SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Stent, Superficial Femoral Artery
Device Trade Name:	GORE TIGRIS Vascular Stent
Device Product Code:	NIP
Applicant's Name and Address:	W.L. Gore & Associates, Inc. 3250 West Kiltie Lane, P.O. Box 2400 Flagstaff, AZ 86005
Date(s) of Panel Recommendation:	None
Premarket Approval Application (PMA) Number:	P160004
Date of FDA Notice of Approval:	July 27, 2016
Priority Review:	No

II. INDICATIONS FOR USE

The GORE TIGRIS Vascular Stent is intended to improve luminal diameter in patients with symptomatic de-novo or restenotic lesions or occlusions in the native superficial femoral artery (SFA) and proximal popliteal artery (PPA) with reference vessel diameters ranging from 4.0-6.5 mm and lesion lengths up to 240 mm.

III. CONTRAINDICATIONS

The GORE TIGRIS Vascular Stent is contraindicated for non-compliant lesions where full expansion of an angioplasty balloon catheter was not achieved during pre-dilatation or where lesions cannot be dilated sufficiently to allow passage of the delivery system.

The GORE TIGRIS Vascular Stent is contraindicated in patients with contraindication to antiplatelet and/or anticoagulation therapy.

Do not use the GORE TIGRIS Vascular Stent in patients with known hypersensitivity to heparin, including those patients who have had a previous incident of Heparin-Induced Thrombocytopenia (HIT) type II.

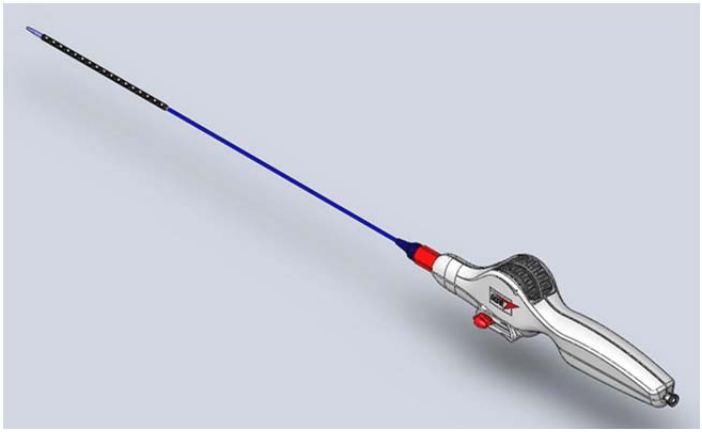
IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the GORE TIGRIS Vascular Stent labeling.

V. DEVICE DESCRIPTION

The GORE TIGRIS Vascular Stent consists of an implantable self-expanding stent and a catheter delivery system (**Figure 1** below). The catheter delivery system is used to intravascularly position the TIGRIS stent, constrained at a smaller introductory profile, at the target lesion and to release it into position.

Figure 1: GORE TIGRIS Vascular Stent System (Stent and Catheter Delivery System)



The GORE TIGRIS Vascular Stent is offered in the device configurations shown in **Table 1**. All of the device configurations are compatible with 6 French introducer sheaths.

Table 1: Stent Configurations

Device Diameter	Device Length				
	30 mm	40 mm	60 mm	80 mm	100 mm
5 mm	X	X	X	X	X
6 mm	X	X	X	X	X
7 mm	X	X	X	X	X

A. Description of the Stent

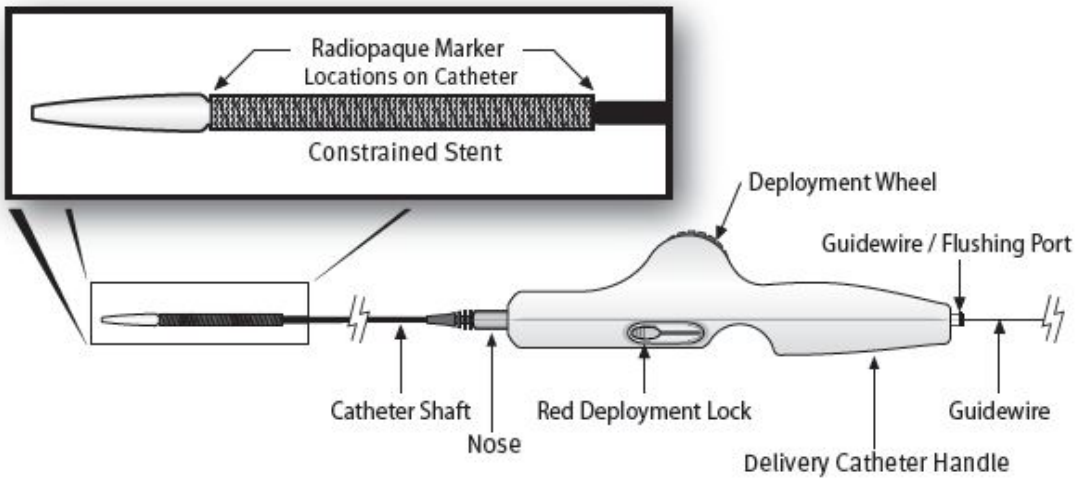
The stent (**Figure 2** below) is comprised of a sinusoidal wound, nitinol (NiTi) wire frame with a polymer secondary linkage. An immobilized heparin surface, the CBAS Heparin Surface, is applied to all surfaces of the stent.

Figure 2: Detail View of the TIGRIS Stent

B. Description of the Delivery Catheter

The catheter delivery system is comprised of a tri-axial catheter assembly that transmits deployment force from a proximal handle to the constrained stent at the distal end (**Figure 3** below).

Figure 3: TIGRIS Delivery Catheter



A helically-pleated tube constrains the stent at the reduced profile at the distal end of the catheter. When deployment is actuated by turning the deployment wheel at the handle, the inner layer unpleats to progressively release the stent.

C. CARMEDA BioActive Surface (CBAS) Heparin Surface

The CBAS Heparin Surface consists of heparin molecules that are covalently bonded to all stent surfaces by an "end-point attachment" method. USP heparin sodium API of porcine origin is used in the manufacture of the CBAS Heparin Surface. The heparin sodium API has been tested and certified to meet USP/EP requirements. The heparin sodium API is entirely of North American origin and is subsequently derivatized by a proprietary process established by Carmeda AB, Uplands Väsby, Sweden. Heparin bioactivity (ability to bind antithrombin III) is retained in the binding process due to the end-point covalent attachment that does not interfere with the heparin active site.

D. Principle of Operation

For implantation, the physician gains guidewire access to the target location. The physician pre-dilates the target lesion by inflating a PTA balloon catheter and makes angiographic measurements to select the appropriate size endoprosthesis. The catheter-mounted stent is delivered to the target location over the guidewire and positioned at the target lesion. The stent is deployed from the delivery catheter. The physician seats the device against the vessel wall by inflating an angioplasty balloon within the stent. When fully deployed and seated, the stent supports the target vessel.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Alternative procedures for treatment of symptomatic de novo or restenotic native lesions or occlusions of the superficial femoral artery (SFA) and/or proximal popliteal artery include use of other commercially available stents (both bare metal stents and drug-eluting stents) and stent-grafts, percutaneous transluminal angioplasty (PTA), medical management, exercise therapy, atherectomy, and bypass graft surgery. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with a physician to select that method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The GORE TIGRIS Vascular Stent is currently available and marketed for vascular use in the European Union, where the CE mark was obtained in 2011. These countries include the following: Austria, Belgium, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Italy, Luxembourg, Monaco, the Netherlands, Norway, Portugal, Spain, Sweden, Switzerland, and the United Kingdom. There was a single recall of one lot (11 devices) in January 2015 due to possible separation of the distal catheter tip. Potential tip separation was due to a failure of a component in the bonding process equipment. The equipment was replaced and additional equipment monitoring has been added.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

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

Table 2: List of Procedure and Device Related Potential Adverse Effects

Procedure Related	Device Related
Access site infection	Allergic reaction
Entry site bleeding and / or hematoma	Hematoma
Hemorrhage	Stenosis
Nausea or vomiting	Restenosis
Vasospasm	Thrombosis or occlusion
Vessel thrombosis	Distal embolism
Occlusion	Vessel wall injury, including perforation, trauma, dissection, and rupture
Pseudoaneurysm, aneurysm, and trauma to the vessel wall (including rupture or dissection)	False aneurysm
Distal embolization	Infection
The need for urgent intervention or surgery	Inflammation
Arteriovenous fistula formation	Fever and / or pain in the absence of infection
Drug reactions	Deployment failure

Procedure Related	Device Related
Hypotension / hypertension	Migration
Transient or permanent contrast induced renal failure	Stent fracture
Renal toxicity	Target lesion revascularization
Sepsis	Device failure
Shock	A possible complication which may occur in conjunction with the use of any heparin-containing product: HIT type II
Radiation injury	
Fever	
Pain	
Arrhythmia	
Bradycardia	
Angina	
Myocardial infarction	
Stroke	
Leg pain or claudication	
Extremity ischemia or amputation	
Tissue ischemia or necrosis	
Cerebral vascular accident	
Malposition	
Malapposition	
Inflammation	
Death	

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

IX. SUMMARY OF PRECLINICAL STUDIES

A. Biocompatibility Studies

Biocompatibility testing was conducted on the GORE TIGRIS Vascular Stent in accordance with applicable Good Laboratory Practices (21 CRF §58) and ISO 10993-1: 2009, *Biological Evaluation of Medical Devices*. Tests were conducted separately on product manufactured, packaged and sterilized using materials and procedures intended for the marketed product for the 1) TIGRIS catheter delivery system and 2) TIGRIS stent.

The TIGRIS catheter delivery system was classified as an externally communicating device in limited contact (< 24 hrs) with circulating blood. The TIGRIS stent was classified as an implant device in permanent contact (> 30 days) with blood. A summary of the biocompatibility testing conducted can be found in **Table 3** below.

Table 3: Summary of GORE TIGRIS Vascular Stent 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	Material-Mediated Pyrogenicity	X	X	Non-pyrogenic
Acute Systemic Toxicity	ISO Systemic Toxicity Study	X	X	Non-toxic
Subchronic Toxicity	14 Day Repeat Dose Intravascular and Intraperitoneal Toxicity Study	X	N/A	Non-toxic
Implantation	Intravascular Implantation Study – 4 Weeks	X[a]	N/A	Non-toxic
	Intravascular Implantation Study – 13 Weeks	X[a]	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	X[a]	X[b]	Non-thrombogenic
Genotoxicity	Bacterial Reverse Mutation (Ames) Assay	X	N/A	Non-mutagenic
	Mouse Lymphoma Assay	X	N/A	Non-genotoxic
	Mouse Micronucleus Assay	X	N/A	Non-genotoxic

[a] Evaluated as part of the animal studies outlined in Section C, below.
[b] Delivery system tested in the absence and presence of anticoagulation. In the absence of anticoagulation, significant thrombus was observed on the test and control articles. However, with anticoagulation, no thrombus was seen. The GORE TIGRIS Vascular Stent is contraindicated in patients with contraindication to antiplatelet and/or anticoagulation 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 C below. These additional animal studies demonstrated a lack of significant thrombus formation when stents were implanted in a clinically-relevant vascular implant location.

