PQ Bypass Stent Graft System
Long Segment Lesion Peripheral Artery
Revascularization Feasibility Study

Signature Page

CLINICAL PROTOCOL Number: STP 185 Rev B6

Issue Date: 02 May 2017

Approved by: [redacted] Date: [redacted]

The trial will be performed in accordance with the relevant parts of Title 21 CFR Parts 812, 50,54, 56 and ISO 14155:2011:01; the ICH Guidelines for Good Clinical Practices (E6), the Declaration of Helsinki, and any regional and/or national regulations.

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1.0 PRIMARY CONTACTS

Sponsor and Data Management	**PQ Bypass, Inc.** 269 N. Mathilda Avenue Sunnyvale, CA 94086 United States [redacted] Ziad Rouag Vice President Clinical and Regulatory Affairs PQ Bypass, Inc. [redacted]
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Protocol Summary

PQ BYPASS	PROTOCOL SUMMARY
Title	Long Segment Lesion Peripheral Artery Revascularization Study
Protocol Number	185
Device	PQ Bypass™ Stent Graft System
Intended Use	The 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.
Regulatory Status	Investigational Device.
Number of Centers	A maximum of 15 international sites (non U.S.).
Subject Population	Up to **65** subjects may be enrolled. A total of **60** evaluable subjects with a documented, atherosclerotic lesion of the native superficial femoral artery (SFA) or the superficial femoral and proximal popliteal arteries, suitable for treatment with PQ Bypass™ Stent Graft System.
Study Design	Prospective, single-arm, multi-center, international, non-randomized, pre-market, safety and effectiveness clinical investigation.
Study Objectives	The primary objective of the feasibility study is to evaluate the safety and effectiveness of the PQ Bypass Stent Graft System in the treatment of atherosclerotic lesions of the native superficial femoral artery (SFA) or the superficial femoral and proximal popliteal arteries.

Primary Safety Endpoint	The primary safety endpoint for this study is 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.
Primary Effectiveness Endpoint	The primary effectiveness endpoint is defined as stent patency as evidenced by a peak systolic velocity ratio (PSVR) < 2.5 from DUS obtained within the 12-month visit window with no clinically-driven re-intervention within the stented segment.
Secondary Safety Endpoints	Secondary safety endpoints will be evaluated and include: 1. The combined rate of death at 30 days, target lesion revascularization (TLR), index limb amputation, and an increase in Rutherford-Becker Classification by 2 classes (comparing pre- to post-procedural assessments) at 12 months. 2. Major adverse vascular event (MAVE) at 30 days, 6 months and 12 months defined as stent thrombosis, target limb amputation, clinically apparent distal embolization, defined as causing end-organ damage (e.g. lower extremity ulceration, tissue necrosis, or gangrene), procedure related arterial rupture, acute limb ischemia or bleeding event requiring transfusion. 3. The combined rate of serious procedural adverse events, including death, myocardial infarction, index limb amputation, and access site and treatment site complications requiring surgery, blood transfusion (>2 units of PRBC), or prolonged hospital stay within 30 days of the index procedure.
Secondary Effectiveness Endpoints	Secondary effectiveness endpoints include: 1. Acute technical (lesion) success, procedural success and device success 2. Ankle-Brachial Index (ABI) and Toe-Brachial Index (TBI) at 1, 6 and 12 months 3. Target vessel revascularization (TVR) at 6 and 12 months 4. Limb ischemia by Rutherford-Becker Classification at Baseline, 1, 6, and 12 months. 5. Number of any type of index limb amputations at 6 and 12 months 6. Absolute Claudication Distance as measured by the Exercise Tolerance Test (TASCII) assessed in subjects at baseline, 1, 6, and 12 months. 7. Target lesion revascularization (TLR) at 1, 6 and 12 months. 8. The rate of primary assisted patency through follow-up defined as: revascularization of non-occlusive (<99%) stenosis within the stent graft or immediately above or below the treated arterial segment with less than 50% residual stenosis. 9. The rate of secondary patency through follow-up defined as: revascularization of occlusion (100%) within the stent graft or immediately above or below the treated arterial segment with less than 50% residual stenosis.
Additional Endpoints	The following additional endpoints will also be reported: 1. A combined rate of death at 30 days, or TLR, index limb amputation, and an increase in Rutherford-Becker Classification by 2 classes (comparing pre- to post-procedural assessments) measured at 24 months.

