The TORUS 2 IDE Clinical Study

The PQ Bypass piv**O**tal IDE intra-a**R**terial stent graft study for occl**U**sive and re-**S**tenotic fem-pop revascularization – **2** Trial: TORUS 2

Rev. D

Sponsor:
PQ Bypass, Inc.
1971 Milmont Drive
Milpitas, CA 95035

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CONFIDENTIAL

INVESTIGATOR SIGNATURE PAGE

STUDY TITLE: The TORUS 2 IDE Clinical Study

PROTOCOL NUMBER & ISSUE: CLN 227-D, August 01, 2020

STUDY INVESTIGATIONAL SITE: _____
(Print name of study investigational site)

I, the undersigned, have read and understand the protocol specified above and agree with its content. I agree to perform and conduct the Study as described in the protocol. In addition, when applicable, I agree to enlist sub-investigators who also agree to perform and conduct the Study as described in the protocol. I will provide copies of this Protocol and all pertinent information to the Study personnel under my supervision and my hospital Institutional Review Board/ Independent Ethics Committee. I will discuss this material with them and ensure they are fully informed regarding the PQ Bypass TORUS Stent Graft System investigational device and the conduct of the Study according to Good Clinical Practice (GCP), Declaration of Helsinki, 21 CFR Parts 50, 54, 56 and 812, ISO 14155:2011 (OUS sites only), and any local regulations.

Site PI Name: _____

Site PI Signature: _____ **Date:** _____

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TORUS 2 IDE Clinical Study

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1.0 PROTOCOL SYNOPSIS

torus2	
Protocol Number	CLN-227-D
Device	TORUS Stent Graft System, provided in diameters ranging from 5.5 – 6.7 mm and lengths up to 200 mm
Primary Purpose	The primary objective of the TORUS 2 IDE Clinical Study is to evaluate the safety and effectiveness of the TORUS Stent Graft System in the treatment of obstructive atherosclerotic lesions of the native SFA or the superficial femoral and/or proximal popliteal arteries.
Study Design	TORUS 2 IDE Clinical Study is a global, prospective, single-arm, multi-center, safety and effectiveness clinical investigation. The safety and effectiveness of the Torus Stent Graft System will be established by comparing the primary safety and effectiveness endpoints to safety and effectiveness Performance Goals (PG) from the published literature.
Follow-Up Schedule	Office visits will occur at 1 month (30 days ±7 days), 6 months (180 days ±30 days), 12 months (360 days ±30 days), 24 months (720 days ±60 days) and 36 months (1080 days ±60 days) post-index procedure to review medications and adverse events, perform clinical assessments and functional status. See **Table 1** for a complete schedule of assessments.
Study Duration	Patients enrolled in the trial will participate for approximately 36 months (3 years).
Number of Patients	188 patients: • Rutherford 2 to 4 • Lesion lengths ≥ 80 mm to ≤ 180 mm • Reference Vessel Diameters 5.0 -6.7 mm
Number of Sites	A maximum of 40 investigational sites globally (North America and Europe)
Primary Safety Endpoint	Freedom from a major adverse event (MAE) at 30 days post-procedure defined as any occurrence of the following events: all-cause death, target limb major amputation and clinically-driven target lesion revascularization (CD-TLR).
Primary Effectiveness Endpoint	Primary patency at 12-months which is defined as the absence of clinically-driven target lesion revascularization (CD-TLR) and absence of recurrent target lesion diameter stenosis >50% by duplex ultrasound with a peak systolic velocity ratio of >2.5.

Secondary Endpoints	• Technical Success defined as the ability to cross and dilate the lesion to achieve residual stenosis of ≤30%. • Procedural Success defined as technical success with out any MAEs within 24 hours of the procedure. • MAE rate at 12 months post-index procedure, defined as a composite rate of all-cause death, target limb major amputation and clinically-driven target lesion revascularization (CD-TLR). • Patency rate through 36 months (absence of CD-TLR and absence of recurrent target lesion diameter stenosis >50% by duplex ultrasound with a peak systolic velocity ratio of >2.5). • Assisted Primary Patency rate through 36 months (revascularization of non-occlusive (<99%) stenosis within the stent graft or immediately above or below the treated arterial segment (end of the graft and 1cm of artery beyond) with less than 50% residual stenosis). • Secondary Patency rate through 36 months (revascularization of occlusion (100%) within the stent graft or immediately above or below the treated arterial segment (end of the graft and 1cm of artery beyond) with less than 50% residual stenosis.) • Alternative Patency rate through 36 months (patency of target vessel based on systolic velocity ratio ≤ 2.0 and absence of CD-TLR). • Walking Improvement assessed by the Walking Impairment Questionnaire (WIQ) from pre-procedure to 1, 6 and 12 months. • Improved Quality of Life assessed by the EQ-5D from pre-procedure to 1, 6, and 12 months. • Rate of CD-TLR through 36 months. • Rate of Target Vessel Resvascularization (TVR) through 36 months. • Rate of major amputation on target limb through 36 months. • Stent Fracture Rate utilizing VIVA definitions at 12 months in US subjects only. • Change in ankle-brachial index (ABI) and toe pressures from pre-procedure through 36 months. • Change in Rutherford clinical classification from pre-procedure through 36 months. • Adverse event rates through 36 months.
Clinical Inclusion Criteria	1. Patient is male or female, with age > 18 and ≤ 90 years at date of enrollment. 2. Patient provides written informed consent before any study-specific investigations or procedures. 3. Patient is willing to undergo all follow-up assessments according to the specified schedule over 36 months. 4. Patient is a suitable candidate for angiography and endovascular intervention.

	5. Patient has symptomatic peripheral arterial disease (PAD) of the lower extremities requiring intervention to relieve de novo obstruction or occlusion or restenosis of the native femoropopliteal artery. 6. Patient has PAD classified as Rutherford classification 2, 3 or 4. 7. Patient has documented PAD by either (i) a resting ankle-brachial index (ABI) of ≤ 0.90 (or ≤ 0.75 after exercise of the target limb). Resting toe brachial index (TBI) is performed only if unable to reliably assess ABI. TBI must be <0.70; or (ii) Normal ABI with angiographic,ultrasound, MRA, or CT evidence of ≥ 60% diameter stenosis.
Angiographic Inclusion Criteria	8. Patient has single or multiple stenotic, restenotic or occlusive lesions within the native femoropopliteal artery("target lesions") that can be crossed with a guidewire and fully dilated. 9. Single target lesion must be covered by a single stent graft. Tandem target lesions are considered a single continuous lesion if the gap between lesions is ≤ 5 cm and > 30% diameter stenosis between the lesion(s). 10. Target lesion(s) eligible for treatment under the protocol are at least 3 cm above the bottom of the femur. 11. Target lesion(s) reference vessel diameter is between 5.0 mm and 6.7 mm by operator's visual estimate. 12. Target lesion measures ≥ 80 mm to ≤ 180 mm in overall length, with ≥ 60% diameter stenosis by operator's visual estimate. Tandem target lesions are considered a single continuous lesion if the gap between lesions is ≤ 5 cm and > 30% diameter stenosis between the lesion(s). 13. Patient has a patent popliteal artery (no stenosis ≥ 50%) distal to the treated segment. 14. Patient has at least one patent infrapopliteal vessel (< 50% stenosis) with run-off to the ankle.
Clinical Exclusion Criteria	1. Patient is unable or is unwilling to comply with the procedural requirements of the study protocol or will have difficulty in complying with the requirements for attending follow-up visits. 2. Patient has a comorbidity that in the investigator's opinion would limit life expectancy to less than 12 months. 3. Patient has any planned major surgical procedure (including any amputation of the target limb) within 30 days after the index procedure for this study.

Clinical Exclusion Criteria	4. Patient has a target vessel that has been treated with any type of surgical procedure prior to enrollment. 5. Patient has a target vessel that has been treated with bypass surgery. 6. Patient has PAD classified as Rutherford classification 0, 1, 5 or 6. 7. Patient has known or suspected active systemic infection at the time of enrollment. 8. Patient has a known coagulopathy or has bleeding diatheses, thrombocytopenia with platelet count less than 100,000/microliter or INR (international normalized ratio) > 1.8. 9. Patient has a stroke diagnosis within three months prior to enrollment. 10. Patient has a history of unstable angina or myocardial infarction within 60 days prior to enrollment. 11. Patient has a contraindication to antiplatelet, anticoagulant or thrombolytic therapies. 12. Patient has known allergy to contrast agents or medications used to perform endovascular intervention that cannot be adequately pre-medicated. 13. Patient has known allergy to titanium, nickel or tantalum (does not include mild contact dermatitis due to nickel allergy). 14. Patient has received thrombolysis within 72 hours prior to the index procedure. 15. Patient has acute or chronic renal disease (e.g., as measured by a serum creatinine of > 2.5 mg/dL or > 220 µmol/L or GFR < 30 ml/min), or on peritoneal or hemodialysis. 16. Patient requiring coronary intervention within seven days prior to enrollment. 17. Patient is pregnant or breast-feeding. 18. Patient is participating in another research study involving an investigational product (pharmaceutical, biologic or medical device). 19. Patient has other medical, social or psychological problems that, in the opinion of the investigator, preclude them from receiving this treatment, and the procedures and evaluations pre- and post-treatment.
Angiographic Exclusion Criteria	20. Patient has significant disease or obstruction (≥ 50%) of the inflow tract that has not been successfully treated at the time of the index procedure (success measured as ≤ 30% residual stenosis, without complication). 21. Patient has no patent (≥ 50% stenosis) outflow vessel providing run-off to the ankle. 22. There is a lack of full expansion in the predilatation balloon. 23. Evidence of aneurysm or acute thrombus in the target vessel.

Table 1: Schedule of Assessments

	SCREEN/BASELINE	INDEX PROCEDURE	PRE DISCHARGE	1 Month (30 days)	6 MONTHS (180 days)	12 MONTHS (360 days)	24 MONTHS (720 days)	36 MONTHS (1080 days)
Visit Window	Within 30 days			± 7 days	± 30 days	± 30 days	± 60 days	± 60 days
Visit Type	Office	Hospital	Hospital	Office	Office	Office	Office	Office
Informed Consent & Medical History	X							
General Inclusion and Exclusion Criteria	X							
Angiographic Inclusion and Exclusion Criteria		X						
Pregnancy Test (if applicable)	X							
Anticoagulant and Antiplatelet	X	X	X	X	X	X	X	X
Physical assessment	X			X	X	X	X	X
Serum Creatinine/eGFR	X							
CBC (WBC, HGB, HCT and Platelets)	X							
Duplex Ultrasound (DUS) Examination				X	X	X	X	X
Index Angiogram/Stent Deployment		X						
Ankle-Brachial Index (or Toe-Brachial Index)	X			X	X	X	X	X
Stent Graft X-Ray						X		
Rutherford Clinical Classification	X			X	X	X	X	X
Walking Impairement Questionaire (WIQ)	X			X	X	X		
EQ-5D	X			X	X	X		
Adverse Events		X	X	X	X	X	X	X

2.0 INTRODUCTION

2.1 BACKGROUND AND RATIONALE

2.1.1. PERIPHERAL ARTERY DISEASE (PAD)

Atherosclerosis is a systemic disease process of plaque build-up within arterial vessels.[1] This plaque consists of fat deposits, cholesterol, calcium and other substances, and when plaque continues to accumulate, the vessel can become hardened, narrowed and/or completely occluded. The subsequent manifestation of narrowed arteries is a reduction of oxygen-rich blood flow to organs and other parts of the body.[2] In peripheral arterial disease (PAD), the accumulation of plaque blocks or reduces the flow of oxygen-rich blood to the arms, legs and pelvis, which can lead to numbness, pain and dangerous infections.[2] Removal of these narrowings or obstructions is critical to restoring adequate blood flow, maintaining healthy vessels, tissues and organs.

The most common risk factors for developing PAD are diabetes mellitus, cigarette smoking, advanced age, hyperlipidemia and hypertension.[3] In 2003, it was estimated that more than 27 million people in North America and Europe were affected by PAD,[4] and in 2007, it was estimated that PAD affects more than one in five people over the age of 70.[5] Despite the risk factors, less than 50 percent of patients with PAD know that they have the condition.[5] Patients suffering from PAD may also have symptomatic or asymptomatic coronary and/or carotid arterial disease and are three to six times more likely to experience a heart attack or stroke than patients without PAD.[5]

2.1.2. CURRENT TREATMENT OPTIONS

PAD, specifically in the superficial femoral arteries (SFA) and proximal popliteal arteries, are treated by a range of alternative practices and procedures for the patient population identified in the indications for use statement. Non-invasive approaches include exercise and drug therapy.