The omission of chronic toxicity and carcinogenicity testing for the stent was supported by information regarding the starting materials, processing of the finished device compared to a marketed device, genotoxicity testing, the GLP animal study, and/or toxicity data from the literature.

The information provided demonstrates that the GORE TIGRIS Vascular Stent is biocompatible.

B. *In vitro* Engineering Testing

In vitro bench testing to support the GORE TIGRIS Vascular Stent was developed based on the device risk assessment and is consistent with *FDA Non-Clinical Tests and Recommended Labeling of Intravascular Stents and Associated Delivery Systems*, April 18, 2010 and its addendum, *Select Updates for Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems*, August 30, 2013.

The relevant *in vitro* tests outlined in the guidance document and included in support of the TIGRIS devices are summarized in **Table 4** below. Unless otherwise specified, all test units were sterilized using a validated Ethylene Oxide sterilization process.

Table 4: Summary of *in vitro* Test Results

Test	Purpose	Acceptance Criteria	Results
Material Composition	Characterize the stent material composition to ensure it is acceptable for the intended use.	ASTM F2063-05	The stent material conforms to implant material standards.
Shape Memory & Superelasticity	The stent must be in its austenitic phase at body temperature to behave superelastically.	A_f must be body temperature.	Each lot of nitinol wire used for the production of stents is tested for austenitic finish temperature (Af). The stent retains its specified size and shape by superelasticity.
Corrosion Resistance	The stent must resist corrosion following implantation.	The deployed stent must exhibit equivalent or superior breakdown potentials as compared to an appropriate reference device per ASTM F2129-08 The deployed stent must not exhibit evidence of corrosion after fatigue testing in an overlapped configuration (see below).	The stent exhibits acceptable corrosion resistance based on testing per ASTM F2129-08. No wire discontinuities or fractures were observed on any of the devices. No evidence of abrasion, corrosion, or other irregularities was observed on devices after fatigue testing (see below).

<table>
<tr><th>Test</th><th>Purpose</th><th>Acceptance Criteria</th><th>Results</th></tr>
<tr><td>Nickel Elution</td><td>The stent must have acceptable levels of nickel elution.</td><td>The stent must not elute nickel beyond the acute and chronic tolerable intakes.</td><td>All stents meet the acceptance criteria for acute and chronic nickel elution.</td></tr>
<tr><td>Dimensional Verification (stent diameter)</td><td>The deployed stent outer diameter must be at least the maximum intended vessel diameter.</td><td><table><tr><th>Stent Diameter (mm)</th><th>Intended Vessel Diameter (mm)</th><th>Min. Stent OD (mm)</th></tr><tr><td>5</td><td>4.0-4.7</td><td>4.7</td></tr><tr><td>6</td><td>4.8-5.5</td><td>5.5</td></tr><tr><td>7</td><td>5.6-6.5</td><td>6.5</td></tr></table></td><td>All measurements pass the applicable requirement for stent outer diameter.</td></tr>
<tr><td>Dimensional Verification (stent length)</td><td>The stent must be within the dimensional specification when implanted.</td><td><table><tr><th>Labeled Stent Length (cm)</th><th>Acceptable Deployed Length (cm)</th></tr><tr><td>3</td><td>2.8-3.2</td></tr><tr><td>4</td><td>3.8-4.2</td></tr><tr><td>6</td><td>5.7-6.3</td></tr><tr><td>8</td><td>7.6-8.4</td></tr><tr><td>10</td><td>9.5-10.5</td></tr></table></td><td>All measurements passed the applicable requirement for deployed length.</td></tr>
<tr><td>Percent Surface Area of Stent</td><td>To determine the stent free surface area of the implanted stent.</td><td>Stents were characterized for information only.</td><td>The stent free surface area was calculated and ranges from 42% to 56% depending on device diameter and vessel oversizing.</td></tr>
<tr><td>Foreshortening</td><td>To determine the foreshortening of the stent from the catheter constrained diameter to the use diameter.</td><td>Stents were characterized for information only. See deployed length.</td><td>Foreshortening values range between -1.8% and 0.5% depending on labeled stent length (negative numbers indicate an increase in length post-deployment).</td></tr>
<tr><td>Stent Integrity</td><td>To verify the stent has no clinically significant defects or flaws after deployment.</td><td>The stent must have no completely severed linkages, no broken or bent struts, and no unacceptable contamination or delamination.</td><td>Stents meet the established acceptance criteria.</td></tr>
<tr><td>Coating Integrity</td><td>To characterize the CBAS heparin surface of the stent.</td><td>Stents were characterized for information only.</td><td>Based on the image analysis, the coating integrity of the CBAS Heparin Surface is maintained throughout aging, across device size configurations. There was no apparent gross heterogeneity in the presence or uniformity of the coating.</td></tr>
</table>

Test	Purpose	Acceptance Criteria	Results
Radial Resistive Force	To measure the stent resistance to radial compression.	Stent resistance to circumferential compression must be ≥ 0.16kgf/cm^2.	Stents meet the established acceptance criteria.
Chronic Outward Force	To characterize the stent outward force before expanding to nominal diameter.	Stents were characterized for information only.	Chronic outward forces ranged from 0.11kgf/cm^2 to 0.42kgf/cm^2, depending on device diameter and vessel oversizing.
Material Mechanical Properties	Characterize the stent materials mechanical properties to ensure they are acceptable for the intended use.	ASTM F2063-05	The stent material conforms to implant material standards ASTM F2063-05 for material properties.
Strain and Fatigue Analysis/Finite Element Analysis	To determine the location and magnitude of the maximum principal strains in the stents, under expected clinical use conditions, through the use of Finite Element Analysis (FEA).	Strains are calculated for: A) radial in-vivo pulsatile loading conditions when deployed in a host vessel at maximum and minimum product specification diameters, B) radial compressions due to catheter loading and C) multi-modal loading conditions when subjected to pulsatile loading conditions that are combined with bending, torsion and axial compression.	The location and magnitude of the maximum principle strains have been calculated and the strain states are below the endurance limit for the Nitinol material.
Accelerated Durability Testing	To evaluate the simulated 10 year durability of stents under expected clinical use conditions, including pulsatile and relative SFA physiological motions.	Acceptance criteria: The following acceptance criteria are used for the pulsatile fatigue test: • The stent must exhibit acceptable simulated 10 year fatigue durability. • There can be no damage that results in complete separation of the stent.	Stents meet the established acceptance criteria.
Magnetic Resonance Imaging Compatibility	To evaluate the MRI safety and compatibility of the stent.	The implant must not present additional risk to the patient when exposed to static magnetic field strengths of 1.5 and 3.0 Tesla.	The stent does not pose additional risk to patients and may be labeled MR Conditional according to ASTM 2503.

Test	Purpose	Acceptance Criteria	Results
Radiopacity	Determine the visibility of the stent and catheter delivery system under fluoroscopy.	The catheter delivery system must enable fluoroscopic visualization of the delivery catheter. The stent radiopacity must be characterized.	The catheter delivery system meets the established acceptance criteria. Stent radiopacity was characterized.
Crush Resistance	Demonstrate the ability of the stent to recover its desired size and shape after application and removal of external loads, deformations, or both.	The stent must recover its desired shape after application and removal of external loads, deformation, or both.	The stent fully recovers its diameter and length following deployment from the constrained profile and passed all acceptance criteria for accelerated durability testing.
Kink Resistance	To determine the radius of curvature at which the GORE TIGRIS Vascular Stent kinks.	Stents were characterized for information only.	Stents have kink radii below 0.2inches. All devices returned to original geometry after testing.
Dimensional Verification (Profile)	To verify the maximum diameter of the catheter delivery system and constrained stent and assure compatibility with recommended sheaths.	The catheter delivery system and constrained stent must be able to pass through a 6.4Fr profile block and through 6Fr introducer sheaths. The catheter delivery system must successfully withdraw through the introducer sheath following stent deployment. The catheter delivery system and constrained stent maximum diameter = 2.13mm (0.84″)	The catheter delivery system and constrained stents meet the acceptance criteria.
Dimensional Verification (Working Length)	Delivery catheter working length enables treatment of the intended site.	The delivery catheter working length must be 118-125cm.	The delivery catheter meets the acceptance criteria for working length.

<table>
<tr><th>Test</th><th>Purpose</th><th>Acceptance Criteria</th><th>Results</th></tr>
<tr><td>Delivery, Deployment, and Retraction</td><td>To assess the ability of the catheter delivery system to deliver the stent to the intended location and deploy the stent.</td><td>The catheter delivery system must be able to reliably:
• Access the target location.
• Deploy the stent by withdrawing the tear tube.
• Retract the intact catheter without dislodging the stent.
The delivery system must deploy the stent with acceptable deployment accuracy and force (deployment force ≤3.3kgf).</td><td>The catheter delivery system meets the established acceptance criteria.</td></tr>
<tr><td>Delivery Catheter Bond Strengths</td><td>Evaluate the tensile strength of delivery catheter bonds.</td><td>The delivery catheter must maintain its function during access, deployment, and retraction.<table><tr><th>Bond</th><th>Bond Strength Accept. Criteria (kgf)</th></tr><tr><td>Tip bond</td><td>≥0.51</td></tr><tr><td>Coupler bond</td><td>≥1.02</td></tr><tr><td>Strain relief bond</td><td>≥1.53</td></tr><tr><td>Thumbwheel linkage</td><td>≥1.7</td></tr><tr><td>Hub bond</td><td>≥0.51</td></tr></table></td><td>Tensile strengths for all delivery catheter samples across all bond locations pass the applicable acceptance criteria</td></tr>
<tr><td>Catheter Buckle Strength</td><td>Evaluate the force required to buckle the catheter</td><td>Buckle force must be >3.3kgf.</td><td>The catheter delivery system meets the established acceptance criteria for buckle force.</td></tr>
<tr><td>Catheter Delivery System Flexibility & Kink</td><td>To verify the catheter delivery system is able to reliably track through tortuous, clinically relevant anatomy and delivery the stent to its intended location.</td><td>The catheter delivery system must be able to reliably:
• Access the target location.
• Deploy the stent by withdrawing the tear tube.
• Retract the intact catheter without dislodging the stent.</td><td>The catheter delivery system meets the established acceptance criteria.</td></tr>
<tr><td>Torqueability</td><td>Assess the catheter delivery system ability to maintain function while torqued.</td><td>Catheter delivery system shall maintain the ability to deploy with the handle rotated 360° during deployment.</td><td>The catheter delivery system meets the established acceptance criteria.</td></tr>
</table>

Test	Purpose	Acceptance Criteria	Results
Torque Strength	To evaluate the number of turns to failure for the catheter delivery system.	Catheter delivery systems were characterized for information only.	The catheter delivery system rotates an average of approximately 8 or 13 full turns prior to failure, depending on catheter working length.

