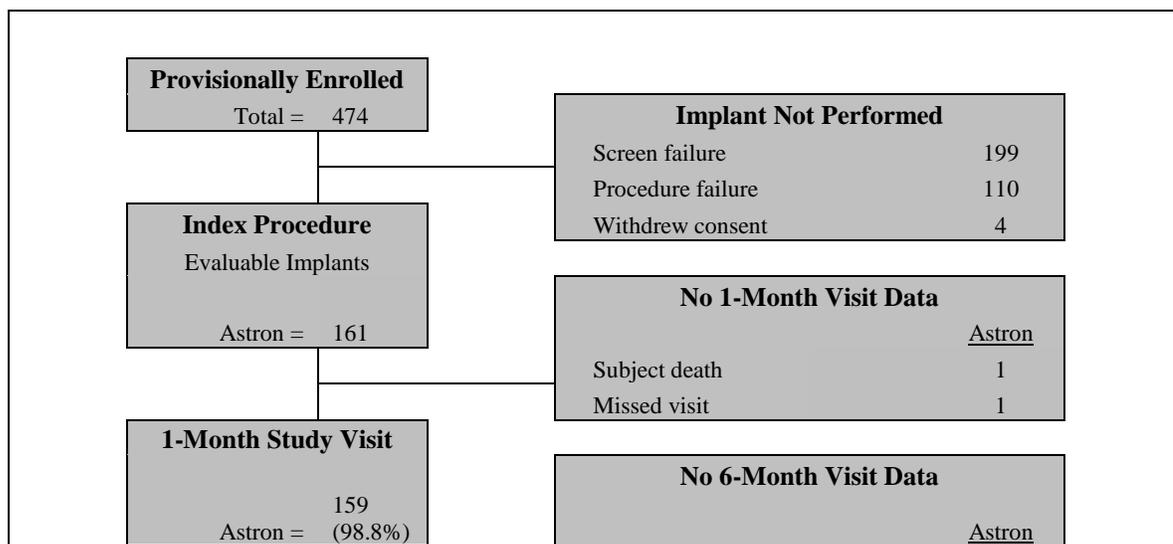
The primary analyses were performed on an intent-to-treat basis. Secondary analyses using multiple imputations were performed to address the impact of missing data on the primary study endpoints.

4. External Evaluation Groups:

All site-reported MAEs or possible MAEs, including deaths, were adjudicated as to their relationship to the procedure or stent by an independent Clinical Events Committee (CEC) composed of physicians knowledgeable in the treatment of Peripheral Artery Disease (PAD).

B. PATIENT ASSESSMENT / ACCOUNTABILITY OF PMA COHORT

Of the 161 evaluable subjects in the iliac cohort, 99.4% (160/161) had an Astron stent implanted; 98.8% (159/161) completed the 1 month follow-up visit; 92.5% (149/161) completed the 6-month follow up visit; and 90.1% (145/161) completed the 12-month follow-up visit. A patient accountability tree is provided in [Figure 2](#).