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[1]American Heart Association. What is PAD? Available at: http://www.americanheart.org/print_presenter.jhtml?identifier=3020249. Accessed June 3, 2013.
[2]National Institutes of Health. National Heart, Lung, and Blood Institute. Diseases and Conditions Index. What is Atherosclerosis? Available at: http://www.nhlbi.nih.gov/health/dci/Diseases/Atherosclerosis/Atherosclerosis_WhatIs.html. Accessed June 3, 2013.
[3]Chi Y and Jaff M. Optimal risk factor modification and medical management of the patient with peripheral arterial disease. Catheterization and Cardiovascular Interventions. 2008;71(4);475-89.
[4]Bashir R and Cooper C. Evaluation and medical treatment of peripheral arterial disease. Current opinion in cardiology. 2003;18(6):436-43.
[5]Gornik H and Beckman J. Peripheral Arterial Disease. Circulation. 2005;111;e169-e172.

Minimally-invasive approaches include endovascular intervention using percutaneous transluminal angioplasty using a plain or drug-coated balloon, stents (bare metal, drug-eluting and covered) and various modalities of atherectomy. The Gore VIABAHN is the only SFA Stent Graft System with PMA approval in the United States and has been commercially available since 2004. The safety and effectiveness of VIABAHN in the treatment of SFA disease is well-established, with more than 2,000 scientific publications[6] and more than 500,000 implanted in patients worldwide[6]. PQ Bypass believes that the 15-year clinical history of VIABAHN demonstrates that this device type is well understood, and the benefits and risks are well-characterized, i.e. mature technology. Given the similarities between the technical characteristics and intended patient population between TORUS and VIABAHN, PQ Bypass believes that the clinical performance of the TORUS stent would be comparable to the VIABAHN stent. The TORUS 2 IDE Clinical Study will confirm this and is designed to demonstrate the safety and effectiveness of the TORUS Stent Graft System in patients with SFA and/or proximal popliteal artery disease.

2.2 DEVICE DESCRIPTION

PQ Bypass designs and manufactures the Torus Stent Graft System. The Torus Stent Graft System is comprised of the TORUS Stent Graft and the Torus Stent Graft Delivery System. The TORUS Stent Graft device characteristics are listed in Table 2.

Table 2: TORUS Stent Graft Device Characteristics

Characteristic	Description
Model Name	TORUS Stent Graft System
Design	Single or Modular
Radiopaque Markers	Yes
Implant Materials	Expanded polytetrafluoroethylene and fluorinated ethylene propylene (ePTFE and FEP) graft material with a nitinol stent.
Stent Graft Construction	Layer of ePTFE wrapped on both inner and outer Nitinol stent structure, with FEP wrap on both ends
Stent Graft Porosity	No
Expansion Design	Self-expanding
Fixation Mechanism	Radial force
Anatomic Site	Femoral artery
Femoral Vessel Size Compatibility	5.0 – 6.7 mm
Method of Placement	Over-the-wire with percutaneous access
Method of Visualization	Radiopaque markers under fluoroscopy
MRI Compatibility	MR Conditional
Mechanics of Action	Catheter assisted, self-expanding stent with radial force
Size: Length	100, 150 & 200 mm
Size Diameter	5.5, 6.0, & 6.7 mm
Catheter Profile	8Fr

[6] HTTPS://WWW.GOREMEDICAL.COM/PRODUCTS/VIABAHN

2.2.1. TORUS STENT GRAFT

TORUS Stent Graft The TORUS Stent Graft **(Figure 1)** is a flexible, self-expanding composite structure made of a NiTi-wire frame encapsulated in an expanded Polytetrafluorethylene (ePTFE) film.

Figure 1: The TORUS Stent Graft

The TORUS Stent Graft is available in diameters and lengths listed below in **Table 3** and with model numbers in **Table 4**.

Table 3: TORUS Stent Graft Device Size Matrix

Labeled Device Diameter (mm)	Recommended Vessel Diameter (mm)	Available Device Nominal Lengths (mm)	Recommended Balloon Diameter for Post-Deployment Touch-up (mm)
5.5	5.0 – 5.5	200	5.5
6.0	5.6-6.0	100, 150, 200	6
6.7	6.1-6.7	100, 150, 200	7

Table 4: TORUS Stent Graft Model Numbers

Catalog/Model Number	Description
SGS-5.5X200	Stent Graft System – 5.5mm X 200mm
SGS-6.0X100	Stent Graft System – 6.0mm X 100mm
SGS-6.0X150	Stent Graft System – 6.0mm X 150mm
SGS-6.0X200	Stent Graft System – 6.0mm X 200mm
SGS-6.7X100	Stent Graft System – 6.7mm X 100mm
SGS-6.7X150	Stent Graft System – 6.7mm X 150mm
SGS-6.7X200	Stent Graft System – 6.7mm X 200mm

2.2.2. TORUS STENT GRAFT DELIVERY SYSTEM

The TORUS Stent Graft Delivery System (Figure 2) is an 8Fr system. It is 0.035" guidewire compatible and has a 135 cm working length. The TORUS Stent Graft System is a familiar design which uses an outer sheath to maintain the TORUS Stent Graft in a compressed state. The delivery system has radiopaque markers on both the proximal and distal ends of the TORUS Stent Graft landing zone (area where stent graft is located), as well as a marker band on the outer sheath to allow visualization of the sheath during deployment.

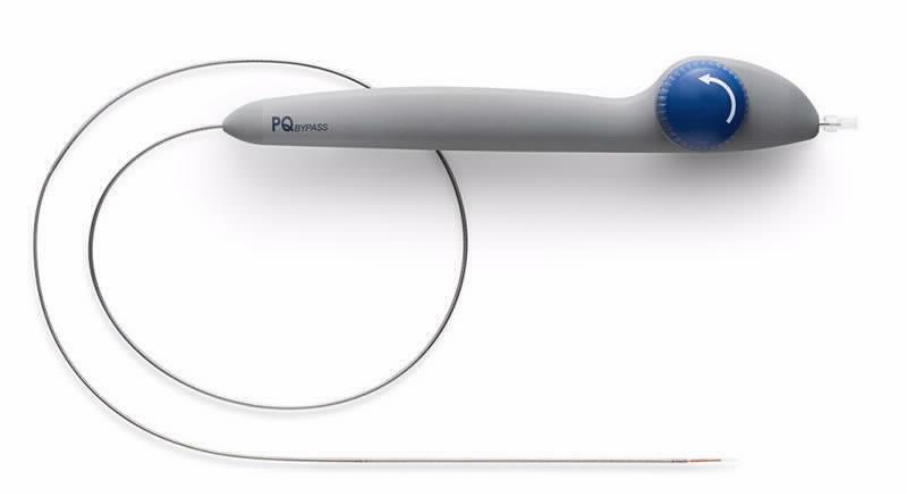

Figure 2: TORUS Stent Graft Delivery System

2.3 REGULATORY STATUS

The Torus Stent Graft system received CE Mark in March 2017 for femoral popliteal bypass indication (Detour I study).

The Torus Stent Graft system has not been submitted for CE review and approval for a femoralpopliteal arterial indication at the time of this protocol.

2.4 PROPOSED INTENDED USE

The TORUS Stent Graft System (formerly PQ Bypass™ Stent Graft System) is indicated to improve luminal diameter in the treatment of patients with symptomatic de novo or restenotic native lesions or occlusions of the superficial

femoral artery (SFA) and/or proximal popliteal artery, with reference vessel diameters of 5.0 to 6.7 mm and lesion lengths up to 180 mm.

2.5 ONGOING CLINICAL INVESTIGATIONS FOR THE TORUS STENT GRAFT SYSTEM

2.5.1. DETOUR STUDIES

The DETOUR Clinical Program was designed to evaluate the safety and effectiveness the PQ Bypass System to access, deliver guidewires and implant stent grafts for a percutaneous femoropopliteal (fem-pop) bypass and is comprised of two (2) studies with 159 patients implanted with the TORUS Stent Graft to date. Both studies are being conducted with robust controls including angiographic and duplex ultrasound core laboratory oversight, clinical events committee adjudication and monitoring of source data to confirm accuracy of the data.

A total of 78 Patients were enrolled in the DETOUR 1 study, and 77 Patients (81 limbs) were treated with the TORUS Stent Graft. Follow-up to one year has been completed, and follow-up to three years is ongoing.

The DETOUR 1 Primary Performance Endpoint is Primary patency at 6 months defined as: no evidence of clinically significant stenosis (≥50%) within the stent graft or immediately above or below the treated arterial segment based on duplex ultrasound (systolic velocity ratio of >2.5).

The DETOUR 1 Primary Safety Endpoint is the rate of in-hospital Major Adverse Clinical Events (MACE) or 6-month MACE, defined as: death, target limb amputation, target vessel revascularization (TVR), major bleeding (transfusion of >2 units packed red blood cells), or deep vein thrombosis on ipsilateral limb.

The DETOUR 2 IDE Clinical Study was initially approved on November 20, 2017 and is ongoing. To date, 81 Patients have been enrolled and treated with the TORUS Stent Graft. Follow-up is through three years.

The DETOUR 2 Primary Efficacy Endpoint is the absence of clinically-driven target lesion revascularizton (CD-TLR) and absence of recurrent target lesion diameter stenosis > 50% by imaging (e.g., duplex ultrasound peak systolic velocity ratio >2.5 or invasive angiography) within the stent or immediately 1 cm above or below the treated segment.

The DETOUR 2 Primary Safety Endpoint is Freedom from a major adverse event (MAE) at 30 days post-procedure defined as any occurrence of the following events: death, CD-TLR, Amputation of the Treated Limb, Symptomatic Deep Vein

Thrombosis (DVT), Pulmonary Embolism or procedure-related bleeding requiring any transfusion of packed red blood cells or surgery.

2.5.2. TORUS 1 STUDY

TORUS 1 is a prospective, single-arm, multi-center, international, non-randomized, premarket study intended to evaluate the safety and effectiveness TORUS Stent Graft in the treatment of atherosclerotic lesions up to 180 mm in length in native superficial femoral artery (SFA) or the superficial femoral and proximal popliteal arteries. A total of sixty (60) Patients have been enrolled to date. Thirty-two (32) patients have had a six-month followup, and twenty-two (22) have had a 12-month follow-up.

The primary safety endpoint is defined as freedom from a major adverse event (MAE) at 30 days post-procedure. An MAE is defined as TLR, amputation of the treated limb or death. The primary effectiveness is defined as stent patency as evidenced by a peak systolic velocity ratio (PSVR) < 2.5 from duplex ultrasound (DUS) obtained within the 12- month visit window with no clinically driven re-intervention within the stented segment.

2.6 RISKS AND BENEFITS

2.6.1. RISKS

As with all procedures that utilize techniques for introducing a catheter into a vessel and a stent implantation into a vessel, complications may occur. These complications include, but are not limited to: access vessel (arterial/venous) occlusion; amputation; aneurysm or pseudoaneurysm; arteriovenous fistula; bleeding complications; death; device or deployment malfunction/failure; drug reactions to antiplatelet agents or contrast medium; embolism (peripheral or pulmonary); fever in absence of infection; hemorrhage or hematoma; hypotension/hypertension; infection, local or systemic, including bacteremia or septicemia; malapposition or migration; malposition; myocardial infarction; pain (insertion site, leg and/or foot); renal insufficiency or failure secondary to contract medium; shock; side branch occlusion; stroke or transient ischemic attack; thrombosis; vessel wall trauma (dissection, perforation or rupture); vessel spasm; venous flow disruption (deep vein thrombosis, phlebitis, leg swelling and/or development of varicose veins); and/or worsening claudication. These are well known and similar to other stent graft devices. All reasonable efforts have been taken to minimize risk for the clinical study in accordance with the applicable regulations, and the risk-benefit ratio is as positive as possible without further clinical data.

Despite our best efforts, however, and the application of relevant standards and scientific knowledge, there may be risks that are unknown due to the investigational nature of the device. To date, there have been no unforeseen risks identified in the clinical investigation. PQ Bypass will continue to evaluate adverse events and device experiences throughout the study and update the risk profile and/or modify the study design as applicable.

2.6.2. BENEFITS

This investigation will allow the Sponsor to collect clinical safety and effectiveness data to support a Premarket Application for a second-to-market stent graft system.

3.0 TRIAL OBJECTIVES

The objectives of the TORUS 2 IDE Clinical Study are to evaluate the safety and effectiveness of the Torus Stent Graft System in patients with femoral popliteal arterial disease. The safety and effectiveness of the TORUS Stent Graft System will be established by comparing the primary safety and effectiveness endpoints to safety and effectiveness Performance Goals (PG).