C. Animal Studies

The GORE TIGRIS Vascular Stent was subjected to a series of three (acute, subacute and chronic) GLP animal studies. The *in vivo* animal studies demonstrated the safety and overall product performance of the GORE TIGRIS Vascular Stent *in vivo* in a total of 19 canine models and 6 porcine models. **Table 5** summarizes the results of the GLP studies conducted on finished, sterile devices.

Table 5: Summary Results of the GLP Animal Studies

Study Type	Study Numbers Test or Control	Evaluations	Outcome
2003SC Chronic Safety Study in Canine Ilio- femoral Artery (30 and 90 days implantation)	15 Canines were implanted with 5mm x 40mm or 6mm x40mm TIGRIS and 5mm x 50mm or 6mm x 50mm Control devices	Patency Histological Parameters	The GORE TIGRIS Vascular Stent demonstrated similar/superior results when compared to the Control device for patency, measured by percent diameter stenosis, at 90 ± 3 days. Histologically, injury and inflammation scores were similar between Test and Control devices.
2075SC Acute Safety/ Deliverability Study in Canine Ilio-femoral Artery	4 Canines were implanted with a total of 12 TIGRIS devices. Diameters were 5mm, 6mm, 7mm, or 8mm. Device lengths were 30mm and 100mm.	Device Deliverability Deployment Accuracy	All devices deployed as intended. All twelve devices were deployed and remained within 5mm of the target site.

Study Type	Study Numbers Test or Control	Evaluations	Outcome
2110SC Chronic Safety Study in the Swine Ilio- femoral Artery (30 and 90 days implantation)	Six swine were implanted with a total of 12 TIGRIS Devices and 12 Control devices. Each study animal received two overlapping TIGRIS and two overlapping Control devices. Devices were 6mm or 7mm in diameter and 30mm in length.	Patency Histological Parameters Delivery and Deployment Stent Integrity	The GORE TIGRIS Vascular Stent demonstrated similar results when compared to the Control device for patency, measured by percent diameter stenosis, at 90 ± 3 days. Histologically, neointimal thickness and percent area stenosis scores were similar between Test and Control devices. All TIGRIS devices received passing scores for delivery and deployment. No fractures were detected in the test or control

D. Sterilization, Packaging, and Shelf-Life

The GORE TIGRIS Vascular Stent is sterilized by ethylene oxide. Validation of the sterilization method to ensure a Sterility Assurance Level (SAL) of 10^{-6} has been conducted in accordance 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*.

Packaging qualification and device verification testing was performed on the GORE TIGRIS Vascular Stent at baseline and on aged product. The device is packaged in a backer card, sealed in a foil-tyvek primary pouch, and a poly-Tyvek secondary pouch. The packaged device is then placed in a carton.

A shelf life of 3 years has been established for the GORE TIGRIS Vascular Stent based on product and package shelf life testing.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant conducted a prospective, multi-center, randomized control clinical study in the United States (US) and European Union (EU) to establish a reasonable assurance of safety and effectiveness for the use of the GORE TIGRIS Vascular Stent for in the treatment of de novo and restenotic atherosclerotic lesions, ≤24 cm in length, in the superficial femoral and proximal popliteal arteries (SFA/PPA) of patients with symptomatic peripheral arterial disease (PAD). The design and results of this investigational device exemption (IDE) study are summarized in **Table 6**.

Table 6: Primary Clinical Study Synopsis

Title of study	Evaluation of the GORE TIGRIS Vascular Stent in the Treatment of Atherosclerotic Lesions of the Superficial Femoral and Proximal Popliteal Arteries
Protocol number	PCE 09-02
Study sites	33 study sites in the US and 3 study sites in the EU
Study objective	The primary objective of the randomized study is to evaluate the safety and effectiveness of the TIGRIS Vascular Stent in the treatment of de novo and restenotic atherosclerotic lesions, ≤24 cm in length, in the SFA/PPA of patients with symptomatic PAD.
Study design	Prospective, multi-center, randomized control clinical study comparing outcomes in subjects randomly assigned to treatment with the GORE TIGRIS Vascular Stent to those assigned to treatment with the control device, the Bard LifeStent Vascular Stent (Control). Randomization was 3:1 (TIGRIS Vascular Stent:Control).
Number of subjects	**Planned**: 269 subjects meeting study eligibility criteria **Enrolled:** Total: 274 subjects TIGRIS Vascular Stent Group: 203 subjects Control Device Group: 71 subjects **Analyzed:** 274 subjects in intent-to-treat (ITT) analysis population 267 subjects in per-protocol (PP) analysis population
Follow-up evaluation intervals	1, 6, 12, 24, and 36 months
Criteria for evaluation	**Primary Safety Endpoint:** A composite 30-day safety endpoint of freedom from Major Adverse Events (MAE), defined as death, target vessel revascularization (TVR), and amputation above the metatarsals in the treated leg (index limb amputation). **Primary Effectiveness Endpoint:** Primary patency at 12 months after implantation, defined as uninterrupted patency without target lesion revascularization (TLR), including the proximal and distal margins, and no restenosis as documented by a peak systolic velocity ratio (PSVR) ≤2.5 by Color Doppler Ultrasound (CDUS).

Results Summary	**Safety Results:** The safety of the TIGRIS Vascular Stent was found to be statistically non-inferior to that of the Control device, using a 12% margin, measured 30 days after implant ($p<0.001$). In the TIGRIS Vascular Stent group, 99.5% (187/188) of subjects were free from MAEs at 30 days, as compared to 100.0% (69/69) of subjects in the Control device group. **Effectiveness Results:** The effectiveness of the TIGRIS Vascular Stent was found to be statistically non-inferior to that of the Control device, using a 19% margin, measured 12 months after implant ($p=0.002$). In the TIGRIS Vascular Stent group, 57.1% (97/170) of subjects maintained primary patency at 12 months, whereas 54.7% (35/64) of subjects in the Control device group maintained primary patency at this time point.

A. Study Design

The PCE 09-02 clinical study was a prospective, unblinded, multi-center, randomized control study comparing outcomes in subjects randomly assigned to treatment with the GORE TIGRIS Vascular Stent to those assigned to treatment with the control device, the Bard LifeStent Vascular Stent (Control), randomized at a 3:1 ratio (TIGRIS Vascular Stent:Control device). The primary objective of the study was to evaluate the safety and effectiveness of the TIGRIS Vascular Stent in the treatment of de novo and restenotic atherosclerotic lesions, ≤24 cm in length, in the superficial femoral and proximal popliteal arteries (SFA/PPA) of patients with symptomatic PAD.

A sample size of 269 subjects meeting study eligibility criteria was established to obtain 80% power to statistically demonstrate non-inferiority of the safety and effectiveness of the TIGRIS Vascular Stent as compared to the Control device.

Two independent core laboratories were contracted to provide objective analysis of all study imaging (one core lab analyzed angiographic images, and another analyzed ultrasound and X-ray images). An independent DSMB composed of five members was established for this study to provide continuing review of study conduct with respect to subject safety and data integrity.

1. Clinical Inclusion and Exclusion Criteria

Inclusion Criteria

Patients eligible for inclusion in the study were required to possess all of the following characteristics:

1. Rutherford Class 2 - 4.
2. Abnormal ankle-brachial index (ABI ≤0.9). If ABI was not measurable due to medial calcinosis, an abnormal toe brachial index (TBI ≤0.7) could be substituted.
3. At least 21 years of age.
4. Subject or legal representative willing to give written informed consent.
5. Reasonable expectation of survival of at least 12 months after the procedure.

6. Male, infertile female, or female practicing an effective method of preventing pregnancy.

   [NOTE: Women of childbearing potential were required to have a negative pregnancy test.]
7. Ability to participate in follow-up visits as required by the protocol.
8. Met angiographic inclusion criteria. Criteria used to establish that the patient was a candidate for treatment by stenting within the limits of this protocol were assessed angiographically at the time of stent implantation. To be eligible for inclusion in the study, patients were required to meet all of the following angiographic criteria:
   - 8(a). One de novo or restenotic lesion of the SFA/PPA with a cumulative length visually estimated to be ≤24 cm, with one or more regions of focal luminal narrowing ≥50%. The lesion must have been located in the region beginning approximately 1 cm below the origin of the profunda femoris artery and ending approximately 1 cm above the intercondylar notch.
   - 8(b). Arteries with reference vessel diameter of 4.0 – 6.5 mm within the SFA/PPA, estimated visually.
   - 8(c). Angiographic evidence of at least one patent tibial artery (<50% stenosis angiographically) from the origin to the ankle that did not require planned intervention at the time of procedure or within 12 months of enrollment.
   - 8(d). Guidewire had successfully traversed the lesion to be treated and was within the true lumen of the distal vessel.
   - 8(e). Lesion had been pre-dilated before stent deployment as required in study protocol Section 4.3.4.

Exclusion Criteria

Patients were not considered eligible for inclusion in the study if they possessed any of the following characteristics:

1. Prior enrollment in this study.
2. Vascular access/catheterization in the target leg within 30 days of study enrollment.

   [NOTE: Diagnostic catheterizations done for the purposes of planning and scheduling the interventional procedure were allowed.]
3. Prior treatment of the SFA/PPA in the target leg with stenting or bypass.
4. Flow-limiting aortoiliac disease.

   [NOTE: Patients receiving successful treatment of iliac disease during the same procedure could be enrolled in the study if all other inclusion/exclusion criteria had been met.]
5. Additional ipsilateral femoropopliteal or tibial disease, outside of the lesion to be stented, requiring intervention.
6. Arterial aneurysm in the target leg.