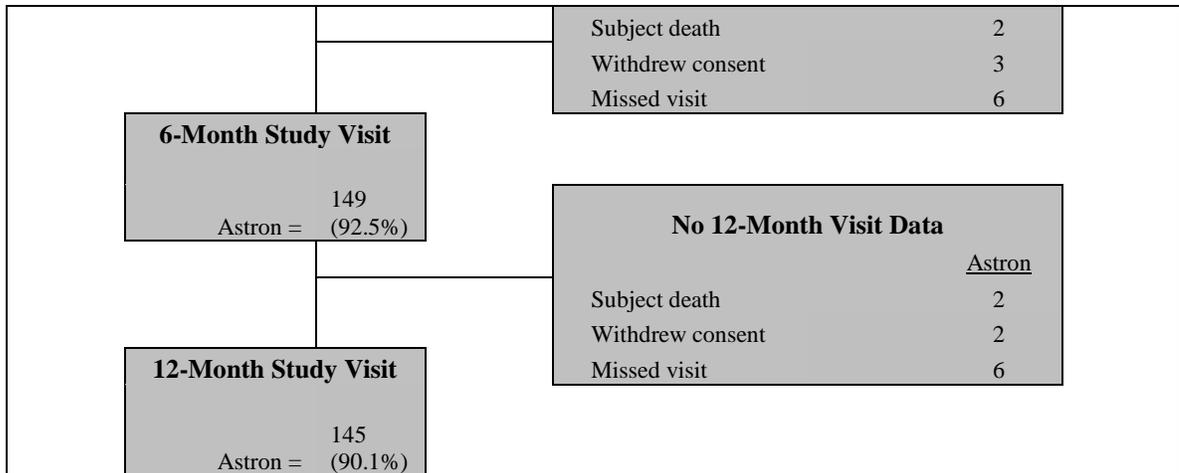


Figure 2: Detailed subject accountability

C. STUDY POPULATION DEMOGRAPHICS & BASELINE PARAMETERS

Table 10 provides a summary of the subject demographics and clinical characteristics enrollment/baseline visit for all evaluable subjects in the Astron stent group.

Table 10: Astron Stent Group Baseline Demographics and Clinical Characteristics

Parameter	Astron Evaluable n=161	
Age in years at enrollment		
Mean ± SD	63.6 ± 10.1	
Range (Min/Max)	40.9 - 91.9	
Gender (n, %)		
Male	105	65.2%
Female	56	34.8%
Race (n, %)		
White	152	94.4%
Black or African American	4	2.5%
Asian	4	2.5%
American Indian or Alaska Native	1	0.6%
Native Hawaiian or other Pacific Islander	0	0.0%
Hispanic Ethnicity (n, %)		
Hispanic	18	11.2%
Non-Hispanic	143	88.8%
General Medical History (n, %)		
Diabetes	32	19.9%

Table 10: Astron Stent Group Baseline Demographics and Clinical Characteristics

Parameter	Astron Evaluable n=161	
Hypertension	117	72.7%
Hyperlipidemia	125	77.6%
Smoking status		
Current	78	48.4%
Within last 5 years	36	22.4%
Never/not within last 5 years	47	29.2%
Cerebrovascular disease	22	13.7%
History of congestive heart failure	11	6.8%
History of ischemic heart disease	69	42.9%
History of coronary revascularization	54	33.5%
Renal insufficiency	11	6.8%

***Definitions:** Hypertension and Hyperlipidemia - requiring treatment with a prescription medication; cerebrovascular disease - carotid artery disease and history of stroke or TIA; congestive heart failure - ejection fraction < 40% or heart failure diagnosis; ischemic heart disease - myocardial infarction, angina pectoris, percutaneous or surgical coronary revascularization, positive exercise test or anti-anginal therapy; renal insufficiency - creatinine \geq 1.5 mg/dL (last measurement prior to baseline).

Table 51 and **Table 12** summarizes the baseline lesion characteristics (core lab and site-reported) for all evaluable subjects obtained from the baseline angiogram at the index procedure.

Table 51: Astron Stent Group Baseline Lesion Characteristics – Core Lab

Lesion Characteristic	Category	Astron n =161	
Lesion location (n, %)	Common iliac	107	66.5%
	External iliac	54	33.5%
Lesion calcification (n, %)	None	47	29.2%
	Moderate	68	42.2%
	Severe	46	28.6%
Lesion length (mm)	mean \pm SD range	35.9 \pm 21.3 8.6 to 105.1	
Pre-deployment minimum lumen diameter (mm)	mean \pm SD range	2.1 \pm 1.3 0 – 5.68	
Post-deployment minimum lumen diameter (mm)	mean \pm SD range	6.0 \pm 1.2 2.9 - 9.1	
Reference vessel diameter (mm)	mean \pm SD range	7.6 \pm 1.5 4.3 - 12.2	
Distal vessel runoff (n, %)	Not Available	35	21.7%
	0 vessel	9	5.6%
	1 vessel	32	19.9%
	2 vessel	48	29.8%
	3 vessel	37	23.0%