	2. Target vessel revascularization (TVR) at 24-month post-procedure. 3. Limb ischemia improvement by Rutherford-Becker (improvement in scale by ≥ 1) at 24 months. 4. Major Adverse Vascular Event (MAVE) by 24 months, defined as: Stent thrombosis, target limb amputation, or clinically apparent distal embolization, defined as causing end-organ damage (e.g. lower extremity ulceration, tissue necrosis, or gangrene). 5. Procedure related arterial rupture, acute limb ischemia, or bleeding event requiring transfusion. Number of any type of index limb amputations at 24-month follow-up. Target lesion revascularization (TLR) at 24 months post-procedure.
Inclusion Criteria	The subject must meet **all** of the following criteria at the time of eligibility: 1. Age ≥ 18 years and of age of legal consent. 2. Women of child bearing potential must have a negative pregnancy test within 7 days prior to the index procedure. 3. Subject has lifestyle limiting claudication or rest pain (Rutherford Becker scale 2-4)* with a resting ABI < 0.9. Resting TBI is utilized only if unable to reliably assess ABI. TBI must be <0.7. These assessments are required for the target limb, but both limbs are preferred. 4. A superficial femoral artery lesion with >50% stenosis or occlusion which requires treatment. 5. Stenotic lesion(s) or occluded length within the same vessel (one long or multiple serial lesions) ≥ 80mm to ≤180mm. 6. Reference vessel diameter (RVD) ≥ 5.0mm and ≤ 6.7 mm, angiographically/CTA/MRA defined. 7. Patent popliteal artery 3 cm proximal to tibial plateau 8. At least 1 patent tibial artery to the foot (<50% stenosis) 9. The target lesion(s) can be successfully crossed with a guide wire and dilated. 10. Adequate aortoiliac or common femoral "inflow" is defined as <30% stenosis after either PTA or stenting of the inflow lesion. After treatment of the inflow lesion, the residual pressure gradient across the target lesion will be obtained and if the peak to peak pressure gradient is < 20mmHg, the subject will be included in the study. Subjects enrolled with aortoiliac or common femoral artery lesions resulting in poor inflow, must be treated prior to receiving the study treatment. (Same Day or earlier) 11. If a subject has bilateral obstructive SFA disease, only 1 leg may be treated with the investigational device in the study. a. If the study leg is treated first, the contra-lateral procedure should not be performed until at least 30 days after the index procedure (staged); and should only be performed with an approved (CE Marked) device. b. If the contra-lateral leg is treated with an approved (CE Marked) device prior to treatment of the study leg, treatment of the contra-lateral leg should be performed at least 15 days prior to the treatment of the study leg. 12. The subject is eligible for standard surgical repair, if necessary. 13. A subject who requires a coronary intervention should have it performed at least 30 days prior or 30 days post the treatment of the target lesion.

	14. Subject must provide written informed consent. 15. Subject must be willing to comply with the specified follow-up evaluation schedule. *Note – Patients with stage 2 Rutherford classification can be included when conservative physical and drug therapy have been unsuccessful.
Exclusion Criteria	The following must NOT be present at the time of subject eligibility: 1. Age greater than 90 2. Thrombophlebitis, within the previous 30 days. 3. Receiving dialysis or immunosuppressant therapy within the previous 30 days. 4. Thrombolysis of the target vessel within 72 hours prior to the index procedure, where complete resolution of the thrombus was not achieved. 5. Stroke within the previous 90 days. 6. Ipsilateral femoral aneurysm or aneurysm in the SFA or popliteal artery. 7. Required stent placement via a popliteal approach. 8. Procedures which are pre-determined to require stent-in-stent placement to obtain patency, such as in-stent restenosis. 9. Significant vessel tortuosity or other parameters prohibiting access to the lesion or 90° tortuosity which would prevent delivery of the stent device. 10. Required stent placement within 1 cm of a previously deployed stent. 11. Known allergies to any of the following: aspirin and clopidogrel bisulfate (Plavix®), ticlopidine (Ticlid ®), and prasugrel (Effient®); heparin; Nitinol (nickel titanium); or contrast agent, that cannot be medically managed. 12. Presence of thrombus prior to crossing the lesion. 13. Known or suspected active infection at the time of the procedure. 14. Use of cryoplasty, laser, or atherectomy devices in the target vessel at the time of index procedure. 15. Restenotic lesion that had previously been treated by atherectomy, laser or cryoplasty within 3 months of the index procedure. 16. History of neutropenia, coagulopathy, or thrombocytopenia that was unexplained or is considered to be at risk for reoccurrence. 17. Known bleeding or hypercoagulability disorder or significant anemia (Hb<8.0) that cannot be corrected. 18. Subject has the following laboratory values: a. platelet count less than 80,000/µL, b. international normalized ratio (INR) greater than 1.5, c. serum creatinine level greater than 2.0 mg/dL. 19. Subject requires general anesthesia for the procedure. 20. Major distal amputation (above the transmetatarsal) in the study or non-study limb. 21. Patient has had a revascularization procedure on the target limb within 30 days of the planned index procedure 22. Patient has a planned amputation of the target limb 23. Previous bypass surgery on the target limb 24. Subject is pregnant or plans to become pregnant during the study.

	25. Subject has a co-morbid illness that may result in a life expectancy of less than 1 year. 26. Subject is participating in an investigational study of a new drug, biologic or device at the time of study screening.
Estimated Enrollment Period	Twelve (12) months
Study Duration for Each Subject	Two (2) years
Proposed Study Duration	Approximately three (3) years or longer (1 year for subject recruitment and 2 years follow-up)
Sponsor	PQ Bypass Medical, Inc. 269 N. Mathilda Avenue Sunnyvale, CA 94086 USA Contact : Ziad Rouag Tel : +1 (415) 531-4647 Email: zrouag@pqbypass.com
Data Management	Data Management will be conducted by an independent data management organization.
Core Imaging Laboratory	An independent duplex ultrasound and angiographic core laboratory will review and analyze key study variables.
Clinical Events Committee	An independent Clinical Events Committee (CEC) or Independent Medical Reviewer will be used to review and adjudicate primary and secondary safety endpoints (including major adverse events), serious adverse events and device related adverse events.
DSMB	An independent Data Safety Monitoring Board (DSMB) will be used to review study data on an ongoing basis and identify any potential safety trends.
Monitoring	The study will be monitored by independent contract monitors.