- The primary safety endpoint will compare freedom from Major Adverse Event (MAE) at 30 days to a safety Performance Goal (PG) derived from literature, including an aggregate of published trial data and the Summary of Safety and Effectiveness Data (SSED) of the PMAs of approved devices.
- The primary effectiveness endpoint will compare primary patency at 12 months to an effectiveness PG derived from literature, including an aggregate of published trial data and the Summary of Safety and Effectiveness Data (SSED) of the PMAs of approved devices.

4.0 SELECTION AND WITHDRAWAL OF PATIENTS

4.1 INCLUSION CRITERIA

All Patients are required to meet the following inclusion criteria in order to be considered eligible for participation in this trial:

Clinical Inclusion Criteria

1. Patient is male or female, with age > 18 and ≤ 90 years at date of enrollment.
2. Patient provides written informed consent before any study-specific investigations or procedures.
3. Patient is willing to undergo all follow-up assessments according to the specified schedule over 36 months.

4. Patient is a suitable candidate for angiography and endovascular intervention and, if required, is eligible for standard surgical repair.
5. Patient has symptomatic peripheral arterial disease (PAD) of the lower extremities requiring intervention to relieve de novo obstruction or occlusion or restenosis of the native femoropopliteal artery.
6. Patient has PAD classified as Rutherford classification 2, 3 or 4.
7. Patient has documented PAD by either (i) a resting ankle-brachial index (ABI) of ≤ 0.90 (or ≤ 0.75 after exercise of the target limb). Resting toe brachial index (TBI) is performed only if unable to reliably assess ABI. TBI must be <0.70; or (ii) Normal ABI with angiographic,ultrasound, MRA, or CT evidence of ≥ 60% diameter stenosis.

Angiographic Inclusion Criteria

8. Patient has single or multiple stenotic, restenotic or occlusive lesions within the native femoropopliteal artery ("target lesions") that can be crossed with a guidewire and fully dilated.
9. Single target lesion must be covered by a single stent. Tandem target lesions are considered a single continuous lesion if the gap between lesions is ≤ 5 cm and > 30% diameter stenosis between the lesion(s).
10. Target lesion(s) eligible for treatment under the protocol are at least least 3 cm above the bottom of the femur.
11. Target lesion(s) reference vessel diameter is between 5.0 mm and 6.7 mm by operator's visual estimate.
12. Target lesions measure ≥ 80 mm to ≤ 180 mm in overall length, with ≥ 60% diameter stenosis by operator's visual estimate. Tandem target lesions are considered a single continuous lesion if the gap between lesions is ≤ 5 cm and > 30% diameter stenosis between the lesion(s).
13. Patient has a patent popliteal artery (no stenosis ≥ 50%) distal to the treated segment.
14. Patient has at least one patent infrapopliteal vessel (< 50% stenosis) with run-off to the ankle.

4.2 EXCLUSION CRITERIA

Patients will be excluded from participating in this trial if they meet any of the following exclusion criteria:

Clinical Exclusion Criteria

1. Patient is unable or is unwilling to comply with the procedural requirements of the study protocol or will have difficulty in complying with the requirements for attending follow-up visits.

2. Patient has a comorbidity that in the investigator's opinion would limit life expectancy to less than 12 months.

3. Patient has any planned major surgical procedure (including any amputation of the target limb) within 30 days after the index procedure for this study.

4. Patient has a target vessel that has been treated with any type of surgical procedure prior to enrollment.

5. Patient has a target vessel that has been treated with bypass surgery.

6. Patient has PAD classified as Rutherford classification 0, 1, 5 or 6.

7. Patient has known or suspected active systemic infection at the time of enrollment.

8. Patient has a known coagulopathy or has bleeding diatheses, thrombocytopenia with platelet count less than 100,000/microliter or INR (international normalized ratio) >1.8.

9. Patient has a stroke diagnosis within three months prior to enrollment.

10. Patient has a history of unstable angina or myocardial infarction within 60 days prior to enrollment.

11. Patient has a contraindication to antiplatelet, anticoagulant or thrombolytic therapies.

12. Patient has known allergy to contrast agents or medications used to perform endovascular intervention that cannot be adequately pre-medicated.

13. Patient has known allergy to titanium, nickel or tantalum (does not include mild contact dermatitis due to nickel allergy).

14. Patient has received thrombolysis within 72 hours prior to the index procedure.

15. Patient has acute or chronic renal disease (e.g., as measured by a serum creatinine of > 2.5 mg/dL or > 220 µmol/L or GFR < 30 ml/min), or on peritoneal or hemodialysis.

16. Patient requiring coronary intervention within seven days prior to enrollment.

17. Patient is pregnant or breast-feeding.

18. Patient is participating in another research study involving an investigational product (pharmaceutical, biologic or medical device).

19. Patient has other medical, social or psychological problems that, in the opinion of the investigator, preclude them from receiving this treatment, and the procedures and evaluations pre- and post-treatment.

Angiographic Exclusion Criteria

20. Patient has significant disease or obstruction (≥ 50%) of the inflow tract that has not been successfully treated at the time of the index procedure (success measured as ≤ 30% residual stenosis, without complication).
21. Patient has no patent (≥ 50% stenosis) outflow vessel providing run-off to the ankle.
22. There is a lack of full expansion in the predilatation balloon.
23. Evidence of aneurysm or acute thrombus in target vessel.

4.3 WITHDRAWAL OF PATIENTS

Each Patient may voluntarily withdraw his/her participation from the study at any time without jeopardy or prejudice. If a Patient prematurely terminates from the study, the reason for study termination will be recorded and the results will be tabulated by number and percent for each category. If termination is a result of an adverse event or death, an Adverse Event Form will also be completed. Patients who withdraw consent after treatment will have their data evaluated until the time of their withdrawal.

The Investigator should follow all unresolved serious adverse events until the events are resolved, the Patient is lost to follow-up, the Patient has withdrawn consent, the Patient completes the study, or the adverse event is otherwise explained.

All reasonable efforts will be made to obtain complete data for all Patients; however, missing observations will occur due to loss to follow-up, withdrawal, or non-adherence with required assessments. Three attempts shall be made to contact Patients who do not return for study follow-up visits. The final attempt shall include a certified letter to the Patient regarding study participation. If these Patients cannot be located, they will be considered lost to follow-up. If they are contacted but refuse to return for visits, they will be considered withdrawals. If they actively request to withdraw from the study, they will be considered withdrawals. Patients shall be encouraged to complete a final study exit visit at the time of withdrawal to assess for safety. Data collected up to the time of loss to follow-up or withdrawal will be maintained in the study database and used for analysis purposes, as appropriate. These Patients will not be replaced.

5.0 TRIAL DESIGN

5.1 DESCRIPTION OF TRIAL DESIGN

The design of the study is a global, prospective, single-arm, multi-center, clinical investigation to evaluate the safety and effectiveness of the Torus Stent Graft System in the treatment of obstructive atherosclerotic lesions of the native SFA or the superficial femoral and/or proximal popliteal arteries.

5.2 TRIAL ENDPOINTS

5.2.1. PRIMARY EFFECTIVENESS ENDPOINT

Primary patency at 12-months which is defined as the absence of clinically-driven target lesion revascularization (CD-TLR) and absence of recurrent target lesion diameter stenosis >50% by duplex ultrasound with a peak systolic velocity ratio of >2.5.

5.2.2. PRIMARY SAFETY ENDPOINT

Freedom from a major adverse event (MAE) at 30 days post-procedure defined as any occurrence of the following events: all-cause death, target limb major amputation and clinically-driven target lesion revascularization (CD-TLR).

5.2.3. SECONDARY ENDPOINTS

Secondary endpoints are defined as the following:

- Technical Success defined as the ability to cross and dilate the lesion to achieve residual stenosis of ≤30%.
- Procedural Success defined as technical success with out any MAEs within 24 hours of the procedure.
- MAE rate at 12 months post-index procedure, defined as a composite rate of all-cause death, target limb major amputation and clinically-driven target lesion revascularization (CD-TLR).
- Patency rate through 36 months (absence of CD-TLR and absence of recurrent target lesion diameter stenosis >50% by duplex ultrasound with a peak systolic velocity ratio of >2.5).
- Assisted Primary Patency rate through 36 months (revascularization of non-occlusive (<99%) stenosis within the stent graft or immediately above or below the treated arterial segment (end of the graft and 1cm of artery beyond) with less than 50% residual stenosis.
- Secondary Patency rate through 36 months (revascularization of occlusion (100%) within the stent graft or immediately above or below the treated arterial segment (end of the graft and 1cm of artery beyond) with less than 50% residual stenosis.
- Alternative Patency rate through 36 months (patency of target vessel based on systolic velocity ratio ≤ 2.0 and absence of CD-TLR).
- Walking Improvement assessed by the Walking Impairment Questionnaire (WIQ) from pre-procedure to 1, 6 and 12 months.

- Improved Quality of Life assessed by the EQ5D from pre-procedure to 1, 6, and 12 months.
- Rate of TLR through 36 months.
- Rate of Target Vessel Resvascularization (TVR) through 36 months.
- Rate of major amputation on target limb through 36 months.
- Stent Fracture Rate utilizing VIVA definitions at 12 months.
- Change in ankle-brachial index (ABI), toe pressures and waveforms from pre-procedure through 36 months.
- Change in Rutherford-Becker clinical classification from pre-procedure through 36 months.
- Adverse event rates through 36 months.

5.3 INVESTIGATIONAL SITES

The clinical study will be conducted at up to 40 investional sites in North America and Europe.

A single investigational site shall not enroll more that 20% of the total planned trial population (i.e., 37 patients) without the prior written approval of the Sponsor.

At least 50% of the enrolled patients will be enrolled in the United States for this study.

5.4 DURATION OF PATIENT PARTICIPATION

Patients enrolled in the trial will participate for approximately 36 months (3 years).

5.5 EARLY STUDY TERMINATION

PQ Bypass reserves the right to terminate the study at any time, but intends only to exercise this right for valid scientific or administrative reasons related to protection of patients. Investigators, IRB/IECs and CA will be notified in writing in the event of termination.

Possible reasons for study termination include:

- The discovery of an unexpected, significant, or unacceptable risk to the patients enrolled in the study
- A decision on the part of PQ Bypass to suspend or discontinue development of the device

5.6 WRITTEN INFORMED CONSENT

Patients who meet general and clincal entry criteria will be asked to sign the study specific IRB/IEC approved Informed Consent Form(s) (**Appendix I**) before any study-specific tests or procedures are performed. Study personnel should explain that even if a patient agrees

to participate in the study and signs an Informed Consent Form, the patient may not be eligible to participate if he/she fails screening criteria.

5.7 ENROLLMENT

Patients who are consented and meet all the study inclusion criteria and none of the study exclusion criteria, arterial access has been achived and study device advanced beyond the sheath will be considered enrolled into the study. Patient eligibility will be confirmed prior to insertion of the study device, based on procedural angiogram and sheath placement.

Therefore, the enrollment date (Day 0) will be the date of the study index procedure; the enrollment date will not be the date of informed consent for this study. Patients in whom the TORUS Stent Graft System is inserted into the vascular and/or the procedure was aborted without treatment with the device shall be followed through discharge for safety only and allowed to exit the study.

5.8 STUDY PROCEDURES

Patients will return to the investigational site at 1 month (30 days ±7 days), 6 months (180 days ±30 days), 12 months (360 days ±30 days), 24 months (720 days ±60 days), and 36 months (1080 days ±60 days) following the procedure for a follow-up evaluation. The Patient will have a clinical examination, undergo lower-extremity arterial duplex ultrasounds, complete QOL surveys and evaluated for any post-procedural complications or adverse events.

5.8.1. INITIAL ELIGIBILITY

After Patients have signed an informed consent form and before the scheduled interventional procedure, patients will undergo an initial eligibility evaluation by the investigator. Medical history and imaging performed within the previous 180 days may be used for this initial eligibility evaluation. The evaluation shall consist of the following:

- Pre-procedural imaging
- Review of inclusion/exclusion criteria

Pre-procedure imaging studies shall be reviewed to assess patient eligibility. This process may be done in collaboration with the sponsor, site investigators, core lab assessment, medical advisory committee, etc. in an effort to assist the investigational sites in eligibility requirements.