TASC II Type (n, %)	Type A	99	61.5%
	Type B	56	34.8%
	Type C	6	3.7%
	Type D	0	0.0%

Table 62: Astron Stent Group Baseline Lesion Characteristics – Site Reported

Variable (site reported)	Category	Astron n =161	
		Target side (n, %)	Right
	Left	74	46.0%
Lesion type (n, %)	De novo	147	91.3%
	Occlusion	13	8.1%
	Restenosis	1	0.6%
Variable (site reported)	Category	Astron n = 161	
Pre-deployment lesion stenosis (%)	mean ± SD	83.1 ± 9.6	
	Range	70 to 100	
Post-deployment lesion stenosis (%)	mean ± SD	4.6 ± 8.1	
	Range	0 to 50	

D. SAFETY AND EFFECTIVENESS RESULTS

1. Primary Endpoint Results

Overall, the Astron stent system demonstrated safety and effectiveness based on the observed performance goal. In the 146 Intent-to-treat (ITT) subjects with 12-month evaluations, the overall device-related and procedure-related MAE rate was 2.1% (3/146), with a 95% confidence interval of (0.4%, 5.9%). The MAE rate was lower than the expected rate of 7.5% and met the performance goal of <15% (p<0.0001).

The primary endpoint for the Astron stent is a composite of the rate of procedure- or stent-related MAEs at 12 months post-index procedure. The MAE rate includes 30-day mortality, along with 12-month rates of TLR and index limb amputation. All MAEs related to the Astron stent were adjudicated as to their relationship to the procedure or stent by an independent CEC composed of physicians knowledgeable in the treatment of PAD.

Table 3 summarizes the MAE rate for the Astron stent group at 12 months post index procedure. The MAE rates are presented based on CEC adjudicated event data.

Table 13: Astron Stent Group Primary Endpoint Results

Category	Rate (%) (95% CI), p-value
Intent-To-Treat Analysis (Primary) n = 146*	
Rate of procedure or stent-related MAE at 12-months	2.1% (3/146) (0.4%, 5.9%), p<0.0001

*Subjects completing the 12-month evaluation.

Error! Reference source not found.4 summarizes the distribution of MAE rates. The 30-day all-cause mortality rate was 0.7% (1/146), 95% CI [0.0%, 3.8%] and the target lesion revascularization (TLR) rates at 12 months were 1.4% (2/146) 95 % CI [0.2%, 4.5%]. No index limb amputation was reported over the 12-month period, and therefore the rate was 0.0% (0/146) 95% CI [0.0%, 2.5%]. The secondary per protocol analysis confirmed similar event instances and rates for the individual components.

The overall rates of the individual components of 30-day all-cause mortality, TLR and index limb amputation were low. There was no evidence that a single individual component contributed more significantly than the other components to the overall MAE rate.

Table 74: Distribution of MAE Rate

Outcome	Rate (95% CI)
Intent-to-Treat Analysis (Primary) n = 146*	
MAE Rate	2.1% (3/146) (0.4%, 5.9%)
30-day mortality	0.7% (1/146) (0.0%, 3.8%)
TLR	1.4% (2/146) (0.2%, 4.5%)
Index limb amputation	0.0% (0/146)

*Subjects completing the 12-month evaluation.

2. Gender Analysis

The heterogeneity of the primary endpoints between males and females was tested with a Fisher's Exact Test. An unadjusted p-value of 0.05 or less was considered evidence of a possible gender difference.

The comparison of the primary endpoint MAE rates in subjects with available data was not significant (p = 1.000, Fisher's Exact Test, 2-sided). The secondary endpoint analysis did not show any significant differences for secondary endpoints 1 through 15.