Schedule of Assessments

Study Task	Pre-Screening	Baseline[1] (Screening)	Procedural	Discharge	30 days (± 7 days)	6 months (± 14 days)	12 months (± 30 days)	24 months (± 60 days)
Informed Consent/HIPAA	X	X						
D agnost c Ang ography/ CTA/MRA	X							
Rev ew of Inc us on/Exc us on Cr ter a	X	X						
Demograph cs and Med ca H story		X						
Br ef Phys ca exam/Hea th Status[2]		X						
Rout ne Laboratory Tests (CBC, P ate et count, Serum creat n ne, INR, Pregnancy test) Phys ca Exam and V ta S gns[1]		X						
CK/CK-MB Enzymes[3]				X				
ECG[4]		X		X	X			
Ang ography			X[5]					
Dev ce Accountab ty			X					
Dup ex U trasound[6]				X	X	X	X	X
X-Ray*							X	
Rutherford- Becker Sca es[7]		X			X	X	X	X
ABI and TBI[8]		X			X	X	X	X
Concom tant Med cat ons[9]		X	X	X	X	X	X	X
Exerc se To erance Test		X			X	X	X	
Adverse Events		X	X	X	X	X	X	X
Protoco Dev at ons		X	X	X	X	X	X	X

*Optional per standard practice. Not applicable if Radiological Safety committee approval is required (e.g. Germany)

[1] Use of retrospect ve assessments, pr or to s gn ng of nformed consent, were used f they were performed as rout ne standard of care

[2] Br ef phys ca exam at base ne s targeted to assess mb schem a and concurrent med ca cond t ons to assess sub ect e g b ty for study part c pat on Hea th status assessment s performed at d scharge and subsequent c n c v s ts to assess for mb schem a and other changes n med ca cond t ons that are reportab e as adverse events

[3] CK at d scharge t me po nt s obta ned on y f sub ect shows s gns or symptoms of card ac schem a CK MB s requ red f CK s e evated (≥ 2X the aboratory upper m t of norma) f CK and CK MB s e evated, and acute myocard a nfarct on s d agnosed, the sub ect w be treated accord ng to hosp ta procedures

[4] 30 day ECG s performed f sub ect exper ences any schem c symptoms s nce d scharge

[5] Ang ography pe formed both pre procedure and post procedure to record data needed for percent d ameter stenos s and other measures Add t ona ang ography may be performed at nvest gator d scret on or to assess events

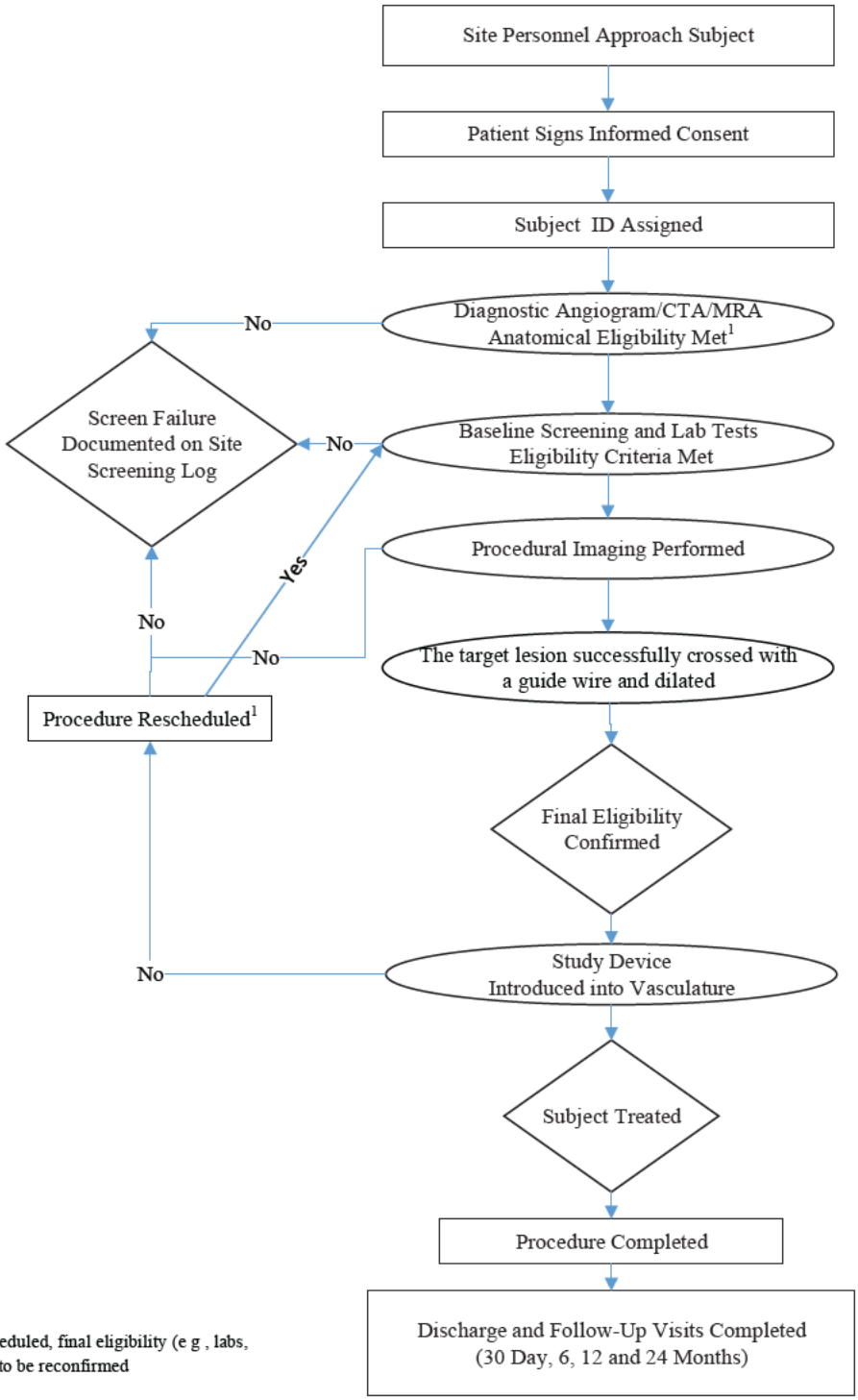
[6] Dup ex U trasound s to be comp eted at each v s t