5.8.2. BASELINE EVALUATION

Patients will undergo a baseline evaluation. This evaluation may be conducted from an office visit within the previous 30 days. The evaluation will consist of the following:

- Review of inclusion/exclusion criteria
- Medical history and demographic data
- Physical examination & health status
- Laboratory Tests
- eGFR
- Ankle Brachial Index or Toe-Brachial Index
- Rutherford clinical category
- Medication history & review (anti-platelet/ anti-coagulation therapy)
- WIQ
- EQ-5D

5.8.3. Vascular Access, Guidewire Delivery and Stent Graft Placement

Investigators will access the target lesion using standard percutaneous techniques and devices. Patient eligibility will be confirmed prior to insertion of the study device, based on procedural imaging and sheath placement. TORUS Stent Grafts of appropriate dimension are selected based on the instructions provided in the TORUS Stent Graft System IFU (**Appendix II**).

5.8.4. Anticoagulation and Antiplatelet Therapy

Effective anticoagulation therapy should be maintained throughout the procedure with heparin (per hospital or institutional standards, recommending a minimum of ACT >250 seconds) or a clinically acceptable alternative of the treating physician's choice. Patients must be treated with antiplatelet and/or anticoagulation through 12 months and then continued per physician/institutional standards of care. .

Table 5 shows the recommendation for administration these medications, but the final decision is up to the operator and may include other antiplatelet or anticoagulation agents not identified.

Antiplatelet medication usage will be collected and reported for compliance for the duration of the trial.

Table 5: Administration of Anticoagulations and Dual Antiplatelet Medications

Medication	Peri-Procedure (< 24 hours of Index Procedure)	Intra-Procedure	Post-Procedure
Aspirin	Minimum loading dose of 81mg required, if not on long-term aspirin therapy	N/A	A minimum of 81 mg per day indefinitely

Clopidogrel * (or similar antiplatelet agent or alternative agent per investigator discretion)	Minimum loading dose of 300-600 mg required, if not on long-term clopidogrel therapy; maybe given within 2 hours after the end of procedure.	N/A	Clopidogrel 75 mg per day for a minimum of 12 months (or per prescribing dose if other similar antiplatelet agent or alternative agent per investigator discretion)
Heparin / Bivalirudin	N/A	Maintain anticoagulation per hospital / institution standard of care (minimum of ACT >250 sec recommended)	N/A

** For patients requiring anticoagulation therapy (NOAC or OAC), antiplatelet monotherapy with either aspirin or clopidogrel for 1 year, followed by aspirin therapy or other anti-coagulant indefinitely is recommended, using investigator discretion for the best interest and safety of the subject.*

5.8.5. PROCEDURAL EVALUATION

Final eligibility will be determined based on imaging study and sheath placement. Information on the lesion being treated and the specific vasculature used in its treatment will be collected. The procedural evaluation and data collection will consist of the following:

- Review of angiographic inclusion/exclusion criteria
- Lesion characteristics
- Access sites used
- Anticoagulation
- Procedure time and floroscopy time
- Contrast volumes
- Study device Information
- Ancillary device information (e.g. balloons, closure devices etc)
- Adverse events and device malfunctions

5.8.6. DISCHARGE EVALUATION

The discharge evaluation will consist of:

- Physical examination and health status
- Anticoagulation and Antiplatelet Medications
- Adverse event assessment

5.8.7. FOLLOW-UP EVALUATIONS

Patients will return to the investigational site for follow-up evaluations at 1 month (30 days ±7 days), 6 months (180 days ±30 days), 12 months (360 days ±30days), 24 months (720 days ±60 days), and 36 months (1080 days ±60 days) post-index procedure. Follow-up evaluations will include:

- Physical examination and health status
- Ankle-Brachial Index/Toe-Brachial Index
- Rutherford score
- Arterial duplex-ultrasound assessment
- Stent Graft X-ray (12 months) in US subjects only.
- Antiplatelet and Anticoagulations Medications
- WIQ (Baseline, 1, 6, 12 months)
- EQ5D (Baseline, 1, 6, 12 months)
- Adverse event assessment

5.8.8. PATIENT LOST TO FOLLOW-UP

A Patient will be considered lost to follow-up and terminated from the study when all of the following criteria have been met:

- Two consecutive study visits missed with supporting documentation of three unsuccessful attempts on three different days over a period of three (3) months at both study visits by the Investigator or his/her designee to contact the patient or next of kin, one of which should be by certified mail with signature confirmation.
- Prior agreement of the Sponsor to remove the patient from the clinical investigation.

5.9 STATISTICS

5.9.1. STATISTICAL HYPOTHESES AND SAMPLE SIZE JUSTIFICATION

There are two primary hypotheses for the study. One is primary patency through 12 months for the primary effectiveness endpoint and the other is freedom from major adverse events (MAE) through 30 days for the primary safety endpoint.

Study sample size is calculated based on formal power calculations for the primary endpoint hypothesis tests. The target power for the primary endpoints is 90%, with

type I error controlled by conducting analyses at a one-sided 2.5% alpha level (equivalent to a two-sided 5% alpha level).

Based on historical published data, the 12 month primary patency rate is estimated at 70%. Therefore, the primary effectiveness endpoint hypothesis test under the expected primary patency rate of 70% against a PG of 57% results in a total evaluable sample size of 159. Accounting for an attrition rate of up to 15% for loss to follow-up or missing endpoint data at 12 months results in an effectiveness sample size requirement of 188. This sample size accounts for the planned group-sequential exact binomial interim analyses described in Section 5.9.2 below.

Based on historical rates of death, TVR or amputations reported in published literature, a conservative assumption for the 30-day MAE rate is given by the sum of the historical rates yielding an estimated rate of 3.5%. The expected rate would be anticipated to be lower than 3.5% since this historical rate includes TVR, which is a broader event category than CD-TLR. Additionally, summing the event rates does not account for the events not being mutually exclusive. For example, a patient that experiences both TVR and amputation would be counted twice when adding the rate of TVR and amputation, leading to an over-estimate of the expected MAE rate.

For primary safety, based on the estimated expected MAE rate through 30 days of 3.5%, the freedom from MAE rate is 96.5%. The 30-day freedom from MAE rate is compared against a PG of 88.0% resulting in an evaluable sample size of 106 based on a single exact binomial analysis with one-sided alpha of 2.5% and power of at least 90%.

Taking the larger of the required sample sizes for the primary effectiveness and safety endpoints results in a final sample size required for enrollment of 188.

5.9.2. PRIMARY EFFECTIVENESS ANALYSES

The primary effectiveness endpoint is primary patency at 12-months defined as the absence of clinically-driven target lesion revascularization (CD-TLR) and absence of recurrent target lesion diameter stenosis >50% by duplex ultrasound with a peak systolic velocity ratio of >2.5.

The statistical hypothesis test for the primary effectiveness endpoint is:

Ho: $p^{effectiveness} \leq 57\%$

Ha: $p^{effectiveness} > 57\%$

where $p^{effectiveness}$ is the primary patency rate at 12 months, and 57% is the pre-specified performance goal (PG). The hypothesis will be evaluated with an exact binomial test including all patients with demonstrated lack of primary patency through 12 months or with follow-up through 12-month duplex ultrasound assessment in the denominator.

The PG for this endpoint is based on the 12 month primary patency PG published by VIVA Physicians, Inc in 2007[7] (VIVA). In this publication, the observed 28% patency rate for the percutaneous balloon angioplasty (PTA) control arm from the three combined PMA trials and the 37% PTA patency rate from the literature analysis yielded a combined patency rate of 33% in lesion lengths ranging from 4 to 15 cm. The observed PTA patency rate for lesions between 6.6 cm to 15 cm was 28% (16/57).

Applying the rule employed by VIVA that the stent PG be twice that of the observed PTA patency rate, the stent PG would be 56%. To ensure consistency with PGs established for similar devices and patient populations, the 12 month primary patency PG is defined as 57%.

A group sequential efficacy analysis will be utilized for the primary effectiveness endpoint with an interim analysis performed once 75% of the study patients have been enrolled and completed 12-month followup. Alpha spending for an additional interim analysis at 30 patients (TORUS 1 patients) is accounted for, but endpoint success will not be declared based on this analysis regardless of results. The group-sequential analysis uses nominal p-value boundaries defined by a Hwang-Shih-DeCani spending function (gamma = -6).

Table 6: Group-Sequential Interim and Final Analysis Success Criteria

Sample Size	Information Fraction	Nominal p-value	Alpha Spending	Post 15% attrition	Minimum Observed Rate
30	16%	0.0001	<0.0001	25	N/A
141	75%	0.0055	0.0051	119	68.9%
188	100%	0.0239	0.0149	159	65.4%
		Total:	0.0201 (one-sided)		

[7]Rocha-Singh, K.J., et al., Performance goals and endpoint assessments for clinical trials of femoropopliteal bare nitinol stents in patients with symptomatic peripheral arterial disease. [with editorial comment]. Catheterization & Cardiovascular Interventions, 2007. 69(6): p. 910-9

Based on the above table, the 75% interim analysis will be performed when 141 patients have been enrolled and completed 12 months of follow-up. Based on an assumed attrition rate of 15%, 119 patients are anticipated for the interim analysis. If 119 patients are analyzed at the interim analysis, the minimum observed rate to meet the PG for this effectiveness analysis is an 68.9% patency at 12 months. If both the primary effectiveness endpoint and primary safety endpoint are met at this interim analysis, the data will be prepared and submitted to the FDA. If the primary effectiveness endpoint is not met at this interim analysis, the final primary effectiveness and safety endpoint analyses will be performed when all patients have been enrolled and completed 12-month follow-up. The minimum observed

12-month primary patentcy rate to meet the performance goal at the final analysis is 65.4% based on an assumed sample size of 159.

5.9.3. PRIMARY SAFETY ANALYSES

The primary safety endpoint is freedom from a major adverse event (MAE) at 30 days post-procedure defined as any occurrence of the following events: all-cause death, target limb major amputation and clinically-driven target lesion revascularization (CD-TLR).

The statistical hypothesis test for the primary safety endpoint is:

Ho: $p^{safety} \leq 88\%$
Ha: $p^{safety} > 88\%$

where p^{safety} is the freedrom from MAE event rate at 30 days and 88% is the pre-specified performance goal (PG). The hypothesis will be evaluated with an exact binomial test including all patients with an MAE or with follow-up through 30 days in the denominator.

The primary safety performance goal of 88% is based on the historical one-sided 95% confidence interval for the 30-day MAE rate published by VIVA.

The primary safety endpoint hypothesis test will be conducted at the 75% interim analysis if the primary effectiveness analysis is met at that interim analysis, since more than the 106 patients required to achieve 90% power will have at least 30 days of follow-up. Otherwise the primary safety endpoint hypothesis test will be conducted at the final analysis. Type I error for the primary safety endpoint analysis is preserved at 2.5% (one-sided) since the analysis is only performed once with the timing determined by the primary effectiveness analysis results.

If the primary safety endpoint is evaluated with 141 patients, the minimum observed 30-day freedom from MAE rate to meet the performance goal is 93.6%. If the primary safety endpoint is evaluated with 188 patients, the minimum observed 30-day freedom from MAE rate to meet the performance goal is 93.1%.

5.9.4. SECONDARY ENDPOINTS AND ADDITIONAL ANALYSES

Secondary and additional analyses will be purely descriptive and are intended solely as supporting analyses. No hypotheses will be tested for secondary endpoints or additional analyses.

5.9.5. ANALYSIS SETS

The study will use intention-to-treat (ITT), modified intention-to-treat (mITT) and per-protocol (PP) analysis sets. The primary endpoint hypotheses will be

conducted based on the modified intention-to-treat analysis set in which patient endpoint outcomes are known. Sensitivity analyses will be performed to account for missing data and explore hypothetical outcomes in the ITT analysis set. Analyses of the PP analysis set will serve as additional sensitivity analyses to explore the impact of protocol non-compliance on primary study endpoints.

Table 7: Analysis Set Definitions

Analysis Set	Definition
ITT	All enrolled patients.
mITT	Subset of ITT set where primary safety and efficacy status are known. For primary safety endpoint, includes all ITT patients evaluated at 30 days post-procedure or with failure prior to 30 days. For primary efficacy endpoint, includes all ITT patients with 12 month duplex ultrasound obtained within the 12 month window or with failure prior to 12 months.
PP	Subset of mITT not found in violation of any inclusion or exclusion criteria post-procedure.

5.9.6. SUBGROUP ANALYSES

A multivariable logistic regression model will be fit with independent variables (unique for safety and effectiveness analyses) for the subgroup levels as well as additional baseline characteristics. Separate sets of baseline characteristics to be included in subgroup logistic regression models will be defined for safety and effectiveness analyses.

With respect to the primary endpoints, the following baseline characteristics will be analyzed as subgroups:

- Gender
- History of diabetes
- Lesion length (cm)
- Rutherford classification

5.9.7. GENERAL STATISTICAL CONSIDERATIONS

Demographic, baseline clinical and disease characteristics and procedural results will be summarized in tables. For continuous variables, the summary will include the number, mean, median, standard deviation, minimum and maximum. Summaries for categorical

variables will include the number and percent of patients in each category. Confidence intervals may be presented, where appropriate, using the t-distribution for continuous data and the Exact binomial method for categorical variables. Statistical analyses will be performed using SAS version 9.4 or higher or other validated statistical software.