The MAE rates were similar between males and females and there was no evidence of a difference in the MAE rate associated with gender. There was no statistical evidence of differences between genders for the primary and secondary endpoints examined.

3. Secondary Effectiveness Results

Secondary endpoints were assessed at the specified time points. Key secondary endpoint safety and efficacy results for the ITT population are summarized in **Table 5**.

Table 15: Key Secondary Endpoint Effectiveness Results

Secondary Endpoint	
Distribution of procedure or stent-related MAE at 12-months	
30-Day mortality	0.7% (1/146)
TLR	1.4% (2/146)
Index limb amputation	0.0% (0/146)
Primary patency rate at 12 months ^a	89.8% (115/128)
Primary assisted patency rate at 12 months ^{b, c}	97.9% (143/146)
Subjects with repeat endovascular procedure on study limb outside of study lesion	2
Subjects with repeat surgical procedure on study limb outside of study lesion	0
Secondary patency rate at 12 months ^{c, d}	99.3% (145 /146)
Subjects requiring bypass on study limb	0
Subjects requiring amputation of study limb	0
Acute procedural success ^{c, e}	153/161 (95.0%)
30-day clinical success ^{c, f}	153/161 (95.0%)
ABI Change from Baseline to 12-month Paired Data (Mean ± SD), n=141	0.23 ± 0.19
Six Minute Walk Test Change from Baseline to 12 months Paired Data (Mean feet ± SD), n=131	157.5 ± 420.6
WIQ Score Changes from Baseline to 12 months Paired Data	
WIQ PAD Specific Score (Mean ± SD), n =143	43.9 ± 36.8
WIQ Walking Distance Score (Mean ± SD), n =144	40.7 ± 38.0
WIQ Walking Speed Score (Mean ± SD), n =143	21.5 ± 27.5
WIQ Stair Climbing Score (Mean ± SD), n=142	26.1 ± 35.6

- a) Freedom from more than 50% restenosis based on the duplex ultrasound peak systolic velocity ratio, comparing data within the treated segment to the proximal normal segment. A peak systolic velocity ratio greater than 2.4 was used to diagnose a stenosis greater than 50% in diameter.
- b) Freedom from a repeat procedure (endovascular or surgical) outside of the initially treated lesion to maintain patency of the target vessel. The treated lesion includes the stented segment plus 5 mm proximal and distal to the stent.
- c) One subject death within 30 days was included in this count.
- d) Freedom from treated lesion abandonment (bypass) or amputation of the target limb.
- e) Completion of the procedure and the stented lesion having less than 30% residual stenosis determined by angiography immediately after stent placement and no MAEs before hospital discharge.
- f) Completion of the procedure and the stented lesion having less than 30% residual stenosis determined by angiography immediately after stent placement and no MAEs within 30 days of the index procedure.

Error! Reference source not found.6 summarizes the adverse events for the ITT population, which a site reported as meeting the above criteria for serious in nature. Note that the total for each category of adverse events is not necessarily a sum of individual events, as it is a count of unique subjects with the adverse event.