[7] At base ne C n ca Category Sca e, dur ng fo ow up, both C n ca Catego y and C n ca mprovement Rutherford Becker Sca es

[8] Pe form Toe Brach a ndex (TB) on y f unab e to re ab y assess AB read ng Tests are performed n rest ng state Post procedure fo ow up assessments depend on wh ch test was performed pre procedure

[9] P av x s recommended for one year post procedure; ASA s recommended for a sub ects ndef n te y

Patient Screening, Enrollment and Follow-Up



[1] If procedure rescheduled, final eligibility (e g , labs, imaging) will need to be reconfirmed

Change History

Revision Letter	Change Description
A	Initial Release
A1	Amendments per Austrian EC requests
B	• Lesion length adjustment • Clinical outcome data update • Device description update • Statistical Plan update from 30 to 60 evaluable patients • Risk benefit update • Addition of x-ray at 12 month follow-up • Minor editorial updates
B1	Added "Section 18 PUBLICATIONS" as requested by Latvian Authorities
B2	Updated statistical plan rationale per Italian EC request using superiority hypothesis instead of a non-inferiority
B3	• Updated EU Rep • Updated X-Ray Language • Updated Reporting SAE (Changed to 7 Days) • Corrected typographical error-No Radiopaque Marker on the graft • Corrected Page numbering (General) • Clarified IC-10
B4	• Updated secondary safety endpoints • Updated Schedule of Assessments • Updated Section 13.0 Monitoring • Added Appendix III – Serious Adverse Event Reporting
B5	• Inclusion criterion #11 modified to reflect that if subject has 2 limbs eligible for the study, only one can be treated in the study. • Exclusion criterion #26 – updated to reflect that subject participating in another study should be excluded. • Section 2.3 – Previous Clinical Experience – Added results from STP 115 to report, including table which compares STP 185 to STP 115 as well as baseline demographics, lesion characteristics, technical success and safety and patency outcomes for the first 60 subjects through 6 months and for n=35 at 12 months. Comparison tables for safety and patency also added. • Section 11 – Statistical Plan – Modified to address BFARM questions with regards to hypothesis testing. • Section 14 - Database Management section updated to address BFARM questions with regards to data management process.
B6	• Section 11 – Statistical Plan – Modified to address BFARM question with regards to statistical tests used

2.0 INTRODUCTION

2.1 Peripheral Artery Disease Background

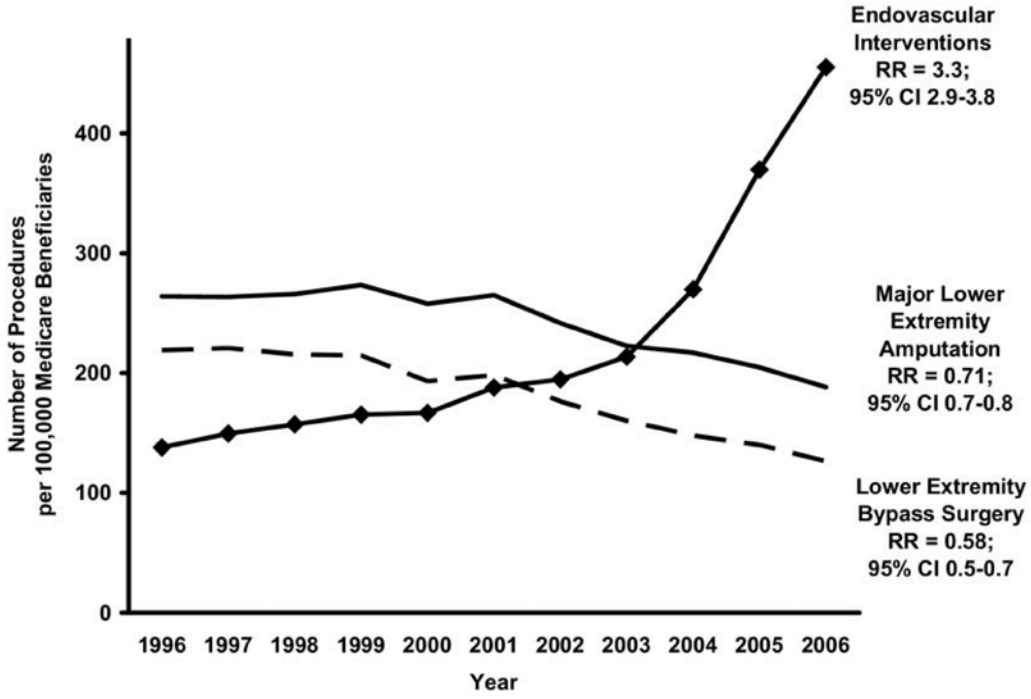
Atherosclerosis is a systemic disease process of plaque build up within arterial vessels.[1] This plaque consists of fat deposits, cholesterol, calcium and other substances, and when plaque continues to accumulate, the vessel can become hardened, narrowed and/or completely occluded. The subsequent manifestation 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]