Additional analysis specifications and considerations will be documented in a separate Statistical Analysis Plan.

6.0 SPONSOR RESPONSIBLITIES

As the Sponsor of this clinical study, PQ Bypass has the overall responsibility for the conduct of the study, including assurance that the study meets the regulatory requirements of the Food and Drug Administration (FDA) and ISO 14155:2011 (Section 8 – OUS sites only). In this study, PQ Bypass will have certain direct responsibilities and will delegate other responsibilities to Independent Contractors. Together, both PQ Bypass and its Independent Contractors will ensure adherence to the sponsor's general duties (21 CFR 812.40; ISO 14155:2011 Section 8), selection of Investigators (21 CFR 812.43; ISO 14155:2011 Section 8.2.1), monitoring (21 CFR 812.46; ISO 14155:2011 Section 8.2.4.2), supplemental applications (21 CFR 812.35 (a) and (b)), record maintenance (21 CFR 812.140 (b)), and report submissions (21 CFR 812.150 (b)).

6.1 GENERAL DUTIES

(21 CFR 812.40; ISO 14155:2011 Section 8)

The Sponsor's general duties consist of submitting the IDE application to FDA, submitting the Investigational Plan to other applicable national regulatory agencies (as applicable), obtaining FDA, other national regulatory (as applicable) and IRB / EC approvals prior to shipping the devices, selecting qualified Investigators, and shipping devices only to those qualified Investigators. As the sponsor, PQ Bypass is also required to obtain signed study agreements, to provide the Investigators with the information necessary to conduct the study and adequate on-site training to conduct the trial, to ensure proper investigational site monitoring, and to provide the required reports to the Investigators, IRBs / ECs, other national regulatory agencies (as applicable), and FDA.

PQ Bypass will be responsible for providing quality data that satisfies federal regulations and informing about serious unanticipated adverse events and deviations from the protocol. Written progress reports and a final report will be prepared in coordination with the Ultrasound, Angiographic and X-Ray Core Laboratories. The final clinical report will be prepared at the conclusion of the trial and copies will be provided to each investigator and to the respective IRBs/ECs.

6.2 SELECTION OF INVESTIGATIONAL SITES & INVESTIGATORS

(21 CFR 812.43; ISO 14155:2011 Section 8.2.1)

PQ Bypass will select qualified investigational sites and Investigators who are experienced with percutaneous transluminal angioplasty and peripheral stenting. The Investigator must work with a qualified IRB / IEC to oversee the rights, safety and welfare of the study participants. The investigational site must also have an adequate patient population and the appropriate staffing and equipment to meet the requirements of the study protocol and the expected enrollment time frames.

6.3 MONITORING

(21 CFR 812.46; ISO 14155:2011 Section 8.2.4.2)

PQ Bypass shall designate a CRO to monitor and oversee the conduct of the TORUS 2 IDE Clinical Study. The Sponsor and/or CRO designee will conduct investigational site monitoring to ensure that all Investigators are in compliance with the Protocol and the Investigators' agreements. The Sponsor and/or CRO designee will monitor the investigational sites to ensure that the completed eCRFs are in agreement with the source documentation and other records, and resolve any differences. Periodic phone contacts and investigational site visits will be conducted to ensure that the Protocol is being followed.

For record verification purposes, the clinical monitor and/or authorized Sponsor representative shall be provided access to hospital records, original laboratory data, and other records and data as they relate to the study and as agreed to with the Investigator prior to the initiation of the trial. The Investigator will also make available to the clinical monitor all regulatory documents, all completed eCRFs, informed consent documents, source documentation and other relevant records for all enrolled patients at the investigational site. It is important that the Investigator and other relevant site personnel are available for consultation with the clinical monitor during the monitoring visits and that sufficient time is devoted at the site to the monitoring process.

If the Sponsor and/or their authorized representative become aware that an Investigator is not complying with the study protocol, the Investigator Agreement, Good Clinical Practices, applicable privacy standards, or any condition of the study imposed by the IRB/IEC, the Sponsor or their authorized representative may immediately secure compliance or discontinue further shipments of the study devices. An inability to secure compliance and/or to complete an investigation into the factors that are inhibiting compliance may result in the Investigator's termination from the study by the Sponsor.

The Sponsor will review significant new information, including unanticipated serious adverse events and ensure that such information is provided to the FDA, other national regulatory agencies (as applicable), the Investigators, and to all reviewing IRB/IECs.

Study close-out visits will be conducted after the final follow-up visit is completed at each investigational site following the resolution of any outstanding data discrepancies and adverse events. The remaining study devices will be the collected and returned to the Sponsor on or before the close out visit. A final study report will be generated and submitted to the Investigator and the appropriate study oversight authorities. Study document retention requirements will be reviewed with each investigational site during the close-out visit.

6.4 Investigational Site Termination

The Sponsor reserves the right to terminate an investigational site from the Study for any of the following reasons:

- Failure to obtain Informed Consent.
- Failure to report Serious Adverse Events within 48 hours of knowledge.
- Loss of or unaccountable device inventory.
- Repeated Protocol violations or safety concerns.
- Repeated failure to complete Case Report Forms.
- Failure to enroll an adequate number of patients

6.5 Informed Consent & Institutional Review Board (IRB) / Independent Ethics Committee (IEC)

(21 CFR Parts 50 & 56; ISO 14155:2011 Section 4)

All patients must provide written informed consent in accordance with the local investigational site's IRB/IEC. A copy of the consent form from each investigational site must be forwarded to the Sponsor for review and approval prior to submitting it to the IRB/IEC. Each investigational site must provide the Sponsor with a copy of the clinical site's IRB/IEC approval letter and the informed consent. Continuing review (e.g., institutional annual review) approvals for the continuation of the trial at each investigational site must also be forwarded to the Sponsor, as applicable.

All Protected Health Information (PHI) to be collected in the study will be described in the informed consent form, and all study data will be managed in accordance with the Privacy Law (HIPAA) or international privacy regulations (GDPR), as applicable.

6.6 Records & Record Retention

(21 CRF 812.140 (b) & (d))

The Sponsor and/or their designated CRO will maintain copies of correspondence, data, device shipments, clinical events (AEs, SAEs, MAEs) and supporting documentation and other records and reports related to this clinical study.

The Sponsor, core laboratories and investigational sites will maintain the TORUS 2 study records until two (2) years after the final study report is completed, or longer if required by local, national or international regulatory agencies. The Sponsor will notify each investigational site regarding the regulatory requirements for record retention during the study close-out visit.

6.7 STUDY REPORTS

(21 CFR 812.150(b))

All information and data generated in association with the study will be held in strict confidence and remains the sole property of the Sponsor. The Investigator agrees to use this information for the sole purpose of completing the study and for no other purpose without prior approval of the Sponsor.

The Sponsor will submit the required FDA reports identified in this section of the regulation. This includes unanticipated serious adverse device effects, withdrawal of IRB/IEC or FDA approval, current 6-month Investigators list, annual progress reports, recall information, final reports, investigators that use the device without obtaining informed consent, and significant risk device determinations.

Upon receipt of the final study data and the final reports from each investigational site, the Sponsor will complete a final study report. Copies of the final report will be provided to each Investigator.

6.8 SUPPLEMENTAL APPLICATIONS

(21 CFR 812.35)

As appropriate, the Sponsor will submit changes to the study Protocol for national approval and subsequently to the Investigators to obtain IRB/IEC approval.

7.0 QUALITY ASSURANCE & ETHICAL STANDARDS

7.1 TRIAL CONDUCT

The trial will be performed in accordance with the relevant parts of the Code of Federal Regulations, ICH Guidelines for Good Clinical Practices, the European Standard ISO 14155:2011 (OUS sites only), the Declaration of Helsinki, and any regional and/or national regulations. As the study Sponsor, PQ Bypass, has the overall responsibility for the conduct of the study, including the assurance that the study is in compliance with these guidelines, standards and requirements.

7.2 INSTITUTIONAL REVIEW BOARDS / INDEPENDENT ETHICS COMMITTEES

Before any patient can be enrolled in this trial, the IRB or IEC for the specific institution must review and approve the protocol and the Informed Consent Form to be used. A patient cannot be asked to sign the Informed Consent Form until the trial has been fully approved by the institution's IRB/IEC. A copy of the study Protocol, proposed Informed Consent form, other written patient information and any proposed advertising material must be submitted to the IRB/IEC for written approval. The Sponsor or their designated CRO will require a copy of any IRB/IEC correspondence, as well as the final IRB/IEC approval letter and the final IRB/IEC approved Informed Consent Form and approvals for protocol and ICF revisions on amendments from each IRB/IEC before recruitment of patients into the study and shipment of investigational product.

The Investigator must submit and, where necessary, obtain approval from the IRB/IEC as well as the FDA, for all subsequent significant protocol amendments and significant changes to the Informed Consent form. The Investigator should notify the IRB/EC of deviations from the protocol or SAEs and UADEs occurring at the investigational site and other SAE/UADE reports received from PQ Bypass in accordance with local procedures.

The Investigator will be responsible for obtaining annual IRB/IEC approval and renewal throughout the duration of the study. Copies of the Investigator's reports and the IRB/IEC continuance of approval must be sent to PQ Bypass.

7.3 INFORMED CONSENT

A sample Informed Consent form template shall be provided to the Investigator to use to prepare for use at his/her investigational site. The written Informed Consent documents should be prepared in the language(s) of the potential patient population.

The reviewing IRB/IEC and the sponsor must first approve the Informed Consent forms that are used. The Informed Consent forms that are used should be in accordance with the current guidelines as outlined by the FDA Regulations, GCP guidelines, Declaration of Helsinki, and ISO Standards (OUS sites only).

Prior to participation in the clinical trial, each patient must give written Informed Consent after the context of the study has been fully explained to the patient in language that is easily understood by the patient. The patients must also be given the opportunity to read the consent, ask questions, and have those questions answered to their satisfaction.

Written Informed Consent must be recorded appropriately by means of the patient's dated signature. The patient will receive a copy of the Informed Consent form.

7.4 PROTOCOL AMENDMENTS

An Investigator may not make changes to this protocol without prior approval by the Sponsor. All significant changes to the protocol that may affect the following must be submitted and approved by the FDA before initiating the change:

- Validity of the data or information resulting from the completion of the approved protocol.
- Relationship of the likely patient risk to benefit relied upon to approve the protocol.
- Scientific soundness of the investigational plan.
- Rights, safety, or welfare of the human patients involved in the investigation.

Any such change to the protocol must be approved by the FDA and submitted and subsequently approved by the investigational site IRB/IEC. PQ Bypass will submit a copy of the protocol amendment to all Investigators for their IRB/IECs to review and ensure the study continues to be conducted consistently across all investigational sites. The investigational sites must send PQ Bypass a copy of the IRB/IEC approval letter for the protocol amendment.

PQ Bypass may make certain administrative changes to the protocol without prior approval of the FDA or IRB/IEC. PQ Bypass will notify all investigational sites of such changes to ensure the study continues to be conducted consistently across all sites. The investigational site IRB/IECs will be notified of these changes.

7.5 EMERGENCY ACTIONS

PQ Bypass accepts the right of the Investigator to deviate from the protocol in an emergency when necessary to safeguard the life or the physical well-being of a study patient. The Investigator must give notice of any emergency deviations and justification for the deviation to PQ Bypass and the IRB/IEC as quickly as possible after the episode, in any event no later than 24 hours after the emergency.

Emergency Use of the investigational device is not permitted in this study.

7.6 DEVIATIONS FROM THE INVESTIGATIONAL PLAN

A protocol deviation is defined as an event where the Investigator or investigational site personnel did not conduct the study according to the protocol.

Investigators shall be required to obtain prior approval from PQ Bypass before knowingly deviating from the protocol, except where necessary to protect the life or physical well-being of a patient in an emergency. Such approval shall be documented in writing and maintained in clinical study management and Investigator files. Prior approval is generally not expected in situations where unforeseen circumstances are beyond the Investigator's

control, (e.g., patient was not available for scheduled follow-up office visit, blood sample lost by laboratory, etc.); however, the event is still considered a deviation and will be reported via the appropriate CRF.