Table 86: Summary of Serious Adverse Events through 12 Month

Category	Number of Evaluable Subjects with Event	Rate of Subjects with Event n = 161 Subjects
Vascular		
Angioplasty on left external iliac and SFA	1	0.62% (1/161)
Occlusion of bypass graft left iliopopliteal bypass conduit	1	0.62% (1/161)
Peripheral ischemia	3	1.86% (3/161)
Pseudoaneurysm	3	1.86% (3/161)
Stenosis or occlusion in contralateral extremity/target lesion within stent segment in the SFA	14	8.70% (14/161)
Stenosis or occlusion in target extremity outside of stent segment	8	4.97% (8/161)
Vessel dissection or perforation during PTA	1	0.62% (1/161)
Worsening of claudication	1	0.62% (1/161)
Total Vascular Events	29	18.01% (29/161)
Stent		
Failure to deliver stent to intended site	1	0.62% (1/161)
Stenosis or occlusion of target lesion within stent segment	2	1.24% (2/161)
Vessel dissection or perforation during stenting procedure	1	0.62% (1/161)
Total Stent Events	4	2.48% (4/161)
Procedure-Related		
Bleeding requiring treatment	2	1.24% (2/161)
Right femoral occlusion	2	1.24% (2/161)
Total Procedure-Related Events	4	2.48% (4/161)
Neurological		
Stroke	1	0.62% (1/161)
Transient ischemic attack	2	1.24% (2/161)
Total Neurological Events	3	1.86% (3/161)
Cardiovascular		
Angina	1	0.62% (1/161)
Atrial arrhythmia	2	1.24% (2/161)
Cardiac arrest	1	0.62% (1/161)
Cardiac catheterization	2	1.24% (2/161)
Chest pain	1	0.62% (1/161)
Coronary artery disease	4	2.48% (4/161)
Dizziness	1	0.62% (1/161)
ICD Device replacement	1	0.62% (1/161)

Myocardial infarction	1	0.62% (1/161)
Pericarditis	1	0.62% (1/161)
Superior mesenteric artery stenosis	1	0.62% (1/161)
Ventricular arrhythmia	1	0.62% (1/161)
Worsening heart failure	2	1.24% (2/161)
Total Cardiovascular Events	12	7.45% (12/161)
Infection		
E. coli infection	1	0.62% (1/161)
Erysipel	1	0.62% (1/161)
Pneumonia	2	1.24% (2/161)
Positive E. faecalis	1	0.62% (1/161)
Purulent drainage from wound	1	0.62% (1/161)
Urinary tract infection	1	0.62% (1/161)
Total Infection Events	5	3.11% (5/161)
Musculoskeletal		
Fracture	1	0.62% (1/161)
Lumbar laminectomy and fusion	1	0.62% (1/161)
Musculoskeletal injury	1	0.62% (1/161)
Musculoskeletal pain	2	1.24% (2/161)
Total Musculoskeletal Events	5	3.11% (5/161)
Gastrointestinal		
Abdominal Pain	3	1.86% (3/161)
Bleeding	5	3.11% (5/161)
Diarrhea	1	0.62% (1/161)
Nausea and/or vomiting	1	0.62% (1/161)
Total Gastrointestinal Events	9	5.59% (9/161)
Renal		
Acute pyelonephritis	1	0.62% (1/161)
Renal failure	1	0.62% (1/161)
Total Renal Events	2	1.24% (2/161)
Respiratory		
Asthma	1	0.62% (1/161)
COPD	2	1.24% (2/161)
Dyspnea	1	0.62% (1/161)
Hemoptysis	1	0.62% (1/161)
Total Respiratory Events	5	3.11% (5/161)
Nervous System		
Axonal sensible polyneuropathy	1	0.62% (1/161)
Total Nervous System Events	1	0.62% (1/161)
Endocrine		
Hyperglycemia	1	0.62% (1/161)

Total Endocrine Events	1	0.62% (1/161)
Other Medical Event		
Allergic reaction	1	0.62% (1/161)
Altered mental status	1	0.62% (1/161)
Anemia	1	0.62% (1/161)
Bleeding left eye	1	0.62% (1/161)
Cancer	6	3.73% (6/161)
Cataract	1	0.62% (1/161)
Electrolyte imbalance	2	1.24% (2/161)
Leucocytosis	1	0.62% (1/161)
Traumatic Injury	1	0.62% (1/161)
Other Adverse Event Total	14	8.70% (14/161)
Overall Serious Adverse Events Totals	67	41.61% (67/161)

4. Applicability to Pediatric Population

Peripheral artery disease is not typically found in pediatric populations. The Astron stent system is not indicated for use in pediatric patients. The BIOFLEX-I study did not evaluate safety and effectiveness in the pediatric population.