7. Co-morbid conditions which would have precluded compliance with study protocol.
8. Obstructive or occlusive non-atherosclerotic disease.
9. Creatinine greater than 2.5 mg/dl.
10. Amputation above the metatarsals, resulting from vascular disease, in the target leg.
11. Septicemia or uncontrolled infection.
12. Contraindication to anticoagulation or antiplatelet therapy, including allergy to heparin, or history of heparin-induced thrombocytopenia (HIT), or a positive PF4 antibody assay.
13. Abnormal platelet levels, i.e., platelet count at Baseline less than 80,000/μL.
14. History of coagulopathy.
15. Participation in any other clinical research study that might confound the endpoints of this study.
16. Any other factor identified by the Investigator that would disqualify the prospective subject from participation in the study.

2. Follow-up Schedule

After the index procedure, enrolled subjects were to return to the enrolling site at five specified intervals for follow-up evaluation: one month (30 ± 7 days), six months (182 ± 30 days), 12 months (365 ± 45 days), 24 months (730 ± 45 days), and 36 months (1095 ± 45 days). The schedule of evaluations to be completed at each study interval is presented in **Table 7**.

Table 7: Evaluations to be Completed at Each Study Interval

Study Interval	Evaluations to be Completed
Baseline	• Demographics • Medical history • Physical exam • CBC, platelets, and creatinine • Rutherford classification • Ankle-Brachial Index (ABI) or Toe-Brachial Index (TBI) • Quality of life (QOL) questionnaires (EQ-5D, PAQ) • Medications
Index Procedure / Discharge	• Angiography / vessel and lesion characteristics • Procedure and device information • Adverse events • X-ray for fracture analysis • Medications
Follow-Up Visits	1-, 6-, 12-, 24-, and 36-month follow-up evaluations: • Physical exam • Adverse events • Rutherford classification • ABI or TBI (whichever was collected at baseline) • QOL questionnaires • Color Doppler ultrasound (CDUS) • Medications Additional 12-, 24-, and 36-month follow-up evaluation: • X-ray
Unscheduled Visits (as available and applicable)	• Physical exam • Adverse events • Rutherford classification • ABI or TBI (whichever was collected at baseline) • QOL questionnaires • Color Doppler ultrasound (CDUS) • Medications • X-ray
Study Completion / Discontinuation	• Reason for discontinuation • Adverse events

3. Clinical Endpoints

Primary Endpoints

The primary safety endpoint in this study was freedom from MAE observed within 30 days of stent implant, with MAE defined as death, target vessel revascularization (TVR), and amputation above the metatarsals in the treated leg (index limb amputation). Analysis of the primary safety endpoint tested the hypothesis that the safety of the TIGRIS Vascular Stent is statistically non-inferior to the Control device, using a 12% margin, measured 30 days after implant.

The primary effectiveness endpoint in this study was primary patency at 12 months after implantation, with primary patency defined as uninterrupted patency without target lesion revascularization (TLR), including the proximal and distal margins, and no restenosis as documented by a peak systolic velocity ratio (PSVR) ≤2.5 by Color Doppler Ultrasound (CDUS). Analysis of the primary effectiveness endpoint tested the hypothesis that the effectiveness of the TIGRIS Vascular Stent is statistically non-inferior to the Control device, using a 19% margin, measured 12 months after implant.

Secondary Endpoints

Secondary endpoints were established to describe functional outcomes of therapy with the TIGRIS Vascular Stent. The study utilized the following secondary endpoints:

1. Freedom from MAE, estimated through time-to-event analysis.
2. Procedural Success: Successful device implantation with a residual stenosis <30% without acute (within 48 hours) serious adverse events (AEs) defined as: death, stroke, myocardial infarction, emergent surgical revascularization, significant distal embolization in the treated leg, or thrombosis of the target vessel occurring after or not successfully treated during the implant procedure.
3. Device Success: Successful delivery of stent to the intended site and successful stent deployment.
4. Freedom from TVR, estimated through time-to-event analysis.
5. Freedom from TLR, estimated through time-to-event analysis.
6. Rutherford improvement: Improvement in Rutherford Classification (from baseline value) by ≥1 class. Any subjects not receiving a Rutherford Classification for the corresponding month visit were not to be used in calculating this statistic.
7. Ankle-Brachial Index (ABI): Descriptive statistics measured at pre-procedure and each follow-up visit. Any subjects not having an ABI measured for a specific visit were not to be used in calculating this statistic at that interval.
8. Quality of Life - Descriptive statistics on change in overall Quality of Life (EQ-5D) and disease-specific Quality of Life (Peripheral Artery Questionnaire [PAQ]) between Baseline and each follow-up visit. Subjects not completing either an EQ-5D or a PAQ for a specific visit were not to be used in calculating this statistic at that interval.
9. Primary patency, estimated through time-to-event analysis.
10. Assisted primary patency, estimated through time-to-event analysis.
11. Secondary patency, estimated through time-to-event analysis.
12. Freedom from stent fracture. All subjects for which fracture is not evaluable at the corresponding time point were not to be used in calculating this statistic.

B. Accountability of PMA Cohort

Between May 2012 and June 2014, a total of 274 subjects were enrolled in the study at 33 study sites in the US and 3 study sites in the EU. The study was designed to enroll 269 subjects meeting all eligibility criteria. Cases of eligibility violations were reviewed and adjudicated by the independent DSMB. Based on this review, and with the approval of the FDA, the enrollment limit was increased by five subjects during the enrollment period to compensate for ineligible subjects that had been enrolled. Of the 274 subjects ultimately enrolled, 267 were determined by the DSMB to have met essential eligibility requirements. The remaining seven subjects were deemed by the DSMB to have had eligibility violations that could affect the evaluation of primary endpoints, and were excluded from the per-protocol (PP) population. All endpoint data reported here are based on the PP population of 267 subjects, unless the intent-to-treat (ITT) population of 274 subjects is specified.

The clinical study report included in the PMA reflects complete follow-up data through at least the 12-month visit for all available subjects. The PCE 09-02 study remains ongoing until all study subjects have completed 36 months of follow-up or have been withdrawn.

Of the 267 subjects determined to meet essential eligibility requirements for inclusion in the study, 25 (9.4%) were withdrawn prior to reaching 365 days after the index procedure. Similar withdrawal percentages were observed between the TIGRIS Vascular Stent and Control device groups at each follow-up interval (**Table 8**).

Table 8: Withdraw Status

	TIGRIS	LIFESTENT	Total
Number of Subjects[1,2]	197	70	267
Subjects Withdrawn prior to 30 Days	2 (1.0%) [197]	0 (0.0%) [70]	2 (0.7%) [267]
Subjects Withdrawn prior to 6 Months	10 (5.1%) [197]	1 (1.4%) [70]	11 (4.1%) [267]
Subjects Withdrawn prior to 12 Months	19 (9.6%) [197]	6 (8.6%) [70]	25 (9.4%) [267]

[1]Numbers indicate subjects withdrawn prior to the exact time point.
[2]Brackets contain subject number eligible for visit according to their study time.

Fourteen deaths had occurred in the study at the time of data lock. Twelve of the deaths occurred in the TIGRIS Vascular Stent group (5.9% of all subjects enrolled in this group), and two occurred in the Control device group (2.8% of all subjects enrolled in this group). No deaths in either group were determined by the DSMB to have a relationship to the study device or procedure. Reported causes of death (by MedDRA Preferred Term code) included myocardial infarction (two cases), ischaemic cardiomyopathy, cardiac failure (acute), cardiac failure (chronic), renal cancer, cardiac arrest (three cases), ventricular fibrillation, septic shock, coronary artery disease, peripheral ischaemia, and cerebrovascular accident.

Of the available subjects that had not withdrawn from the study prior to their 12-month follow-up visit window, 90.8% attended the 12-month follow-up visit. Follow-up visit attendance through 12 months is presented in **Table 9**.

Table 9: Subject Follow-up Visit Attendance

	TIGRIS	LIFESTENT	Total
Number of Subjects[1,2,3]	197	70	267
Attended 30-Day Follow-Up Visit	183 (93.8%) [195]	70 (100.0%) [70]	253 (95.5%) [265]
Attended 6 Month Follow-Up Visit	175 (92.1%) [190]	64 (92.8%) [69]	239 (92.3%) [259]
Attended 12 Month Follow-Up Visit	167 (91.8%) [182]	59 (88.1%) [67]	226 (90.8%) [249]

[1]Numbers indicate subjects whom attended corresponding follow-up visit.
[2](%) indicate the percentage of eligible subjects who attended the corresponding follow-up visit.
[3]Brackets contain number of subjects eligible for the corresponding follow-up visit.

C. Study Population Demographics and Baseline Parameters

The study was conducted in the US and EU. Subject demographics, including a poolability analysis for gender and age by location, are shown in **Table 10** below (ethnicity and race data were not collected in the EU). Subject medical history, including key clinical characteristics at the time of the index procedure, is presented in **Table 11**. Target vessel and lesion characteristics are provided in **Table 12**.

Table 10: Demographics

	TIGRIS	LIFESTENT	P-value
Number of Subjects	197	70	
Gender[1]	197	70	0.878
Female	56 (28.4%)	21 (30.0%)	
Male	141 (71.6%)	49 (70.0%)	
Age at Procedure (years)[2]	195	70	0.385
Mean (Std Dev)	66.8 (9.30)	67.9 (8.87)	
Median	67	69	
Min-Max	45 - 88	47 - 86	
Ethnicity[1,3]	142	54	1.000
Hispanic or Latino	2 (1.4%)	1 (1.9%)	
Not Hispanic or Latino	140 (98.6%)	53 (98.1%)	
Unknown	0 (0.0%)	0 (0.0%)	
Race[1,3]	142	54	0.010
American Indian or Alaskan Native	1 (0.7%)	0 (0.0%)	
Asian	4 (2.8%)	0 (0.0%)	
Black	18 (12.7%)	2 (3.7%)	
Native Hawaiian or Pacific Islander	1 (0.7%)	0 (0.0%)	
White	116 (81.7%)	52 (96.3%)	
Other Race	2 (1.4%)	0 (0.0%)	

	TIGRIS	LIFESTENT	P-value
Gender[4]	US=142 OUS= 55	US= 54 OUS= 16	US=196 OUS= 71
	Interaction P-value = 0.7435		P-value = 0.5878
US	28.9% [41/142]	31.5% [17/ 54]	29.6% [58/196]
OUS	27.3% [15/ 55]	25.0% [4/ 16]	26.8% [19/ 71]
Age[5] **(years)**	US=142 OUS= 55	US= 54 OUS= 16	US=196 OUS= 71
	Interaction P-value = 0.4010		P-value = 0.6751
US	67.0 (0.79)	67.5 (1.25)	67.1 (0.67)
OUS	66.3 (1.25)	69.4 (1.91)	67.0 (1.06)

[1] P-value obtained with the Fisher's Exact Test.
[2] P-value obtained with the t-test.
[3] Measured only in the USA. P-value obtained from testing proportion which are white.
[4] Estimates percent of females [# of subjects which are female / # of subjects]. P-values obtained using logistic regression.
[5] Mean and (standard error) estimates. P-values obtained using analysis of variance.