2.2 Current Treatment Options

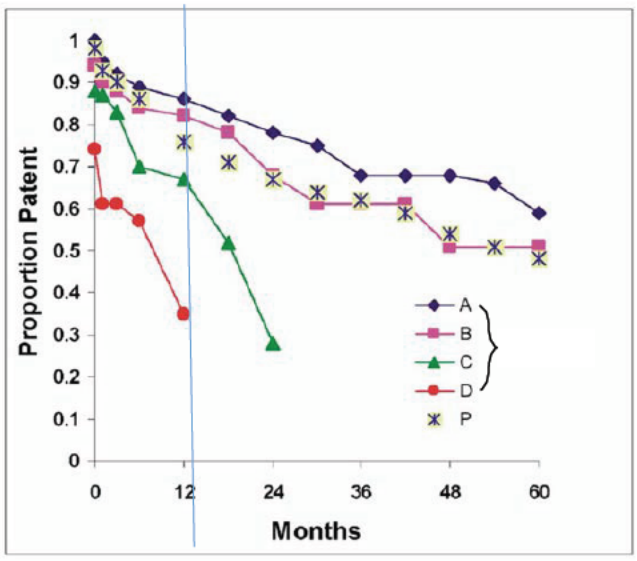
The gold standard for treating lesions in the infrainguinal segment is surgical bypass using an autologous vein. Unfortunately, adequate vein is often unavailable and the long term results of surgical bypasses using synthetic material are less satisfactory.[6] Over the past three decades, advances in endovascular technology, which is less invasive than surgery, have led to increasing use of endovascular tools in lieu of surgical options. Today, treatments are recommended based on specific lesion characteristics. The Trans Atlantic Inter Society Consensus (TASC) group recommends treatment using their Type A D classification system, which incorporates lesion length and lesion type (stenosis vs. occlusion, denovo vs. re stenosis, etc.). In 2000, the first TASC meeting recommended that TASC A lesions be treated endovascularly, TASC D lesions be treated surgically and had no recommendation for TASC B and C lesions due to lack of evidence.[7] In 2007, updated recommendations were published that both modified the classifications and recommended endovascular therapy for TASC B lesions and surgery for TASC C lesions in “good risk” patients.[8] Many in the community felt the TASC II recommendations were not representative of the latest data on novel endovascular methods, prompting critiques in favor of an “endovascular first” approach for all femoropopliteal lesion types.[9, 10,11] These critiques were consistent with the market, which increased use of endovascular therapies by 3x while reducing surgical and amputation rates from 1996 2006.[12] (**Figure 1**).

Figure 1: Trends in endovascular interventions, major amputation and lower extremity bypass surgery



The increasing trend of the "endovascular first" approach is supported by current research on endovascular and surgical outcomes. Which endovascular method to use for which lesion type, however, continues to be a research topic of interest. Percutaneous transluminal angioplasty (PTA) appears most effective in treating relatively short (<5 cm) femoropopliteal lesions with an average 12 month primary patency of 74% (61 84%).[13,14,15,16,17,18,19] With lesions longer than 5 cm, however, PTA primary patency drops to 35% (13 56%).[20,21,22,23,24,25,26,27,28] Stenting after PTA improves primary patency in lesions longer than 5 cm (mean 72%, 54 87%), but PTA and stenting for lesions >10 cm long is less effective (mean 43%, 22 55%).[13,16,18,20,24,29,30,31,32,33] In terms of TASC categories, PTA and/or stenting have outcomes equal to or better than surgery for TASC A and B lesions, but fail to match surgery's patency rates in TASC C or D lesions (**Figure 2**).[34]

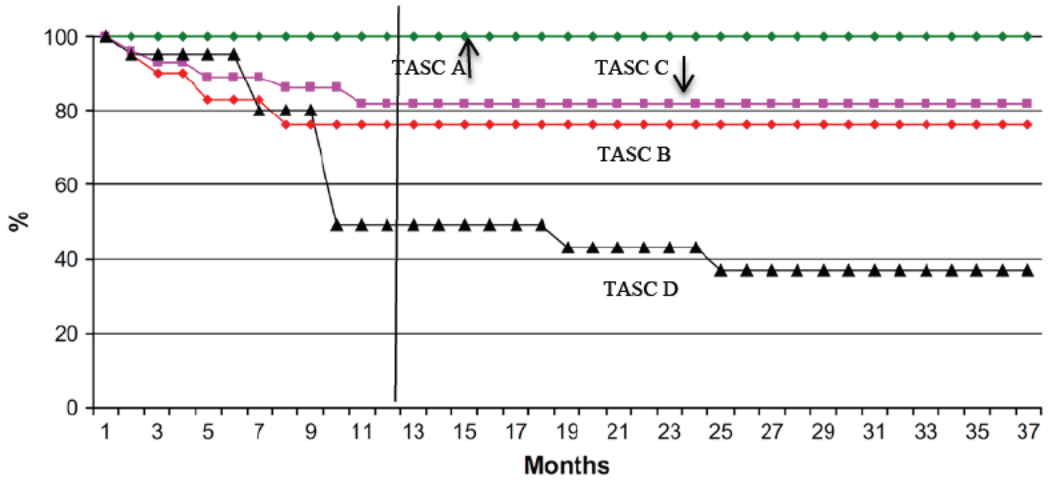
Figure 2: Primary Patency of SFA PTA and/or Stenting (letters indicate TASC lesion types [A-D] and prosthetic bypass surgery [P])



Despite lower patency in endovascular treated TASC C/D groups, investigators are divided on whether to recommend surgery as the primary treatment for long segment disease.[25,27,28,32,33,35, 36] While some cite the superior primary patency of surgical grafts as the principle metric for recommendation, others cite the overall patient experience with surgical and endovascular means and conclude that endovascular methods should be attempted prior to subjecting a patient to the risks of open surgical repair.