E. FINANCIAL DISCLOSURE

There were disclosable financial arrangements which had no effect on the reliability of data. There was one investigator that had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f). There were no investigators who received compensation for conducting the study where the value could be influenced by the outcome of the study, who were full-time or part-time employees of the sponsor, had significant payment of other sorts, had proprietary interest in the product tested, or had significant equity interest in the sponsor of the covered study.

XI. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

No supplemental clinical data was available or needed.

XII. PANEL RECOMMENDATIONS

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

Non-clinical testing performed during the design and development of the Astron stent system confirmed the product design characteristics, specifications, and intended use. The in vitro engineering testing conducted on the stent and delivery system demonstrated that the performance characteristics met the product specifications.

The biocompatibility and in vivo animal testing demonstrated that the acute and chronic in vivo performance characteristics of the Astron stent system provide reasonable assurance of safety and acceptability for clinical use.

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 BIOFLEX-I multi-center clinical study evaluated the safety and effectiveness of the Astron stent system in the treatment of subjects with atherosclerotic disease of the common or external iliac arteries. The performance goal assessment (primary endpoint) for the Astron stent was a composite of the rate of procedure- or stent-related MAEs at 12 months post-index procedure. The MAE rate included 30-day mortality, along with 12-month rates of TLR and index limb amputation. Overall, in the 146 Intention-to-Treat (ITT) subjects with 12-month evaluations, the MAE rate was 2.1% (3 out of 146), with a 95% confidence interval of (0.4%, 5.9%), which was lower than the expected rate of 7.5% and the performance goal of 15% ($p < 0.001$). Three Astron subjects experienced an MAE prior to 12 months, including one death on the day of the index procedure due to a rupture of the contralateral iliac, and two target lesion revascularizations.

B. RISK/BENEFIT ANALYSIS

The probable benefits of the devices are based on the data collected in the clinical study conducted to support PMA approval as described above. The results of the BIOFLEX-I study show positive clinical outcomes in terms of the primary and secondary endpoints (benefits) and outweigh risks when used as intended according to the Instructions for Use, as determined by the product risk analysis.

Additional factors that were considered in determining probable risks and benefits for the Astron Peripheral Self-Expanding Nitinol Stent System included:

- The study was designed based on prior IDE trials conducted to gain PMA approval for other iliac nitinol stents. The primary and secondary endpoints were analyzed and reported differences were found to be significant to a p-value of less than 0.05.
- The study was conducted with similar methodologies as other iliac stent IDE clinical trials using comparable performance goals.

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- The study results were similar to recently-approved nitinol stents for the treatment of iliac atherosclerotic disease. The low observed MAE rate at 12 months and low worldwide complaint history for the Astron stent in the post-market device support the absence of the need for an additional post-market study.
 - The results of the study can be applied to the general population of patients with iliac artery disease. The study was conducted on a typical population of subjects with iliac artery disease. The study did not exclude any typical patient subgroups that would be expected to benefit from treatment.
 - Risks are identifiable and similar to those previously reported and observed for other iliac self-expanding nitinol stents.
 - There are several alternatives for the correction of iliac artery disease, which includes: percutaneous transluminal angioplasty (PTA), stenting with another stent for which there is an approved indication, bypass surgery, lifestyle modifications, and medical therapy. The use of iliac stents in treating iliac artery disease is a preferred alternative in comparison to surgical intervention, given a more favorable risk-benefit profile.

In conclusion, given the available information above, the data supports that the probable benefits outweigh the probable risks for using the device for improving luminal diameter in patients with iliac atherosclerotic lesions in vessel reference diameters between 4.3mm and 9.5mm and lesion lengths up to 105mm.

C. OVERALL CONCLUSIONS

The results from non-clinical and clinical evaluations demonstrate that the Astron stent system provides reasonable assurance of safety and effectiveness when used as indicated and according to the Instructions for Use (IFU).

XIV. CDRH DECISION

CDRH issued an approval order on December 17, 2015.

The applicant's manufacturing facility was 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