Deviations must be reported to PQ Bypass regardless of whether medically justifiable, pre-approved by PQ Bypass or taken to protect the patient in an emergency. Patient specific deviations will be reported on the Protocol Deviation case report form. Non-patient specific deviations, (e.g., unauthorized use of an investigational device outside the study, unauthorized use of an investigational device by a physician who has not signed an Investigator agreement or not been trained in the use of the device, etc.), will be reported to PQ Bypass. Investigators will also adhere to procedures for reporting study deviations to their EC and CA, where required, in accordance with their specific reporting policies and procedures.

Regulations require that Investigators maintain accurate, complete and current records, including documents showing the dates of and reasons for each deviation from the protocol.

7.7 INVESTIGATOR & STAFF TRAINING

To ensure accurate, complete and reliable data, the Sponsor or its representatives will provide instructional material to the investigational sites, as appropriate; instruct the investigators and study personnel on the protocol, the completion of the CRFs, and study procedures; communicate regularly with site personnel via mail, email, telephone, and/or fax; and make periodic monitoring visits to the site. During those visits, the Sponsor or its representatives will monitor the patient data recorded in the CRFs against the source documents at the investigational site.

All participating investigators will be trained in the use of the TORUS Stent Graft System prior to participating in the study. TORUS Stent Graft System training will be conducted by the Sponsor or its representatives. All device training will be documented in a training log that will be maintained in the investigational site regulatory binder.

Procedural technique and experience with the TORUS Stent Graft System may be assessed by clinical/engineering personnel. Observations during the cases will also be discussed with the Investigator and study staff.

7.8 AUDITS AND INSPECTIONS

The principal investigator will also allow representatives of the governing IRB or IEC, the U.S. Food and Drug Administration (FDA), and other applicable regulatory agencies to inspect all study records, CRFs, and corresponding portions of the patient's office and/or hospital medical records at regular intervals throughout the trial. These inspections are for the purpose of verifying adherence to the protocol, completeness, and exactness of

the data being entered onto the CRFs and compliance with FDA or other regulatory agency regulations.

The principal investigator will inform the Sponsor or the Sponsor's designee should they be audited or inspected by any regulatory agencies. The Sponsor or the Sponsor's designee will also inform the investigational site if they are made aware of a pending audit or inspection by a regulatory agency.

The Investigator and/or designees must be available to respond to reasonable requests by authorized Sponsor, CRO and regulatory agency representatives during the monitoring and inspection process. The Investigator must provide the Sponsor with copies of all correspondence that may affect the review of the current study (i.e., Inspection Observations) or their qualification as an Investigator in clinical studies conducted by the Sponsor. The Sponsor will provide any needed assistance to the investigational site for regulatory audits, if any.

7.9 MONITORING PROCEDURES

Monitoring visits to the clinical sites will be made periodically during the study, to ensure that all aspects of the current, approved protocol/amendment(s) are followed. Original source documents shall be reviewed for verification of data in the electronic database according to the defined monitoring plan. The Investigator/institution shall make all attempts to grant direct access to original source documents by PQ Bypass personnel, their designees, and appropriate regulatory authorities. It is recognized that all participating institutions may not have procedures for providing access to electronic health records to non-institutional employees. In such situations, the Sponsor and/or designee shall collaborate with the investigator and institution to ensure alternative access to the complete medical record for enrolled patients. In the event that the original medical records cannot be obtained for a patient that is seen by a non-study physician at a non-study institution, photocopies of the original source documents must be made available for review.

Investigational site visits will be conducted to ensure that the protocol is being followed and that any protocol deviations are properly documented. Additionally, telephone and/or e-mail contact will be conducted on a regular basis with the investigator and the investigational site staff to ensure that the protocol is being followed and to address any issues that may occur during the course of the trial. Clinical monitoring will include a verification that Informed Consent was properly obtained for all enrolled trial participants, a review of clinical records for accuracy and completeness, resolution of missing or inconsistent results and a review of source documents. The clinical monitor will verify that the eCRFs are in agreement with the source documentation and other records. The investigator will make available to the clinical monitor for review all Informed Consent documents, Internet access to completed eCRFs, source

documentation, original laboratory data and other relevant records for all enrolled patients at the investigational site. It is important that the investigator and other relevant investigational site personnel are available for consultation with the clinical monitors during the monitoring visits and that sufficient time is devoted at the site to the monitoring process.

If a deficiency is noted during an on-site visit (or at any other time during the course of the trial), the clinical monitor is required to discuss the situation with the investigator and the Sponsor (if required) to secure compliance.

7.10 Investigational Device Distribution and Accountability

7.10.1. Investigational Device Distribution

PQ Bypass will control the distribution of the investigational devices. Each investigational site will be responsible for ordering the investigational devices for the study. The Investigator is responsible for ensuring that the devices are ordered for shipment to arrive at the hospital before the procedure date. Devices will be shipped with an Investigational Device Shipment Record. This form is to be used by PQ Bypass, or distribution designee, and the investigational site to record any shipments of the investigational device. A copy is to be retained by the shipper and the recipient.

7.10.2. Device Accountability

The Investigator shall maintain adequate records of the receipt and disposition of all investigational devices. The Investigator is responsible for ensuring that the investigational devices are used only under the Investigator's supervision and are only used according to this protocol and any approved amendments. The Investigator will not supply an investigational device to any person not authorized to participate in the study. The Investigator shall document in CRFs the lot numbers of the devices used during a case. In addition, the Investigator shall keep complete and accurate records of all devices used or unused that have been returned to PQ Bypass in a Device Accountability Log provided by PQ Bypass.

7.11 Return of Devices

All unused investigational devices will be returned to the study Sponsor upon completion of the clinical study. All used investigational devices will be properly disposed of, per institutional procedures. Any investigational device that fails to perform correctly will be returned to the study Sponsor for analysis. The Investigator or his/her designated representative is responsible for device accountability and disposition of all used and unused devices. The study Sponsor

or its designated representative will conduct device reconciliation at the completion of patient enrollment or at the conclusion of the study.

IMPORTANT: Please note that the devices must be labeled with a "BIOHAZARD" sticker if there is reasonable belief that the device has come in contact with blood or infectious substances that are known or are believed to cause disease in animals or humans.

7.12 CENTRAL CORE LABS – ANGIOGRAPHY, DUPLEX ULTRASOUND AND X-RAY

In order to ensure that the clinical data and images are analyzed in a controlled, non-biased manner and that the results are analyzed using a standardized process, all angiograms, duplex ultrasound studies and X-rays obtained during this study per study requirements will be submitted to central core labs for analysis.

The core labs will be responsible for analyzing the angiograms and ultrasound images according to the study eligibility criteria, the study endpoints and this study protocol. In addition, they will provide feedback to the investigational sites and Sponsor regarding the quality of the tracings and images. The X-ray core lab will be assessing for stent fracture at the applicable study time points. Final written summary reports of all angiograms, X-rays, and duplex ultrasounds will be provided to the study Sponsor.

7.13 COVERAGE OF EXPENSES

The treated patients may receive nominal compensation for participating in the study and may be reimbursed for study specific out-of-pocket expenses (e.g., parking, lodging, etc) and patient to approval by Sponsor and/or IRB/IEC.

7.14 CONFIDENTIALITY

Confidentiality of patients will be maintained throughout the trial. A unique identification code will be assigned to each patient participating in this trial. Any data that may be published in abstracts, scientific journals, or presented at medical meetings will reference a unique Patient code and will not reveal the patient's identity. The Sponsor will make every reasonable effort to protect the confidentiality of all patients participating in the trial.

8.0 INVESTIGATOR RESPONSIBILITIES, RECORDS & REPORTS

The Investigators are responsible for signing the Investigator Agreement (**Appendix III**) prior to the commencement of the study and for ensuring that this trial is conducted according to this study Protocol, GCPs, Declaration of Helsinki, 21 CFR Parts 50, 54, 56 and 812, ISO 14155:2011 (Section 9 – OUS Sites only) and any other local, national or IRB/IEC requirements that apply to Clinical Investigations at their site.

It is also the Investigator's responsibility to ensure that all sub-investigators and staff assisting with this study have the appropriate qualifications and that they complete training on the protocol, investigational devices and study procedures, and that patient confidentiality is respected.

8.1 Informed Consent & Institutional Review Board / Independent Ethics Committee

(21 CFR Parts 50 & 56; ISO 15144:2011 Section 4)

Because this study is collecting medical data from patients providing written informed consent, the Investigator at each investigational site is responsible for securing IRB/IEC approval for this study protocol and the Informed Consent documents. The local IRB/IEC for each specific institution must review and approve this study protocol and the specific Informed Consent form to be used at that investigational site prior to enrollment of the first patient. The Sponsor must also review and approve the final Informed Consent documents prior to their use. The Sponsor must receive a copy of any IRB/IEC correspondence as well as the final approval letter and the final approved Informed Consent from each IRB/IEC.

The Investigator is responsible for ensuring that all applicable local and national (21 CFR Part 50, ISO 14155:2011 – OUS sites only) requirements, and Declaration of Helsinki are met when completing the informed consent process. Written, informed consent is to be obtained for all patients prior to enrollment.

The Investigator or investigational site staff will not make amendments to this Protocol or the Informed Consent form without PRIOR written approval from the Sponsor. All approved amendments must then be submitted to the local IRB/IEC and national authorities, as appropriate for approval.

8.2 Withdrawal of Approval

If the Investigator's IRB or IEC withdraws their approval to conduct this study for any reason, the Investigator must notify the Sponsor as soon as possible, but in no event later than five working days after the withdrawal of the approval.

8.3 Device Accountability

The Sponsor will ship investigational devices to the designated Investigators participating in this study following IRB/IEC approval. All Investigators will be responsible for providing a secure storage location for the devices, supervising device use, and the disposal and/or return of the devices as instructed by the Sponsor. In addition, all Investigators will maintain records to document the receipt, use and disposition of all devices received by their imvestigational site intended for this study. The Sponsor and/or designee will also maintain records of all shipments and disposition of the investigational devices. The Sponsor and/or their authorized Contract Research Organization (CRO) will routinely

inspect the investigational site inventory records for device accountability at the sites participating in this study.

8.4 Data Handling and Record Keeping

8.4.1. Serious Adverse Events & Major Adverse Events

The Investigator will report to the Sponsor by telephone, email, fax, or electronic CRF submission any SAE or MAE as soon as possible (within 48 hours of the Investigator becoming aware of the event or by the end of the next working day). Additionally, SAEs and MAEs should be reported to the IRB/IEC, if required per the investigational site guidelines or as directed by the Sponsor. The Adverse Event eCRF is to be completed and submitted to the Sponsor within five (5) working days of the event. The contact information for reporting SAEs and MAEs is provided in the study contact section of this protocol.

8.4.2. Device Malfunctions or Failures

The Investigators will report any Device Malfunctions or Failures that occur, to the Sponsor within 24 hours of the Investigator becoming aware of the device malfunction or failure or by the end of the next working day. The report may be made by or within 24 hours via telephone, email or fax. The Investigator or study staff are to return the devices per the Instructions for Use for investigation. The Device Observation eCRF is to be completed and submitted to the Sponsor within five (5) working days of the event. The contact information for reporting Device Performance issues is provided in the study contact section of this protocol.

8.4.3. Deviations from the Investigational Plan

The Investigator must notify the Sponsor of any deviation from the Investigational Plan. The Investigator should also notify the IRB / EC as required per their local requirements or as directed by the Sponsor. This notice must occur as soon as possible, but in no case longer than five (5) working days after the Investigator becomes aware of a major deviation. Major deviations include, but is not limited to, those that involve the informed consent process, the inclusion/exclusion criteria of the study, SAE/MAE reporting, device misuse or device accountability discrepancies, or any deviation that involves or leads to a serious adverse event in a study participant.

8.4.4. Source Documents

The Investigator must maintain detailed source documents on all patients who are enrolled or who undergo screening in the study. Source documents include patient medical records, hospital charts, clinic charts, investigator patient trial

files, as well as the results of diagnostic tests (e.g., laboratory tests, hemodynamic studies).

- The following minimum information should be entered into the patient's medical record:
- The date the patient entered the study and the patient number
- The study protocol number and the name of the Sponsor
- The date that Informed Consent was obtained
- Evidence that the patient meet the study eligibility requirements (e.g., medical history, study procedures and/or evaluations)
- The dates of all study related patient visits
- Evidence that required procedures and/or evaluations were completed
- Use of any concurrent medications
- Documentation of specific device used
- Occurrence and status of any adverse events (AEs)

The date the patient exited the study and a notation as to whether the patient completed the trial or was discontinued, including the reason for discontinuation.

8.4.5. CLINICAL DATA COLLECTION

Standardized electronic case report forms (eCRF) will be used to collect complete and accurate records of the clinical data from the TORUS 2 trial according to the GCPs requirements. The Investigator and/or study staff under his/her direction is responsible for accurately recording the clinical data for this study and submitting it to the Sponsor in a timely manner.