New evidence using "covered stents"/stent grafts may provide another useful variable to consider in treating TASC C/D lesions, or long segment disease. Like bare metal stents, covered stents/stent grafts are preceded by PTA. Unlike traditional stents, however, these devices are covered with a synthetic material; most commonly polytetrafluoroethylene (PTFE) or Dacron (knitted polyester), the same materials used for prosthetic surgical bypass. Much like investigators who theorized that a subintimal approach to long segment angioplasty would lead to better outcomes by precluding the existing atheroma from the new lumen, covered stents eliminate the previously atherosclerotic vessel from direct communication with the blood which may eliminate some of the limitations experienced by other endovascular therapies in longer lesions.[27, 37] Some of the earliest work reported in the literature began in the mid 1990's and found 79% patency at 12 months in lesions averaging 13.1cm in length (5 40cm).[37] These initial results compare very favorably to stents and PTA, both of which fail to reach 50% patency at 12 months in lesions longer than 10 cm. Since that time, a number of additional studies using stent grafts have been conducted supporting their effectiveness in long lesions; average 12 month patency is 73% in lesions between 10 15 cm and 71% in lesions between 15 26 cm.[26, 38,39, 40, 41, 42, 43, 44, 45, 46] In terms of TASC Classification, stent grafts continue to demonstrate excellent patency in more complex lesions (**Figure 3**).[38]

Figure 3: Primary Patency of SFA Stent Grafting



While TASC D patients continue to have poor prognosis compared to TASC A C, the patency rates for all lesion types are improved relative to stenting and PTA. These apparent improvements in patency have also been confirmed in prospective comparisons. One study identified 12 month patency of 75% and 28% for stent grafts and PTA, respectively, in the treatment of long segment lesions (>15 cm).[26] Another study found an equally dramatic difference with 12 month patency of 87% at 2 years in the stent graft group versus 23% with PTA in relatively short lesions (6.9 cm).[22] The leading stent graft on the market obtained FDA approval demonstrating a more modest difference in 12 month primary patency (stent grafts – 62%, PTA – 40%).[21] In the same study, the difference was more striking in long lesions (>13 cm) where the stent graft group maintained patency at a rate of 54% where the PTA group fell to 17% at 12 months. Stent grafts also fare well when compared to synthetic bypass grafting in femoropopliteal occlusive disease. A recently published four year randomized study found no difference between the stent graft and synthetic surgical bypass groups at any follow up period from 1 to 4 years in patients with an average lesion length of 25 +/ 15 cm (SD) and TASC scores distributed equally among A through D.[47]

While these findings are very promising, reports do exist that suggest stent grafts may not have an advantage over more conventional therapy. In a randomized evaluation of stent grafts and bare metal stents in long segment femoropopliteal disease (18 19 cm), no difference was identified between the two treatment groups over three years; primary patency at 3 years was 24.2% and 25.9% for the stent graft and bare metal stents, respectively.[48]

While this report highlights the difficulty in treating long lesions with either endovascular method, the collective evidence supports using stent grafts in long lesions over traditional PTA and stenting.

The PQ Bypass Stent Graft System is intended 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, covering TASC A C lesions.

There are a currently a number of similarly indicated SFA stents currently on the U.S.

market. There is however only one (1) similarly indicated stent graft one (1) on the U.S. market, the Gore Viabahn Endoprosthesis. **Table 1** summarizes the similarities and differences in technical features between the PQ Bypass Stent Graft System and the Gore Viabahn.

Table 1 Technical Features Comparison

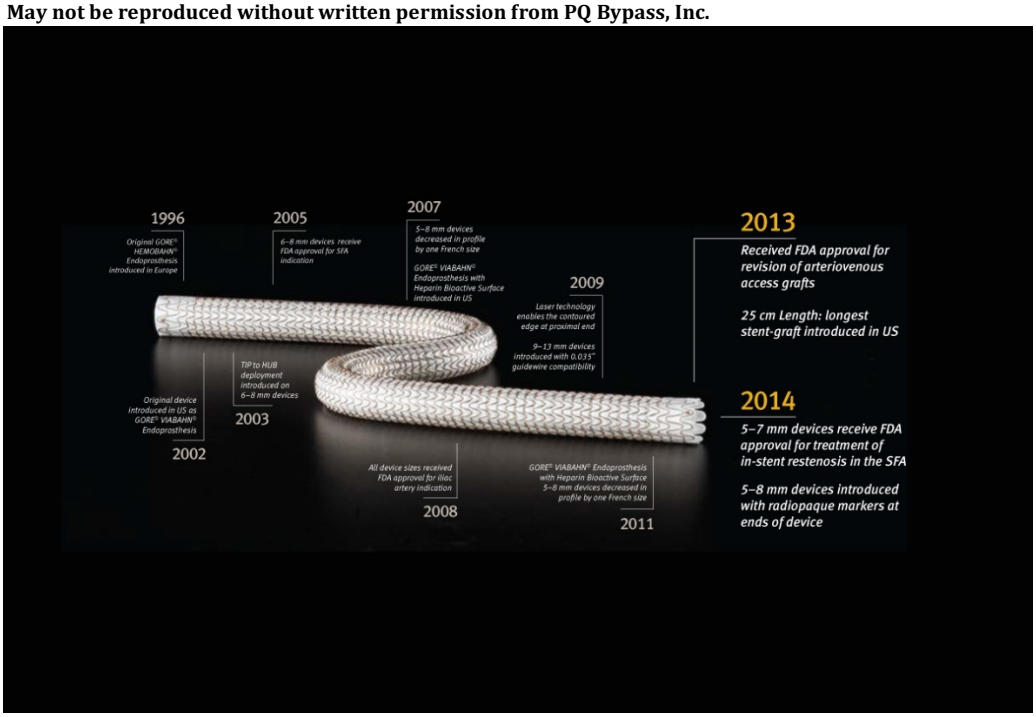
Manufacture		GORE	PQ BYPASS
Model Name		**Viabahn**	**Stent Graft System**
Market Approval		US: P040037	N/A
Design		**Single or Modular**	**Single or Modular**
Radiopaque Markers		Yes	No
Implant Materials		Expanded polytetrafluoroethylene and fluorinated ethylene propylene (**ePTFE** and **FEP**) graft material with a Nitinol stent.	Expanded polytetrafluoroethylene and fluorinated ethylene propylene (**ePTFE** and **FEP**) graft material with a Nitinol stent
Heparin coating		Yes	No
Stent Graft Construction		Expanded polytetrafluoroethylene (ePTFE) liner attached to an external nitinol stent structure	Layer of ePTFE wrapped on both inner and outer Nitinol stent structure, with FEP wrap at both ends
Stent Encapsulation		No	Yes
Expansion Design		Self-expanding	Self-expanding
Fixation Mechanism		Radial force	Radial force
Sizes	**Length cm**	2.5, 5, 10, 15, 25	10, 15, 20
	Diameter (mm)	5, 6, 7, 8, 9, 10, 11, 13	5.5, 6, 7
Catheter Profile (Fr)		7, 8, 9, 11, 12	8
Device Image			