Table 2: Subject Medical History and Baseline Characteristics

	TIGRIS	LIFESTENT	P-value
Number of Subjects	197	70	
Smoking History[1]	197	70	0.460
Never Smoked	17 (8.6%)	10 (14.3%)	
Current Smoker	76 (38.6%)	23 (32.9%)	
Former Smoker	104 (52.8%)	37 (52.9%)	
Quit ≤ 1 year ago[2]	18 (17.3%)	5 (13.5%)	
Quit ≤ 5 years ago[2]	14 (13.5%)	8 (21.6%)	
Quit > 5 years ago[2]	72 (69.2%)	24 (64.9%)	
Diabetes Mellitus[1]	197	70	0.777
Yes	79 (40.1%)	30 (42.9%)	
No	118 (59.9%)	40 (57.1%)	
Hypertension[1]	197	70	0.122
Yes	171 (86.8%)	55 (78.6%)	
No	26 (13.2%)	15 (21.4%)	
Hyperlipidemia[1]	197	70	0.881
Yes	137 (69.5%)	48 (68.6%)	
No	60 (30.5%)	22 (31.4%)	
Coronary Artery Disease[1]	197	70	0.580
Yes	98 (49.7%)	32 (45.7%)	
No	99 (50.3%)	38 (54.3%)	

	TIGRIS	LIFESTENT	P-value
Myocardial Infarction (MI)[1]	197	70	0.581
Yes	36 (18.3%)	10 (14.3%)	
No	161 (81.7%)	60 (85.7%)	
BMI[3]	197	70	0.626
Mean (Std Dev)	28.0 (5.0)	28.4 (6.0)	
Median	27.5	28.8	
Min-Max	16.2 - 47.5	15.5 - 46.9	
Baseline Rutherford Category[1]	197	70	0.772
Category 2	62 (31.5%)	22 (31.4%)	
Category 3	125 (63.5%)	43 (61.4%)	
Category 4	10 (5.1%)	5 (7.1%)	

[1] P-value obtained with the Fisher's Exact Test.
[2] Percent measured out of former smokers.
[3] P-value obtained with the t-test.

Table 3: Target Lesion and Vessel Characteristics

	TIGRIS	LIFESTENT	P-Value
Number of Subjects	**197**	**70**	
Final Lesion Length (mm)[1]	197	70	0.075
Mean (Std Dev)	107.0 (69.5)	124.6 (73.4)	
Median	90	120	
Min-Max	5 - 260	10 - 240	
Lesion Type[1]	197	70	0.483
Occlusion	83 (42.1%)	26 (37.1%)	
Stenosis	114 (57.9%)	44 (62.9%)	
If Stenosis, Maximum Percent[2]	114	44	0.143
Mean (Std Dev)	74.4 (9.27)	72.0 (8.57)	
Median	75.0	73.8	
Min-Max	51.0 - 91.7	52.8 - 86.6	
Lesion Calcification[1]	189	66	0.442
None	95 (50.3%)	28 (42.4%)	
Mild	4 (2.1%)	0 (0.0%)	
Moderate	48 (25.4%)	21 (31.8%)	
Severe	42 (22.2%)	17 (25.8%)	
Reference Diameter Proximal to Lesion (mm)[1]	196	70	0.698
Mean (Std Dev)	5.4 (0.65)	5.5 (0.65)	
Median	5.5	5.5	
Min-Max	4.0 - 6.5	4.0 - 6.5	
Reference Diameter Distal to Lesion (mm)[1]	196	70	0.671
Mean (Std Dev)	5.4 (0.69)	5.4 (0.62)	
Median	5.5	5.5	
Min-Max	4.0 - 6.5	4.0 - 6.5	
Tibial Runoff Vessels[1]	187	69	0.156
1	21 (11.2%)	11 (15.9%)	
2	106 (56.7%)	30 (43.5%)	
3	60 (32.1%)	28 (40.6%)	

[1] P-value obtained with the t-test.
[2] P-value obtained with the Fisher's Exact Test.

D. Safety and Effectiveness Results

1. Safety Results

Primary Safety Endpoint

The primary safety endpoint of the PCE 09-02 study, freedom from MAE observed within 30 days of stent implant was met. The safety of the TIGRIS Vascular Stent was found to be statistically non-inferior to that of the Control device, using a 12% margin, measured 30 days after implant ($p<0.001$; **Table 13**). **Table 13** represents the primary safety endpoint analysis for the PP population; analyses of ITT and As-treated (AT) populations demonstrated similar results for this endpoint.

MAEs were defined in this study as death, TVR, and index limb amputation. One MAE was reported within the first 30 days after the index procedure. This MAE, in the TIGRIS Vascular Stent group, consisted of a TVR performed on the day of the procedure to treat a procedural complication. After deployment of the TIGRIS Vascular Stent, occlusion of the popliteal artery was noted above the knee but distal to the margins of the deployed TIGRIS Vascular Stent. A guidewire was passed through the occlusion to restore flow, and a prophylactic balloon angioplasty was performed in the peroneal and distal popliteal arteries.

Table 13: Freedom from Major Adverse Events at 30 Days

	TIGRIS	LIFESTENT	P-value*
Freedom from MAE	N=188	N=69	< 0.001
Yes	187 (99.5%)	69 (100.0%)	
95% Confidence Interval**	[97.1%, 100.0%]	[94.8%, 100.0%]	

*The non-inferiority test with a 12% margin is performed using a one-sided z-test with a pooled variance estimate.
**Confidence interval calculated using binomial exact test.

Secondary Safety Endpoint

Freedom from MAE through 12 months after implant, estimated through time-to-event analysis, is presented in **Table 14**.

Table 14: Kaplan-Meier Estimates of Freedom from MAE

Time Post Treatment (days)	# at Risk Interval Start	Events Number (Cumulative)	Censored Number (Cumulative)	Survival Probability	95% C.I.
Treatment Group: Bard LifeStent Vascular Stent (N=70)					
0	70	0 (0)	0 (0)	100.0%	(100.0%, 100.0%)
[1-30]	70	0 (0)	1 (1)	100.0%	(100.0%, 100.0%)
[31-183]	69	4 (4)	1 (2)	94.1%	(85.1%, 97.8%)
[184-365]	64	9 (13)	15 (17)	80.1%	(68.0%, 87.9%)
Treatment Group: GORE TIGRIS Vascular Stent (N=197)					
0	197	1 (1)	6 (6)	99.5%	(96.5%, 99.9%)
[1-30]	190	0 (1)	3 (9)	99.5%	(96.5%, 99.9%)
[31-183]	187	13 (14)	5 (14)	92.4%	(87.5%, 95.4%)
[184-365]	169	36 (50)	22 (36)	72.3%	(65.1%, 78.2%)

Device- or procedure-related Serious Adverse Events

Listings of all reported device- or procedure-related serious adverse events (SAEs) as classified via MedDRA System Organ Class (SOC), High Level Term (HLT), and Preferred Term (PT) for each follow-up interval are provided in **Tables 15 and 16**. The percentage of subjects experiencing a device- or procedure-related SAE was similarly low for both treatment groups at each interval, ranging from a low of 1.4% (TIGRIS Vascular Stent group at procedure day, and Control device group at 30-day interval) to a high of 5.9% (Control device group at 1-year interval) through one year.

The MedDRA SOCs corresponding to the device- or procedure-related SAE category were "General disorders and administration site conditions," (21 total events) "Injury, poisoning and procedural complications," (six total events) and "Vascular disorders" (four total events) (**Tables 15 and 16**).

The MedDRA PTs corresponding to this AE category included the following:

- *Vessel puncture site haematoma* (one event, in the TIGRIS Vascular Stent group),
- *Vessel puncture site haemorrhage* (one event, in the TIGRIS Vascular Stent group),
- *Device breakage* (one event, in the Control device group),
- *Vascular stent restenosis* (17 events, with 11 in the TIGRIS Vascular Stent group and six in the Control device group),
- *Vascular pseudoaneurysm* (five total events, with four in the TIGRIS Vascular Stent group and one in the Control device group),
- *Procedural complication* (one event, in the TIGRIS Vascular Stent group),
- *Vessel perforation* (one event, in the TIGRIS Vascular Stent group),

- *Arteriovenous fistula* (one event, in the TIGRIS Vascular Stent group),
- *Device occlusion* (one event, in the TIGRIS Vascular Stent group), and
- *Intermittent claudication* (two total events, with one in the TIGRIS Vascular Stent group and one in the Control device group).

The frequency and types of the reported device- or procedure-related SAEs in the study are in alignment with what might be expected in the studied patient population and therapeutic area.

Table 15: Summary of All Serious Device and Procedure Related Adverse Events by Early Follow-up Interval (ITT Population)[3,4,5]