8.4.6. INVESTIGATOR FINAL REPORT

The Investigator will report information and events according to the timelines in the Table 7. Within three (3) months of Study completion, the Investigator will provide a final study report that summarizes their enrollment and study participation. This report should include a summary of enrollment, AEs, MAEs, SAEs, UADEs and Device Malfunctions and Failures. This report will be forwarded to the IRB/IEC and the Sponsor after all of the enrolled patients have completed their final follow-up visit or have exited the study and the study close-out visit has been completed, but no later than three (3) months following completion of the last follow-up visit.

Table 8: Investigator Reporting Timelines

Form/Report	Submission Timeframe
Enrollment notification	Completion of Enrollment eCRF within 24 hours of enrollment, or by the end of the next working day.
Electronic CRFs	Completion within 5 working days of study visit.
Angiographic, X-Ray and Duplex Ultrasound Images	Submit to Core Lab within 5 working days of completion.
Adverse Events (non-serious)	Complete eCRF within 14 days of the Investigator becoming aware of the event.
SAEs & MAEs & UADEs	Submit notification to Sponsor within 48 hours of the investigational site becoming aware of the event, or by the end of the next working day; submit to the local IRB/IEC as required or as directed by the Sponsor.
Study Progress Reports	As required by the local IRB/IEC (minimum annually).
Final Report to the IRB / IEC	Within 3 months of Study completion.

9.0 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

The occurrence of Adverse Events will be monitored during this study. All Adverse Events will be collected through 12 month follow-up and recorded on the Adverse Event eCRF at onset and at each follow-up visit until resolved. SAEs, MAEs and UADEs will be collected for the duration of the study. All device- and procedure-related events, all target limb related events, and all potential non-serious events related to study requirement medications shall be reported throughout the trial.

Potential adverse events associated with use of the TORUS Stent Graft System include, but are not limited to the following:

- Access site hemorrhage or hematoma
- Access site pain/infection
- Acute vessel closure
- Aneurysm or pseudoaneurysm formation
- Arteriovenous (AV) fistula
- Death
- Device failure
- Embolism
- Fever/pain in absence of infection
- Infection
- Inflammation
- Malposition
- Myocardial infarction
- Radiation injury
- Renal insufficiency/failure due to excessive contrast load
- Sepsis
- Shock
- Side branch occlusion
- Stenosis or Occlusion
- Thrombosis
- Vessel dissection, perforation or wall trauma

9.1 ADVERSE EVENTS

Any untoward medical occurrence, unintended disease or injury or any untoward clinical signs (including an abnormal laboratory finding) in patients, users or other persons whether or not related to the medical device. This includes events related to the study device or events related to the procedures involved.

Adverse Device Effect: An adverse event related to the use of a medical device, including adverse events resulting from insufficient or inadequate Instructions for Use, deployment, implantation, installation or operation, or any malfunction of the medical device or any event resulting from user error or intentional misuse of the medical device.

The Investigator is responsible for assessing the severity of the AE, the causal relationship between any events and the clinical study procedure, activities or device. Additionally, the Investigator is responsible for providing appropriate treatment for the event and for adequately following the event until resolution. The following categories of adverse event severity are to be used:

- **Mild**: Awareness of a sign or symptom that does not interfere with the patient's usual activity or is transient, resolved without treatment and with no clinical sequelae.
- **Moderate**: Interferes with the patient's usual activity.
- **Severe**: Any fatal or immediately life-threatening clinical experience that requires a patient to be hospitalized, or hospitalization is unduly prolonged because of potential disability or danger to life or because an intervention has been necessitated. This includes any permanently disabling event.

AEs, SAEs and endpoint events will also be classified as to their relationship to the study device and the study procedure as follows:

- **Definitely Related**: The adverse event is directly and clearly related to the investigational device or procedure.
- **Probably Related**: The exact relationship cannot be determined, but it is most likely that the adverse event and the investigational device or procedure are related.
- **Possibly Related**: The exact relationship cannot be determined, but there is a reasonable likelihood that the adverse event and the investigational device or procedure may be related.
- **Not Related**: The adverse event does not have any identified or perceived relationship to the investigational device or procedure.
- **Unknown**: The relationship of the AE to the device or procedure cannot be determined.

Pre-existing medical conditions or a repeat of symptoms reported prior to the TORUS Stent Graft System procedure will not be recorded as an adverse event. Pre-existing conditions that worsen during a study are considered adverse events.

9.2 SERIOUS ADVERSE EVENT (SAE)

A serious adverse event is any problem or unwanted event encountered in a clinical trial or a performance evaluation that has led, or could have led, directly or indirectly to death or to a serious deterioration in the health of a patient or user or any other person, without regard to whether the event was caused by a medical product. The following events (including laboratory results and outcome events) will be considered to be SAEs and must be reported within 48 hours or by the end of the next business day be reported to the study Sponsor. These events must be reported whether or not the Investigator believes they are related to study procedures, activities or device:

- Death
- Serious deterioration in the health of the patient, that either resulted in:
  - a life-threatening illness or injury, or
  - a permanent impairment of a body structure or a body function, or
  - in-patient or prolonged hospitalization,
  - medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function, or
  - led to fetal distress, fetal death, or a congenital abnormality or birth defect.

Serious Adverse Device Effect: An adverse device effect that has resulted in any of the consequences of a Serious Adverse Event.

Note: Planned hospitalization for a pre-existing condition, a condition unrelated to the treatment or a procedure required by this study, that is without serious deterioration in health, is not considered a serious adverse event.

9.3 UNANTICIPATED ADVERSE DEVICE EFFECTS (UADE)

An unanticipated adverse device effects is any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem or death was not previously identified in nature, severity, or degree of incidence in the protocol, investigator's brochure, labeling or published literature, or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of the patients.

9.4 ADVERSE EVENT REPORTING

All adverse events will be captured through the 12-month visit as a part of this clinical study. Following the 12-month visit, only SAEs, MAEs, and UADEs will be collected and reportedfor the duration of the study. All device- and procedure-related events and all target limb related events shall be reported throughout the trial.

At each contact with the patient, the investigator will seek information on adverse device effects by specific questioning and, as appropriate, by examination. Information on all adverse device effects will be recorded immediately in the source document, and also in the appropriate electronic case report form (eCRF). All clearly related signs, symptoms, and abnormal diagnostic procedures results should be recorded in the source documents.

All SAEs, UADEs, MAEs and possible serious device and/or procedure-related adverse events must be reported by the Investigator (or his/her designee) within 48 hours of becoming aware of the event or by the end of the next business day. The report should include: severity, duration, action taken, treatment outcome and relationship to the adverse event to the study device, procedure, anticoagulations and dual antiplatelet Medications, etc. (i.e., unrelated, relation or relationship unknown).

In the case of serious adverse events (SAE), major adverse events (MAE), procedure and/or device failures and malfunctions, medical record documentation (e.g., procedure notes, operative notes, discharge summary, relevant progress notes, imaging or lab studies) must be provided to PQ Bypass or its designee, if requested. If appropriate, PQ Bypass shall inform the Competent Authority and the relevant Ethics Committee about the event within the appropriate timelines. In accordance with MEDDEV 2.7 / 3 rev.3 (May 2015), the sponsor must report:

- all reportable events which indicate an imminent risk of death, serious injury, or serious illness and that requires prompt remedial action for other patients/patients, users or other persons or a new finding to it,
- to the National Competent Authorities where the clinical investigation has commenced,
- immediately, but not later than 2 calendar days after awareness by sponsor of a new reportable event or of new information in relation with an already reported event.

9.5 Reporting of Device Failures and Malfunctions

All reported device malfunctions or failures of the Torus Stent Graft system are required to be documented in the eCRF within 24 hours. Device failures and malfunctions should also be documented in the patient's medical record. Instructions for returning the investigational device will be provided.

NOTE: Device failures or malfunctions are NOT to be reported as adverse events. However, if there is an adverse event that results from a device failure or malfunction, that specific event would be recorded in the usual way.

10.0 Clinical Events Committee

An independent Clinical Events Committee (CEC) will be responsible for a systematic review and the adjudication of all endpoint events.

The CEC shall consist of up to four (4) independent physicians, with experience in interventional peripheral endovascular procedures. In order to enhance objectivity and reduce the potential for bias, the CEC members will not have scientific, financial or other conflicts of interest related to the Sponsor or the study investigators or the investigational sites. The CEC will operate and conduct all meetings and event reviews independent of the Sponsor unless specific expert knowledge regarding the characteristics or the function of study device is requested by the CEC from the Sponsor.

The CEC will adjudicate events through an online system in an ongoing fashion. The adjudication process, event definitions and required source documentation materials for each type of event will be pre-specified in the CEC charter. All adjudication decisions will be made by the CEC in an independent fashion based upon the review of all available medical evidence associated with each event.

11.0 Publication Policy

PQ Bypass intends to submit the results of the primary and secondary endpoints for publication within 12 months of completion of the 12-month follow up. Publication will be pursued whether the 12-month outcomes are positive or negative or early termination of the study. The publications policy for this Study is as follows. Following the earliest of a) publication of the multi-center Study results, b) receipt of a notice from PQ Bypass stating that the multi-center Study has been terminated or, c) twenty-four (24) months after completion or termination of the Study at all Investigational Sites, Investigators shall have the right to publish, in appropriate scientific journals or other professional publications, information and data collected or produced as a result of their participation in the Study, provided that drafts of the publications have been delivered to PQ Bypass for purposes of review and comment at least sixty (60) days prior to the first submission for publication or public release, to which Investigating Parties shall give due

consideration. PQ Bypass shall return comments to the Investigator within forty-five (45) days receipt of the draft. In addition, the Investigator shall delay any proposed publication/presentation in the event PQ Bypass so requests to enable PQ Bypass to secure patent or other proprietary protection. In all such publications, credit shall be given to PQ Bypass for its sponsorship of the Study. Similarly, in publications by PQ Bypass regarding the Study, appropriate recognition will be given of the contribution made by the Institution and Principal Investigator, as applicable. PQ Bypass may use, refer to, and disseminate reprints of scientific, medical, and other published articles relating to the Study, including such reprints that disclose the name of Investigators and/or Institution.

12.0 STUDY DEFINITIONS

Access Site Hemorrhage: Bleeding from the access site which requires transfusion, hospitalization (either admission or extended stay), or further treatment for management.

Acute Limb Ischemia: Results from a sudden decrease in limb perfusion, usually producing new or worsening signs and symptoms, and often threatening limb viability.

Acute Renal Failure: Acute post-operative renal insufficiency resulting in one or more of the following: (a) increase of > 1.0 mg/dl in serum creatinine from most recent prior measured level, and current measured absolute value is > 2.0 mg/dl; (b) a new requirement for dialysis.

Allergic Reaction: An allergic reaction characterized by rash, upper respiratory congestion, urticaria, shortness-of-breath, or general collapse (anaphylaxis).

Amputation:

Major: any requirement for amputation of the target limb above the ankle.

Minor: any requirement for amputation of the of the target limb below the ankle.

Anemia: Decrease from baseline in red blood cells, hemoglobin, or total blood volume that is associated with hemodynamic changes or requires transfusion, or a drop in hematocrit to below 26%.

Angina, unstable: Angina that increases in frequency, intensity, or duration, which occurs at rest, or which is new in onset. Unstable angina is a syndrome that is intermediate between stable angina and myocardial infarction: it is characterized by an accelerating or "crescendo" pattern of chest pain that lasts longer than stable angina, occurs at rest or with less exertion than stable angina, or is less responsive to medication. Unstable angina and myocardial infarction are considered acute coronary syndromes.

Ankle Brachial Index (ABI): The ratio of systolic blood pressure measured at the ankle to systolic blood pressure measured at the brachial artery. It is used to predict the severity of peripheral arterial disease (PAD). ABIs >0.9-1.2 = normal, ≤ 0.9 = peripheral arterial disease, < 0.4 = severe peripheral arterial disease (ischemic pain and ulceration). ABI > 1.2 is likely due to incompressible arteries and is commonly observed in association with long-standing diabetes mellitus, extreme old age, or calcinosis.

Instructions for ABI Calculations:

Obtain systolic blood pressures (SBP) for both arms (brachials) and both ankles [posterior tibials (PT) & dorsalis pedals (DP)].

Divide the higher of the two SBPs for each leg (highest between the PT and DP) by the higher of the two arm pressures to get the right and left ABIs.

Arterial Occlusion / Thrombosis at Groin Puncture Site: Angiographic or ultrasonographic evidence of occlusion at the puncture site limiting antegrade flow to the distal limb.