The Gore Viabahn has a long history of use in the SFA whose results are widely documented in a number of landmark clinical trials:

https://www.goremedical.com/products/viabahn?locale=mpd_na.

The Gore Viabahn has continued to evolve over the year as illustrated in the **Figure 4** below.

Figure 4: Gore Viabahn Evolution



Once CE Marked and FDA approved, the PQ Bypass Stent Graft would constitute a second SFA indicated stent graft. The PQ Bypass stent graft present however several distinct design differences over the Gore Viabahn including:

- A higher radial force designed to reduce kinking and fracture
- Exposed nitinol proximal end edge designed to reduce risk of edge stenosis
- Tapered distal end radial force designed to allow the stent graft to tapper naturally with the vessel diameter
- Nitinol stent encapsulated in ePTFE designed to limit nitinol exposure in the vessel

It is believed that these design differences will result in distinct clinical advantages over the Gore Viabahn

2.3 Previous Clinical Experience

STP - 185

To date only 12 patients have been enrolled in STP 185 study and results are still pending. First Patient for STP 185 was treated in Riga, Latvia on 02 March 2016. **Table 2** summarizes the Clinical Sites currently (conditionally) approved for the STP 185 study.

Table 2: Clinical Sites in STP-185

Number	Clinical Site	Country	Enrolled
01	Stradins University Hospital, Riga, Latvia	Latvia	9
02	Universidad Católica de Chile, Santiago, Chile	Chile	0
03	Poznan University of Medical Sciences, Poznań, Poland	Poland	0
04	Institute of Hematology Medicine, Warsaw, Poland	Poland	0
05	Gdańsk Medical University, Gdańsk, Poland	Poland	0
06	University Leipzig Medical Centre, Leipzig, Germany	Germany	0
08	San Raffaele Scientific Institute Hospital, Ospedale San Raffaele, Milano, Italy	Italy	0
09	Arcispedale Santa Maria Nuova, Reggio Emilia, Italy	Italy	0
10	Mirano Hospital, Mirano, Italy	Italy	0
12	Medical University of Graz, Austria	Austria	1
13	Hanusch Krankenhaus, Vienna, Austria	Austria	0

Table 3 summarizes basic demographic information for the first 10 patients (available data). As the study has just started outcomes will be reported as these become available in the future.

Table 3 : Demographics of First 10 Patients

Demographics	Subjects (N = 10)
Age, (years) Mean	62.5
(Range), N	(53 - 72), 10
Male Gender, (%, m/N)	90% (9/10)
SFA Lesion Length, (cm) Mean	13.8
(Range), N	(7.9 - 19.0), 10
Chronic Total Occlusion, (%, m/N)	75% (6/8)
TASC II Lesion Type, (%, m/N)	
B	30% (3/10)
C	70% (7/10)
Calcification, (%, m/N)	
Mild	29%(2/7)
Moderate	71%(5/7)
Number of Run-Off Vessels, (%, m/N)	
1	10% (1/10)
2	30% (3/10)
3	60% (6/10)

STP - 115

The PQ Bypass Stent Graft System is also currently undergoing a CE Mark study (STP 115) for the PQ Bypass procedure which represents worse case use scenario relative to placing the stent graft across lesions intra arterially.

The PQ Bypass approach to treating PAD builds on the concept of stent grafting by implementing the use of a stent graft in a manner similar to surgical bypass. The PQ Bypass procedure seeks to place stent grafts as a bypass conduit via a percutaneous method. Where standard stent grafts are placed across lesions intra arterially, the PQ Bypass stent grafts exit the artery proximal to the lesion, travel through the adjoining vein and re enter the arterial lumen at the distal reconstitution site, leaving only a small portion of a stented graft inside of the native artery and bypassing the heavily diseased area. A comparison of the two studies is provided in **Table 4.**

Table 4: Study Comparison STP 185 vs. 115

	STP185	STP115
Intended use	Revascularization of restenotic native lesions or occlusions of the SFA	Percutaneous femoropopliteal (fem-pop) bypass
Rutherford Classification	3-5	3-5
TASC II Lesion Classification	B and C	D
Lesion Length	8-18 cm	Avg. length = 28cm
Stent Graft Characteristics	Identical	Identical
Stent Graft Delivery system	Identical	Identical
Other Procedure Related Devices	None	Proximal Anastomosis Device Venous Locator

The CE Mark study is a prospective, multi center, non randomized study evaluating the safety and performance of the PQ Bypass System to access, deliver guidewires and implant stent grafts for a percutaneous femoropopliteal (fem pop) bypass.