			Follow-up Interval			
	Procedure Day		30 Days[1]		6 Months	
	TIGRIS	LIFESTENT	TIGRIS	LIFESTENT	TIGRIS	LIFESTENT
Number of Subjects[2] Available	N = 203	N = 71	N = 203	N = 71	N = 199	N = 70
Number experiencing any event(s)	5 (2.5%) [5]	1 (1.4%) [1]	3 (1.5%) [3]	1 (1.4%) [1]	4 (2.0%) [4]	2 (2.9%) [2]
General disorders and administration site conditions	**2 (1.0%) [2]**	**0 (0.0%) [0]**	**0 (0.0%) [0]**	**1 (1.4%) [1]**	**3 (1.5%) [3]**	**2 (2.9%) [2]**
Administration site reactions NEC	2 (1.0%) [2]	0 (0.0%) [0]	0 (0.0%) [0]	0 (0.0%) [0]	0 (0.0%) [0]	0 (0.0%) [0]
Vessel puncture site haematoma	*1 (0.5%) [1]*	*0 (0.0%) [0]*	*0 (0.0%) [0]*	*0 (0.0%) [0]*	*0 (0.0%) [0]*	*0 (0.0%) [0]*
Vessel puncture site haemorrhage	*1 (0.5%) [1]*	*0 (0.0%) [0]*	*0 (0.0%) [0]*	*0 (0.0%) [0]*	*0 (0.0%) [0]*	*0 (0.0%) [0]*
Device physical property and chemical issues	0 (0.0%) [0]	0 (0.0%) [0]	0 (0.0%) [0]	1 (1.4%) [1]	0 (0.0%) [0]	0 (0.0%) [0]
Device breakage	*0 (0.0%) [0]*	*0 (0.0%) [0]*	*0 (0.0%) [0]*	*1 (1.4%) [1]*	*0 (0.0%) [0]*	*0 (0.0%) [0]*
Vascular complications associated with device	0 (0.0%) [0]	0 (0.0%) [0]	0 (0.0%) [0]	0 (0.0%) [0]	3 (1.5%) [3]	2 (2.9%) [2]
Vascular stent restenosis	*0 (0.0%) [0]*	*0 (0.0%) [0]*	*0 (0.0%) [0]*	*0 (0.0%) [0]*	*3 (1.5%) [3]*	*2 (2.9%) [2]*
Injury, poisoning and procedural complications	**1 (0.5%) [1]**	**1 (1.4%) [1]**	**3 (1.5%) [3]**	**0 (0.0%) [0]**	**1 (0.5%) [1]**	**0 (0.0%) [0]**
Cardiac and vascular procedural complications	0 (0.0%) [0]	1 (1.4%) [1]	3 (1.5%) [3]	0 (0.0%) [0]	1 (0.5%) [1]	0 (0.0%) [0]
Vascular pseudoaneurysm	*0 (0.0%) [0]*	*1 (1.4%) [1]*	*3 (1.5%) [3]*	*0 (0.0%) [0]*	*1 (0.5%) [1]*	*0 (0.0%) [0]*
Non-site specific procedural complications	1 (0.5%) [1]	0 (0.0%) [0]	0 (0.0%) [0]	0 (0.0%) [0]	0 (0.0%) [0]	0 (0.0%) [0]
Procedural complication	*1 (0.5%) [1]*	*0 (0.0%) [0]*	*0 (0.0%) [0]*	*0 (0.0%) [0]*	*0 (0.0%) [0]*	*0 (0.0%) [0]*
Vascular disorders	**2 (1.0%) [2]**	**0 (0.0%) [0]**	**0 (0.0%) [0]**	**0 (0.0%) [0]**	**0 (0.0%) [0]**	**0 (0.0%) [0]**
Vascular injuries NEC	1 (0.5%) [1]	0 (0.0%) [0]	0 (0.0%) [0]	0 (0.0%) [0]	0 (0.0%) [0]	0 (0.0%) [0]
Vessel perforation	*1 (0.5%) [1]*	*0 (0.0%) [0]*	*0 (0.0%) [0]*	*0 (0.0%) [0]*	*0 (0.0%) [0]*	*0 (0.0%) [0]*
Vascular malformations and acquired anomalies	1 (0.5%) [1]	0 (0.0%) [0]	0 (0.0%) [0]	0 (0.0%) [0]	0 (0.0%) [0]	0 (0.0%) [0]
Arteriovenous fistula	*1 (0.5%) [1]*	*0 (0.0%) [0]*	*0 (0.0%) [0]*	*0 (0.0%) [0]*	*0 (0.0%) [0]*	*0 (0.0%) [0]*

[1] This time interval includes Day 0 such that all adverse events counted in the Procedure Day column are also counted 30 Days.
[2]Subject counts at the top of each column are the number of subjects within the study at the beginning of that interval and are the denominator used in calculating percentages in that column.
[3]Time intervals for estimates: Procedure Day (0 Days), 30 Days (Procedure - 30 Days) and 6 Months (31 - 182 Days).
[4]Entries Represent MedDRA System Organ Class, High Level Term and Preferred Term and are identified by font style and increasing level of indentation.
[5]Cells are formatted to display: number of subjects experiencing the event (percentage of subjects experiencing the event) [number of events experienced].

Table 16: Summary of All Serious Device and Procedure Related Adverse Events by Late Follow-up Interval (ITT Population)[2,3,4]

	Follow-up Interval					
	1 Year		2 Years		3 Years	
	TIGRIS	LIFESTENT	TIGRIS	LIFESTENT	TIGRIS	LIFESTENT
Number of Subjects[1] Available	N = 188	N = 68	N = 123	N = 39	N = 22	N = 9
Number experiencing any event(s)	6 (3.2%) [6]	4 (5.9%) [4]	4 (3.3%) [4]	1 (2.6%) [1]	0 (0.0%) [0]	0 (0.0%) [0]
General disorders and administration site conditions	**5 (2.7%) [5]**	**3 (4.4%) [3]**	**4 (3.3%) [4]**	**1 (2.6%) [1]**	**0 (0.0%) [0]**	**0 (0.0%) [0]**
Device malfunction events NEC	0 (0.0%) [0]	0 (0.0%) [0]	1 (0.8%) [1]	0 (0.0%) [0]	0 (0.0%) [0]	0 (0.0%) [0]
Device occlusion	*0 (0.0%) [0]*	*0 (0.0%) [0]*	*1 (0.8%) [1]*	*0 (0.0%) [0]*	*0 (0.0%) [0]*	*0 (0.0%) [0]*
Vascular complications associated with device	5 (2.7%) [5]	3 (4.4%) [3]	3 (2.4%) [3]	1 (2.6%) [1]	0 (0.0%) [0]	0 (0.0%) [0]
Vascular stent restenosis	*5 (2.7%) [5]*	*3 (4.4%) [3]*	*3 (2.4%) [3]*	*1 (2.6%) [1]*	*0 (0.0%) [0]*	*0 (0.0%) [0]*
Vascular disorders	**1 (0.5%) [1]**	**1 (1.5%) [1]**	**0 (0.0%) [0]**	**0 (0.0%) [0]**	**0 (0.0%) [0]**	**0 (0.0%) [0]**
Peripheral vasoconstriction, necrosis and vascular insufficiency	1 (0.5%) [1]	1 (1.5%) [1]	0 (0.0%) [0]	0 (0.0%) [0]	0 (0.0%) [0]	0 (0.0%) [0]
Intermittent claudication	*1 (0.5%) [1]*	*1 (1.5%) [1]*	*0 (0.0%) [0]*	*0 (0.0%) [0]*	*0 (0.0%) [0]*	*0 (0.0%) [0]*

[1]Subject counts at the top of each column are the number of subjects within the study at the beginning of that interval and are the denominator used in calculating percentages in that column.
[2]Time intervals for estimates: 1 Year (213 - 410 Days), 2 Years (411 - 775 Days) and 3 Years (776 - 1140 Days).
[3]Entries Represent MedDRA System Organ Class, High Level Term and Preferred Term and are identified by font style and increasing level of indentation
[4]Cells are formatted to display: number of subjects experiencing the event (percentage of subjects experiencing the event) [number of events experienced].

2. Effectiveness Results

Primary Effectiveness Endpoint

The primary effectiveness endpoint of the PCE 09-02 study, primary patency assessed at 12 months after implant, was met. The effectiveness of the TIGRIS Vascular Stent was found to be statistically non-inferior to that of the Control device, using a 19% margin, measured 12 months after implant (p=0.002; **Table 17**). **Table 17** represents the primary effectiveness endpoint analysis for the PP population; analyses of ITT and AT populations demonstrated similar results for this endpoint.

Table 17: Primary Patency at 12 Months

	TIGRIS	LIFESTENT	P-value*
Patent at 12 Months	N=170	N=64	0.002
Yes	97 (57.1%)	35 (54.7%)	
95% Confidence Interval**	[49.3%, 64.6%]	[41.8%, 67.2%]	

*The non-inferiority test with a 19% margin is performed using a one-sided z-test with a pooled variance estimate.
**Confidence interval calculated using binomial exact test.

Secondary Effectiveness Endpoints

Procedural Success

A large majority of index procedures in both treatment groups were successful in treating the target lesion with no acute, unresolved SAEs. A total of three subjects did not meet the study definition of procedural success, *i.e.*, successful device implantation with a residual stenosis <30% without acute (within 48 hours) serious adverse events (AEs) defined as: death, stroke, myocardial infarction, emergent surgical revascularization, significant distal embolization in the treated leg, or thrombosis of the target vessel occurring after or not successfully treated during the implant procedure (**Table 18**).

Table 18: Procedural Success

	TIGRIS	LIFESTENT
Number of Subjects	197	70
Procedural Success	197	70
Yes	196 (99.5%)	68 (97.1%)
No	1 (0.5%)	2 (2.9%)

Device Success

One subject in the PP group did not have a device implanted successfully (**Table 19**). During the applicant's review of the procedural records in this case, the implanting Investigator noted that this subject had unusually challenging anatomy. All stents were withdrawn, undeployed, from the subject with no clinical sequelae. The implanting Investigator elected to discontinue the procedure without deploying a stent or continuing the procedure with a non-study stent, and the subject was successfully treated using balloon angioplasty only.

Table 19: Device Success

	TIGRIS	LIFESTENT
Number of Subjects	197	70
Device Success	197	70
Yes	196 (99.5%)	70 (100.0%)
No	1 (0.5%)	0 (0.0%)

Freedom from TVR

Freedom from TVR was comparable between treatment groups. Time-to-event analysis of freedom from TVR through 12 months is presented in **Table 20**.

Table 20: Kaplan-Meier Estimates of Freedom From TVR

Time Post Treatment (days)	# at Risk Interval Start	Events Number (Cumulative)	Censored Number (Cumulative)	Survival Probability	95% C.I.
Treatment Group: Bard LifeStent Vascular Stent (N=70)					
0	70	0 (0)	0 (0)	100.0%	(100.0%, 100.0%)
[1-30]	70	0 (0)	1 (1)	100.0%	(100.0%, 100.0%)
[31-183]	69	4 (4)	1 (2)	94.1%	(85.1%, 97.8%)
[184-365]	64	8 (12)	16 (18)	81.9%	(70.3%, 89.3%)
Treatment Group: GORE TIGRIS Vascular Stent (N=197)					
0	197	1 (1)	6 (6)	99.5%	(96.5%, 99.9%)
[1-30]	190	0 (1)	3 (9)	99.5%	(96.5%, 99.9%)
[31-183]	187	10 (11)	8 (17)	94.0%	(89.4%, 96.6%)
[184-365]	169	35 (46)	23 (40)	74.1%	(66.9%, 79.9%)

Freedom from TLR

Freedom from TLR was comparable between treatment groups. Time-to-event analysis of freedom from TLR through 12 months is presented in **Table 21**.