Arterial Perforation/Rupture/Puncture of an Arterial Wall: Classified as follows:

Angiographic perforation: Perforation detected by the investigational site at any point during the procedure.

Clinical perforation: Perforation requiring additional treatment (including efforts to seal the perforation), or resulting in significant extravasation of blood from the investional site, abrupt closure, limb ischemia or death.

Arterial Pseudoaneurysm: Disruption of arterial wall confirmed by imaging study and requiring intervention.

Arteriovenous Fistula (AVF): An abnormal passage or communication between an artery and a vein which may be due to the percutaneous introduction of ancillary devices (e.g., needles, catheters, guide wires) confirmed by imaging studies..

Cardiac Arrhythmia: Electrical disruption of the heart rhythm requiring specific medication, DC shock, or pacemaker insertion to address condition.

Cardiogenic Shock: Patient presents with SBP < 80 mm Hg for more than 30 minutes unresponsive to fluids or requiring intravenous vasopressor agent or an intra-aortic balloon pump (IABP).

Cerebral Vascular Accident (CVA): See Stroke.

Classification of Lesion Morphology (TASC II)

TASC II type A lesions:

Single stenosis ≤ 10 cm in length

Single occlusion ≤ 5 cm in length

TASC II type B lesions:

Multiple lesions (stenosis or occlusions), each ≤ 5 cm

Single stenosis or occlusion ≤ 15 cm not involving the infrageniculate popliteal artery

Single or multiple lesions in the absence of continuous tibial vessels to improve inflow for a distal bypass

Heavily calcified occlusions ≤ 5 cm in length

Single popliteal stenosis

TASC II type C lesions:

Multiple stenosis or occlusions totaling > 15 cm, with or without heavy calcification

Recurrent stenosis or occlusions that need treatment after two endovascular interventions

TASC II type D lesions:

Chronic total occlusion of the common or superficial femoral arteries (> 20 cm, involving the popliteal artery)

Chronic total occlusion of the popliteal artery and proximal trifurcation vessels

Closure, Abrupt: Occurrence of new (during the index procedure), persistent slow, reduced, or loss of flow within the target vessel that requires intervention other than the index or adjunct treatment. Abrupt closure may also be referred to as acute occlusion if there is a total loss of flow.

Closure, Late: Target lesion site occlusion that occurs greater than 30 days after the index procedure is completed (e.g., the patient has left the treatment area).

Closure, Subacute: Target lesion site occlusion that occurs after the index procedure is completed (e.g., the patient has left the treatment area) and within 30 days of procedure.

Contrast-Induced Nephropathy: Associated with contrast agent resulting in > 25% increase in serum creatinine or an absolute value of > 0.5 mg/dl.

Contrast Media Reaction: An allergic reaction, immediate or delayed, associated with the intravascular administration of contrast media that results in symptoms (e.g. itching, hives) or physiologic changes requiring treatment (e.g. anaphylactic reaction) or death.

Critical Limb Ischemia (CLI): Clinical manifestation of peripheral arterial disease characterized by Rutherford Clinical Scale Category of 4-6. For the purposes of this study, only patients with Rutherford Clinical Scale Category of 2, 3 and 4, are eligible for enrollment.

Death: Death is divided into 2 categories:

- ***Cardiovascular death*** is defined as death due to any of the following:
  - Acute myocardial infarction.
  - Sudden cardiac death.
  - Death due to heart failure.
  - Death due to stroke.
  - Death due to other cardiovascular causes (e.g., procedures, hemorrhage, or other cardiovascular causes).
  - Death not attributable to any other cause (e.g., undetermined cause of death).
- ***Non-cardiovascular death*** is defined as a death not due to cardiovascular causes (as listed above).

Deep Vein Thrombosis (DVT): Thrombosis of a deep vein, as confirmed by imaging study or direct visualization.

Femoropopliteal: DVT involvement limited to the superficial femoral or popliteal veins, with or without distal (e.g., toward foot) DVT involvement, based on duplex ultrasound exam.

Iliofemoral: DVT involvement of the common or external iliac veins or the common femoral vein, with or without distal (e.g., toward foot) DVT involvement, based on duplex ultrasound exam.

De Novo Lesion: An obstructive or occlusive lesion without previous endovascular or surgical intervention

Device Failure: A device that is used in accordance with the Instructions for Use, but does not perform according to the Instructions for Use and negatively impacts the treatment.

Device Malfunction: A malfunction of a device is an unexpected change to the device that is contradictory to the Instructions for Use and may or may not affect device performance.

Dissection: Disruption of an arterial wall resulting in separation of the intimal layer. May or may not be flow limiting.

Dissection Classifications (National Heart, Lung and Blood Institute – NHLBI)

Type A: Small radiolucent area within the lumen of the vessel disappearing with the passage of the contrast material.

Type B: Appearance of contrast medium parallel to the lumen of the vessel disappearing within a few cardiac cycles.

Type C: Dissection protruding outside the lumen of the vessel persisting after passage of the contrast material.

Type D: Spiral shaped filling defect with our without delayed run-off of the contrast material in the antegrade flow.

Type E: Persistent luminal filling defect with delayed run-off of the contrast material in the distal lumen.

Type F: Filling defect accompanied by total coronary occlusion.

Embolization, Distal: Any distal emboli confirmed by imaging.

Embolization, Symptomatic: Clinical signs or symptoms of distal emboli detected in the treated limb distal to the treated lesion after the index procedure ***or*** noted angiographically and requiring mechanical or pharmacologic means to improve flow. This includes new abrupt occlusions or filling defects.

Enrollment: Patients who are consented and meet all the study inclusion criteria and none of the study exclusion criteria and are treated or treatment is attempted with the study device will be considered enrolled into the study. Patients who do not meet all inclusion and exclusion criteria (e.g., including ability to cross the lesion with a guidewire, target reference vessel diameter, patent tibioperoneal artery in the target limb, etc.) will be considered an angiographic screen failure and will not be followed in the study (no data will be collected on these patients).

Hematoma: Collection of blood (or its degradation products) that exceeds 8 cm in diameter, requires treatment, or prolongs hospitalization.

Hypertension: Systolic BP >140 mmHg, or diastolic >90 mmHg requiring specific medical therapy.

Hypotension: Any prolonged systolic blood pressure <80 mmHg associated with symptoms and requiring intravenous vasopressor medications.

Infection, access site: Infection at the vascular access site, documented by lab culture or clinical evidence requiring medical treatment (irrigation, debridement, antibiotics, etc.) to resolve.

Infection, systemic: Systemic infection documented by positive lab culture or clinical evidence, requiring medical treatment to treat and resolve.

Intention to Treat (ITT): The principle of including outcomes of all patients in the analysis who are enrolled and treated (attempted or completed) into the study, regardless of noncompliance, Protocol deviations, or withdrawal.

Limb Ischemia: Deficient supply of oxygenated blood to the tissues in the limbs that is due to obstruction of the inflow of arterial blood characterized by pain and/or discoloration of the limb and/or tissue loss.

Luminal Patency: Restenosis <50% as determined by angiography or duplex ultrasound.

Major Adverse Event (MAE): An MAE comprises the following: all-cause death, target limb major amputation and clinically-driven target lesion revascularization (CD-TLR).

Myocardial Infarction (MI): Evidence of myocardial necrosis in a clinical setting consistent with myocardial ischemia, requiring a combination of evidence of myocardial necrosis [either changes in cardiac biomarkers (e.g., troponins or CK-MB) or post-mortem pathological findings] and supporting information devired from the clinical presentation, electrocardiographic changes, or the results of myocardial or coronary artery imaging.

Patency, Primary Vessel: Vessel patency at a given time point will be determined by the absence of clinically-driven target lesion revascularization (CD-TLR) and absence of recurrent target lesion diameter stenosis >50% by duplex ultrasound with a peak systolic velocity ratio of >2.5.

Patency, Tibioperoneal Run-Off: Patient has at least one patent tibioperoneal run-off vessel with <50% stenosis confirmed by angiography at time of enrollment.

Perforation: Puncture of an arterial wall.

Procedural Success: Procedural Success is defined as technical success with out any MAEs within 24 hours of the procedure.

Pseudoaneurysm: Disruption of the arterial wall characterized by an out-pouching or pocket with swirling, flowing blood outside of the confines of the arterial lumen.

Recurrent Occlusion: Occlusion (i.e., total obstruction of vessel lumen) after a successful canalization.

Recurrent Thrombosis: Thrombosis (i.e. sub-total obstruction of vessel lumen) following successful treatment.

Reference Vessel Diameter, Proximal (RVD_{prox}): Diameter of normal vessel immediately proximal to the treated segment.

Reference Vessel Diameter, Distal (RVD_{dist}): Diameter of normal vessel immediately distal to the treated segment.

Renal Failure (Acute): Acute post-operative renal insufficiency resulting in one or more of the following: (a) increase of > 1.0 mg/dl in serum creatinine from most recent prior measured level, and current measured absolute value is > 2.0 mg/dl; (b) a new requirement for dialysis.

Renal Insufficiency: An increase in serum creatinine of ≥ 1.0 mg/dl over previous value requiring medical treatment but which does not require dialysis to resolve.

Respiratory Failure: New onset of respiratory insufficiency that requires placement of endotracheal tube and/or pneumothorax with or without chest tube.

Respiratory Insufficiency: Deterioration of patient's respiratory efforts that require supportive or medical treatment.

Restenosis: Reoccurrence of narrowing or blockage or target lesion. Recurrence of ≥ 50% diameter stenosis within ± 5 mm proximal and/or distal to the target lesion as measured by duplex ultrasound (PSV > 2.5) or angiography (note: in cases where both imaging modalities are available, the angiography will take precedence).

Retroperitoneal Bleed: Bleeding into the back of the abdomen from a vascular access or puncture site.

Rutherford Clinical Category Scale: Clinical scale identifying three grades of claudication and three grades of critical limb ischemia ranging from rest pain alone to minor and major tissue loss.

Category	Clinical Description
0	Asymptomatic
1	Mild claudication
2	Moderate claudication
3	Severe claudication

Category	Clinical Description
4	Ischemic rest pain
5	Minor tissue loss
6	Ulceration or gangrene

Stent Fracture: Defined as clear interruption of stent strut observed in a minimum of two projections, determined by core lab examination of X-ray images. The VIVA paper defines the stent integrity grading scale.

Stent Integrity Grading Scale:

Grading Scale	Clinical Description
Type 0:	No strut fractures
Type I:	Single tine fracture
Type II:	Multiple tine fracture
Type III:	Stent fracture(s) with preserved alignment of the components
Type IV:	Stent fracture(s) with mal-alignment of the components
Type V:	Stent fracture(s) in a trans-axial spiral configuration

Stroke: Any neurological deficit defined as an acute episode of focal or global neurological dysfunction caused by brain, spinal cord, or retinal vascular injury as a result of hemorrhage or infarction. May be further categorized as:

Ischemic Stroke: defined as an acute episode of focal cerebral, spinal, or retinal dysfunction caused by infarction of central nervous system tissue.

Hemorrhagic Stroke: defined as an acute episode of focal or global cerebral or spinal dysfunction caused by intraparenchymal, intraventricular, or subarachnoid hemorrhage.

Target Lesion Revascularization, Clinically-driven (CD-TLR): Clinically-driven target lesion revascularization is defined as target lesion revascularization performed due to target lesion diameter stenosis > 50% AND either evidence of clinical or functional ischemia (e.g., recurrent/progressive intermittent claudication, critical limb ischemia) OR recurrence of the clinical syndrome for which the initial procedure was performed.

Technical Success: Technical Success is defined as the ability to cross and dilate the lesion to achieve residual stenosis of ≤30%.

Thrombocytopenia: A persistent decrease in the number of blood platelets to subnormal levels.

Toe Brachial Index (TBI): A Toe Brachial Index (TBI) is performed when the ABI or Ankle Brachial Index is abnormally high due to plaque and calcification of the arteries in the leg; this is caused by atherosclerosis and is most often found in diabetic patients. The abnormally high ABI is >1.3.

Instructions for TBI Calculations:

Obtain systolic blood pressures (SBP) for both arms (brachials) and both great toes.

Divide the higher of the two SBPs for each leg (highest between the PT and DP) by the great toe pressure to get the right and left TBIs.

Thrombus: Blood clot that obstructs a blood vessel.

Transient Ischemic Attack: A neurological event defined as a transient episode of focal neurological dysfunction caused by brain, spinal cord, or retinal ischemia, without acute infarction.

APPENDIX I: INFORMED CONSENT FORM

APPENDIX II: INSTRUCTIONS FOR USE (IFU)

APPENDIX III: INVESTIGATOR AGREEMENT