Table 21: Kaplan-Meier Estimates of Freedom From TLR

Time Post Treatment (days)	# at Risk Interval Start	Events Number (Cumulative)	Censored Number (Cumulative)	Survival Probability	95% C.I.
Treatment Group: Bard LifeStent Vascular Stent (N=70)					
0	70	0 (0)	0 (0)	100.0%	(100.0%, 100.0%)
[1-30]	70	0 (0)	1 (1)	100.0%	(100.0%, 100.0%)
[31-183]	69	4 (4)	1 (2)	94.1%	(85.1%, 97.8%)
[184-365]	64	8 (12)	16 (18)	81.9%	(70.3%, 89.3%)
Treatment Group: GORE TIGRIS Vascular Stent (N=197)					
0	197	0 (0)	6 (6)	100.0%	(100.0%, 100.0%)
[1-30]	191	0 (0)	3 (9)	100.0%	(100.0%, 100.0%)
[31-183]	188	9 (9)	8 (17)	95.0%	(90.7%, 97.4%)
[184-365]	171	33 (42)	23 (40)	76.3%	(69.3%, 81.9%)

Rutherford Improvement

The TIGRIS Vascular Stent group exhibited a comparable frequency of improvement in Rutherford category, as well as mean change in Rutherford category, to the Control device group at each follow-up interval. Improvement was seen in more than 87% of subjects at all intervals (**Table 22**).

Table 22: Rutherford Improvement[1,2]

	TIGRIS	LIFESTENT
Number of Subjects	197	70
30 Days	182	69
Rutherford Improved	171 (94.0%)	66 (95.7%)
Rutherford Not Improved	11 (6.0%)	3 (4.3%)
6-Months	175	64
Rutherford Improved	155 (88.6%)	59 (92.2%)
Rutherford Not Improved	20 (11.4%)	5 (7.8%)
12-Months	165	58
Rutherford Improved	145 (87.9%)	52 (89.7%)
Rutherford Not Improved	20 (12.1%)	6 (10.3%)

[1]Rutherford Improved requires at least 1 class of improvement in Rutherford Classification versus baseline; otherwise they are counted as Rutherford Not Improved.
[2]Subjects without Rutherford measured at corresponding visit omitted.

Ankle-Brachial Index

Table 23 presents the mean, median, and min-max change in ABI from the pre-procedure baseline value at each follow-up interval. Higher numbers in **Table 23** represent a more favorable clinical outcome, with positive numbers indicating improvement from subjects' pre-procedure condition. The mean change from the baseline value is positive at each interval for both treatment groups, and similar between groups.

Table 23: Change in ABI

	TIGRIS	LIFESTENT
Number of Subjects	197	70
30-Days	178	70
Mean (Std Dev)	0.310 (0.1897)	0.332 (0.1902)
Median	0.280	0.350
Min-Max	-0.130 - 1.000	-0.050 - 0.820
6-Month	172	61
Mean (Std Dev)	0.241 (0.2364)	0.232 (0.2399)
Median	0.210	0.210
Min-Max	-0.410 - 0.900	-0.260 - 1.000
12-Month	160	57
Mean (Std Dev)	0.249 (0.2269)	0.314 (0.2107)
Median	0.215	0.270
Min-Max	-0.350 - 1.200	0.000 - 1.000

Quality of Life

This endpoint was established in order to evaluate the quality of life (QOL) improvement brought about by improvement of symptoms following treatment with the TIGRIS Vascular Stent as compared to the Control device. The QOL questionnaire results obtained at each visit following the index procedure were compared with those obtained pre-procedure.

In this study, the Peripheral Artery Questionnaire (PAQ) and EQ-5D Questionnaire were used. For both questionnaires, higher scores reflect a better quality of life. Scores for both treatment arms showed a trend of consistent post-procedure improvement as compared to baseline, and there was no statistically significant difference between the two groups at any interval.

Primary Patency

Kaplan-Meier estimates of primary patency are presented in **Table 24**. Estimates of primary patency (survival probability) are similar between the two treatment groups through 12 months.

Table 24: Kaplan-Meier Estimates of Primary Patency

Time Post Treatment (days)	# at Risk Interval Start	Events Number (Cumulative)	Censored Number (Cumulative)	Survival Probability	95% C.I.
Treatment Group: Bard LifeStent Vascular Stent (N=70)					
0	70	0 (0)	0 (0)	100.0%	(100.0%, 100.0%)
[1-30]	70	1 (1)	3 (3)	98.6%	(90.2%, 99.8%)
[31-183]	66	8 (9)	3 (6)	86.2%	(75.2%, 92.6%)
[184-365]	55	14 (23)	10 (16)	63.7%	(50.5%, 74.3%)
Treatment Group: GORE TIGRIS Vascular Stent (N=197)					
0	197	0 (0)	11 (11)	100.0%	(100.0%, 100.0%)
[1-30]	186	0 (0)	2 (13)	100.0%	(100.0%, 100.0%)
[31-183]	184	23 (23)	8 (21)	87.0%	(81.1%, 91.2%)
[184-365]	153	45 (68)	30 (51)	60.2%	(52.4%, 67.1%)

Assisted Primary Patency

Kaplan-Meier estimates of assisted primary patency are presented in **Table 25**. Estimates of assisted primary patency (survival probability) are similar between the two treatment groups through 12 months.

Table 25: Kaplan-Meier Estimates of Assisted Primary Patency

Time Post Treatment (days)	# at Risk Interval Start	Events Number (Cumulative)	Censored Number (Cumulative)	Survival Probability	95% C.I.
Treatment Group: Bard LifeStent Vascular Stent (N=70)					
0	70	0 (0)	0 (0)	100.0%	(100.0%, 100.0%)
[1-30]	70	0 (0)	3 (3)	100.0%	(100.0%, 100.0%)
[31-183]	67	0 (0)	6 (9)	100.0%	(100.0%, 100.0%)
[184-365]	61	4 (4)	12 (21)	93.4%	(83.3%, 97.5%)
Treatment Group: GORE TIGRIS Vascular Stent (N=197)					
0	197	0 (0)	9 (9)	100.0%	(100.0%, 100.0%)
[1-30]	188	0 (0)	2 (11)	100.0%	(100.0%, 100.0%)
[31-183]	186	3 (3)	12 (23)	98.3%	(94.9%, 99.5%)
[184-365]	171	8 (11)	46 (69)	93.3%	(88.3%, 96.3%)

Secondary Patency

Kaplan-Meier estimates of secondary patency are presented in **Table 26**. Estimates of secondary patency (survival probability) are similar between the two treatment groups through 12 months.

Table 26: Kaplan-Meier Estimates of Secondary Patency

Time Post Treatment (days)	# at Risk Interval Start	Events Number (Cumulative)	Censored Number (Cumulative)	Survival Probability	95% C.I.
Treatment Group: Bard LifeStent Vascular Stent (N=70)					
0	70	0 (0)	0 (0)	100.0%	(100.0%, 100.0%)
[1-30]	70	0 (0)	1 (1)	100.0%	(100.0%, 100.0%)
[31-183]	69	0 (0)	1 (2)	100.0%	(100.0%, 100.0%)
[184-365]	68	1 (1)	18 (20)	98.3%	(88.4%, 99.8%)
Treatment Group: GORE TIGRIS Vascular Stent (N=197)					
0	197	0 (0)	6 (6)	100.0%	(100.0%, 100.0%)
[1-30]	191	0 (0)	3 (9)	100.0%	(100.0%, 100.0%)
[31-183]	188	1 (1)	9 (18)	99.5%	(96.2%, 99.9%)
[184-365]	178	1 (2)	29 (47)	98.9%	(95.5%, 99.7%)

Freedom from Stent Fracture

The presence/absence of stent fracture was evaluated by the core lab using X-ray imaging analysis. No fractures were identified in the TIGRIS Vascular Stent group at the 12- month interval. In the Control device group, 18 subjects (34.6%) with stent fractures were identified at 12 months (**Table 27**). Over 88% of the 19 Control devices observed to have fractured were classified by the core lab as either type III (a complete transverse fracture), type IV (two transverse fractures bounding a displaced section of the stent), or type V (spiral dissection of the stent) (**Table 28**).

Table 27: Stent Fractures (Reported by Subject)

	TIGRIS	LIFESTENT
Number of Subjects	197	70
12-Month	158	52
Fracture	0 (0.0%)	18 (34.6%)
No Fracture	158 (100.0%)	34 (65.4%)

Table 28: Fracture Grades (Reported by Device)

	TIGRIS	LIFESTENT
Number of Devices Analyzed at 12-Months	270	70
Number of Fractures	0 (0.0%)	19 (27.1%)
Fracture Grades		
Grade 1: Single strut fracture only	0 (0.0%)	1 (1.4%)
Grade 2: Multiple single strut fractures that occur at different sites	0 (0.0%)	1 (1.4%)
Grade 3: Multiple strut fractures resulting in complete transection of the stent, without displacement of the stent segment	0 (0.0%)	7 (10.0%)
Grade 4: Multiple strut fractures resulting in displacement of segment(s) of the stent	0 (0.0%)	5 (7.1%)
Grade 5: Spiral dissection of the stent	0 (0.0%)	5 (7.1%)

3. Subgroup Analyses

Primary Endpoints Stratified by Lesion Length

Both the primary effectiveness and the primary safety endpoints were re-estimated and stratified by lesion lengths, including 95% confidence intervals around the estimates (**Table 29**).

Table 29: Primary Endpoints Stratified by Lesion Length

	TIGRIS	LIFESTENT
Number of Subjects	197	70
Primary Patency at 12 months[1]		
≤ 16 cm	134	43
Patent at 12 Months	82 (61.2%)	27 (62.8%)
95% C. I.	[52.4%, 69.5%]	[46.7%, 77.0%]
> 16 cm	36	21
Patent at 12 Months	15 (41.7%)	8 (38.1%)
95% C. I.	[25.5%, 59.2%]	[18.1%, 61.6%]
(16 cm - 20 cm)	17	7
Patent at 12 Months	7 (41.2%)	0 (0.0%)
95% C. I.	[18.4%, 67.1%]	[59.0%,100.0%]
> 20 cm	19	14
Patent at 12 Months	8 (42.1%)	8 (57.1%)
95% C. I.	[20.3%, 66.5%]	[28.9%, 82.3%]
Freedom from MAEs at 30 days[1]		
≤ 16 cm	146	47
Free from MAE	145 (99.3%)	47 (100.0%)
95% C. I.	[96.2%,100.0%]	[92.5%,100.0%]
16 cm - 20 cm	20	8
Free from MAE	20 (100.0%)	8 (100.0%)
95% C. I.	[83.2%,100.0%]	[63.1%,100.0%]
> 20 cm	22	14
Free from MAE	22 (100.0%)	14 (100.0%)
95% C. I.	[84.6%,100.0%]	[76.8%,100.0%]

[1]Confidence intervals calculated using binomial exact test.

Primary Endpoints Stratified by Gender and Race

Both primary endpoints were re-estimated, stratified by gender and race separately, including 95% confidence intervals around the estimates.

For the primary effectiveness endpoint, the primary patency at 12 months was similar between treatment groups in males and females. Although males were observed to have a slightly higher primary patency than females, there was a substantial degree of overlap in the confidence intervals between the genders for both groups (**Table 30**). Primary patency at 12 months was similar between treatment groups for White

subjects, but it is difficult to compare treatment groups for non-White subjects due to the low number of subjects identified as non-White in the Control device group. This low number reflects the exclusion of subjects enrolled in the EU, where race data was not collected (**Table 30**).

Table 30: Primary Patency at 12 Months by Gender and Race

	TIGRIS	LIFESTENT
Number of Subjects	197	70
Primary Patency at 12 Months by Gender[2]		
Females	47	19
Patent at 12 Months	25 (53.2%)	9 (47.4%)
95% C. I.	[38.1%, 67.9%]	[24.5%, 71.1%]
Males	123	45
Patent at 12 Months	72 (58.5%)	26 (57.8%)
95% C. I.	[49.3%, 67.4%]	[42.2%, 72.3%]
Primary Patency at 12 Months by Race[1,2]		
White	100	49
Patent at 12 Months	56 (56.0%)	26 (53.1%)
95% C. I.	[45.7%, 65.9%]	[38.3%, 67.5%]
Non-white	21	1
Patent at 12 Months	9 (42.9%)	0 (0.0%)
95% C. I.	[21.8%, 66.0%]	[2.5%,100.0%]

[1]Subjects from Europe are omitted, as race data was not collected at EU study sites.
[2]Confidence intervals calculated using binomial exact test.

For the primary safety endpoint, the 30-day freedom from MAE percentage was similar between treatment groups with respect to both gender and race, with only one subject (a White female) experiencing an MAE within 30 days of the index procedure (**Table 31**).

Table 31: Freedom from Major Adverse Events at 30 Days by Gender and Race

	TIGRIS	LIFESTENT
Number of Subjects	197	70
Freedom from MAEs at 30 days by Gender[2]		
Females	54	21
Free from MAE	53 (98.1%)	21 (100.0%)
95% C. I.	[90.1%,100.0%]	[83.9%,100.0%]
Males	134	48
Free from MAE	134 (100.0%)	48 (100.0%)
95% C. I.	[97.3%,100.0%]	[92.6%,100.0%]
Freedom from MAEs at 30 days by Race[1,2]		
White	112	51
Free from MAE	111 (99.1%)	51 (100.0%)
95% C. I.	[95.1%,100.0%]	[93.0%,100.0%]
Non-white	25	2
Free from MAE	25 (100.0%)	2 (100.0%)
95% C. I.	[86.3%,100.0%]	[15.8%,100.0%]

[1]Subjects from Europe are omitted, as race data was not collected at EU study sites.
[2]Confidence intervals calculated using binomial exact test.

Additional Efficacy Analyses Stratified by Lesion Length

Additional efficacy analyses are summarized in **Tables 32-34** below. All analyses by lesion length are Kaplan-Meier time-to-event analyses using site-reported lesion lengths, and include day 360 and day 720 performance estimates. Subjects are considered to have known status if they either lost patency prior to day 720 or had a follow-up visit with the required testing performed at or after the start of the two-year window (730-45 days). For example, there were 63.7% (170/267) of subjects who met these conditions for primary patency at the time of the data lock.

Table 32: Primary Patency by Lesion Length

Time Point	**Day 360**			**Day 720**		
Lesion Lengths	**0-16cm**	**17-24cm**	**All**	**0-16cm**	**17-24cm**	**All**
GORE TIGRIS Device	68.3%	43.6%	63.0%	59.9%	34.9%	54.9%
Control Device	74.6%	52.4%	67.4%	57.4%	23.3%	45.5%

Table 33: Freedom from TLR by Lesion Length

Time Point	Day 360			Day 720		
Lesion Lengths	**0-16cm**	**17-24cm**	**All**	**0-16cm**	**17-24cm**	**All**
GORE TIGRIS Device	82.1%	57.9%	76.9%	73.6%	51.5%	68.8%
Control Device	82.0%	81.6%	81.9%	70.9%	49.1%	63.6%

Table 34: Secondary Patency by Lesion Length

Time Point	Day 360			Day 720		
Lesion Lengths	**0-16cm**	**17-24cm**	**All**	**0-16cm**	**17-24cm**	**All**
GORE TIGRIS Device	99.3%	97.4%	98.9%	99.3%	97.4%	98.9%
Control Device	97.4%	100.0%	98.3%	97.4%	85.7%	95.1%

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 PCE 09-02 clinical study included six investigators who had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: None
- Significant payment of other sorts: six investigators
- Proprietary interest in the product tested held by the investigator: None
- Significant equity interest held by investigator in sponsor of covered study: None

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. 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

Non-clinical testing performed during the design and development of the TIGRIS Vascular Stent system confirmed the product design characteristics, specifications, and intended use. The non-clinical 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 TIGRIS Vascular 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 primary effectiveness endpoint in the pivotal clinical study of the TIGRIS Vascular Stent was primary patency at 12 months after implantation, with primary patency defined as uninterrupted patency without target lesion revascularization (TLR), including the proximal and distal margins, and no restenosis as documented by a peak systolic velocity ratio (PSVR) $\leq$2.5 by Color Doppler Ultrasound (CDUS). The effectiveness of the TIGRIS Vascular Stent (57.1%; 97/170) was found to be statistically non-inferior to that of the Control device (54.7%; 35/64), using a 19% margin, measured 12 months after implant (p=0.002).

Secondary effectiveness endpoints evaluated in the pivotal clinical study of the TIGRIS Vascular Stent were intended to describe functional outcomes of treatment with the device over the course of the study. Key secondary endpoints included procedural success; device success; freedom from target vessel and target lesion revascularization (TVR and TLR); change in Rutherford classification; change in ankle-brachial index values; change in quality of life; primary, assisted primary, and secondary patency; and freedom from stent fracture.

For all secondary endpoints, study data indicate that the effectiveness of the GORE TIGRIS Vascular Stent is non-inferior to that of the FDA-approved Control device. These results suggest that the GORE TIGRIS Vascular Stent is effective at treating the proposed indication for the studied patient population.

B. Safety Conclusions

The primary safety endpoint, freedom from MAE, defined in this clinical study as death, TVR, and index limb amputation observed within 30 days of stent implant, was met. The safety of the TIGRIS Vascular Stent (99.5%; 187/188) was found to be statistically non-inferior to that of the Control device (100%; 69/69), using a 12% margin, measured 30 days after implant (p<0.001).

Furthermore, the frequency and types of all reported AEs comparable between the two treatment groups, and no unanticipated device- or procedure-related events were reported. Fourteen deaths have been reported in the study, and there is no indication that any of

these deaths are related to study participation. These results suggest that the GORE TIGRIS Vascular Stent is safe for use in the proposed indication and patient population

C. Benefit-Risk Conclusions

The primary potential benefit of the GORE TIGRIS Vascular Stent is the improvement or restoration of blood flow in peripheral arteries with impeded or absent blood flow related to peripheral arterial disease (PAD).

The risks associated with peripheral self-expanding stents are well-understood. Specifically, with respect to the TIGRIS Vascular Stent, the frequency and types of the adverse events reported throughout the pivotal clinical study are in alignment with what might be expected in the studied patient population and therapeutic area. No unanticipated device- or procedure-related adverse events were reported in the study.

Given the available information above, the data support that the probable benefits outweigh the probable risks for using the TIGRIS Vascular Stent to improve luminal diameter in patients with symptomatic de-novo or restenotic lesions or occlusions in the native superficial femoral artery (SFA) and proximal popliteal artery (PPA) with reference vessel diameters ranging from 4.0-6.5 mm and lesion lengths up to 240 mm.

1. Patient Perspectives

The study included protocol driven questionnaires in order to asses Quality of Life (QOL), specifically the EQ-5D and PAQ. Scores for both treatment arms showed a trend of consistent post-procedure improvement as compared to baseline, and there was no statistically significant difference between the two groups at any interval. It is expected that patients would place value on this treatment, are willing to take the risk of this treatment to achieve the benefit and would be able to understand the benefits and risks of treatment with the TIGRIS Vascular Stent without difficulty.

D. Overall Conclusions

The clinical and non-clinical data in this application provide a reasonable assurance that the device is safe and effective. The clinical study met the pre-specified safety and effectiveness endpoints. Therefore, it is reasonable to conclude that the benefits of use of the device for the target population outweigh the risk of illness or injury when used as indicated in accordance with the labeling and Instructions for Use (IFU).

XIII. CDRH DECISION

CDRH issued an approval order on July 27, 2016. The final conditions of approval cited in the approval order are described below.

Continued Follow-up Study: This study must be conducted per protocol PCE 09-02 (dated August 3, 2012) and the Post-Approval Study Analysis Plan (dated January 15, 2016). This study is a prospective, randomized, multi-center follow-up of the PCE 09-02 pivotal study. It will evaluate the long term safety and effectiveness of the GORE

TIGRIS vascular stent. All 218 remaining subjects (56 subjects have completed or withdrawn from the study) of the 274 original study subjects (with either the TIGRIS or Bard LifeStent comparator device) enrolled in the PCE 09-02 study from 36 investigational sites will be followed up to 3 years post-implant.

A. **Primary Effectiveness endpoint**

- Primary patency is defined as uninterrupted patency without target lesion revascularization (TLR), including the proximal and distal margins, and no restenosis as documented by a peak systolic velocity ratio (PSVR) ≤2.5 by Color Doppler Ultrasound (CDUS). In cases where PSVR cannot be determined, or is determined to be inaccurate by the independent ultrasound core laboratory, reduction in luminal diameter within the stented region must be ≤50% as adjudicated by the core laboratory. Primary patency will be reported at 3 years post-implant.

B. Secondary Endpoints (at 2 and 3 years post-implant)

- Freedom from MAE (death, TVR, or index limb amputation)
- Freedom from TVR
- Freedom from TLR
- Rutherford Improvement: Improvement in Rutherford Classification by at least 1 class
- Ankle-Brachial Index (ABI) from pre-procedure
- Quality of Life: Change in overall Quality of Life (EQ-5D) and disease-specific Quality of Life (Peripheral Artery Questionnaire [PAQ]) from Baseline
- Primary patency at 24 months
- Assisted primary patency
- Secondary patency Freedom from fracture

The applicant's manufacturing facility(ies) has/have 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.