Table 5 below is a summary of the STP 115 protocol. As noted in the inclusion exclusion criteria the population being treated involves TASC D long lesions (avg. = 28 cm) including CTOs. The results from the CE Mark study serve to support the safety profile of the Stent Graft System.

Table 5: STP 115 Protocol Summary

PQ BYPASS	PROTOCOL SUMMARY
Title:	PQ Bypass Systems for Femoropopliteal Bypass II (PQB 4 FP II)
Protocol Number	STP 115 Rev D
Study Design:	Prospective, single-arm, multi-center, international, non-randomized, pre-market, safety and effectiveness clinical investigation evaluating the PQ Bypass Systems to access, deliver guidewires and implant stent grafts for a percutaneous femoropopliteal (fem- pop) bypass.
Study Objective:	To assess the safety and performance of the PQ Bypass System to access, deliver guidewires and implant stent grafts for a percutaneous fem-pop bypass.
Enrollment:	Up to 60 subjects will undergo a percutaneous fem-pop bypass, including up to 30 subjects in Germany.
Number of Sites	Up to 17 international sites (non U.S. sites).
Study Enrollment	12-month enrollment period: • Initial enrollment: Proposed Q4, 2014 • Last enrollment: Proposed Q3, 2015
Study Duration	36 months (12-month enrollment and 24-month follow-up)
Primary Safety Endpoint:	Major Adverse Clinical Events (MACE) at 6 months. MACE is a composite endpoint defined as: 1. Death 2. Target limb amputation 3. Target vessel revascularization (TVR) 4. Major bleeding (transfusion of >2 units PRBC) 5. Deep vein thrombosis on ipsilateral limb
Primary Performance Endpoint:	The rate of primary patency at 6 months. Primary patency 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 primary effectiveness endpoint will be assessed by an independent Core Lab.
Secondary Safety Endpoints:	Major Adverse Clinical Events (MACE) will be evaluated at: 1. Discharge 2. 12 months 3. 18 months 4. 24 months
Secondary Effectiveness Endpoints:	• Technical Success defined as: successful delivery, access and placement of the investigational devices and successful removal of delivery system. • Procedural Success defined as: successful delivery, access and placement of the investigational devices in the absence of in-hospital MACE. • Clinical Success defined as improvement of at least one category using the Rutherford Clinical Severity Scale through follow-up. • The rate of primary assisted patency through follow-up defined as: revascularization of non-occlusive (<99%) stenosis within the stent graft or immediately above or

	below the treated arterial segment with less than 50% residual stenosis. • The rate of secondary patency through follow-up defined as: revascularization of occlusion (100%) within the stent graft or immediately above or below the treated arterial segment with less than 50% residual stenosis.
DSMB	A Data Safety Monitoring Board (DSMB) consisting of non-Investigator experts, will review safety data from the study and establish stopping rules for early termination of the trial. The DSMB will make recommendations based upon the safety analysis of adverse events, protocol deviations, and device failures. The DSMB will function in accordance with SOPs and applicable regulatory guidelines.
CEC	A Clinical Events Committee will review and adjudicate primary and secondary safety endpoints (including major adverse events), serious adverse events and device related adverse events.
Inclusion Criteria:	• Willing and able to provide informed consent • Age 18 or older • Rutherford Classification of 3-5 • Patent iliac and femoral arteries/veins and access vessels, of sufficient size and morphology (including tortuosity), to allow endovascular access with 8 Fr. introducer sheath • Femoro-popliteal lesions ≥10 cm in length considered to be: o Chronic total occlusion (100% stenosis) o Diffuse stenosis (>50% stenosis) with moderate to heavy calcification o In-stent restenosis (>50% stenosis) • Proximal and distal target vessels are 5.4-7.0 mm in diameter • Orifice and proximal 1 cm of SFA is patent • Patent popliteal artery 3 cm proximal to tibial plateau • At least 1 patent tibial artery to the foot • Patent femoral vein ≥ 10 mm in diameter or duplicate femoral vein • Subject has > one-year life expectancy
Exclusion Criteria:	• Age greater than 90 • Bypass length required > 30 cm • History of deep vein thrombosis • Has known hypersensitivities, allergies or contraindications to: nitinol, PTFE; aspirin, heparin, antiplatelet, anticoagulant or thrombolytic therapy; or anticoagulation or contrast media • Has a known history of intracranial bleeding or aneurysm, myocardial infarction or stroke within the last 3 months • Pregnant or nursing • Untreated flow-limiting aortoiliac occlusive disease • Has renal failure (eGFR < 30mL/min) • Major distal amputation (above the transmetatarsal) in the study or non-study limb • Patient has had a revascularization procedure on the target limb within 30 days of the planned index procedure • Patient has a planned amputation of the target limb • Previous bypass surgery on the target limb • Patient is participating in another clinical study for which follow-up is currently on going

	• Patient has a condition that in the view of the investigator precludes participation in this study
Follow-Up:	• Discharge • 30 days ± 7 days (optional, per physician practice) • 3 months ± 14 days • 6 months ± 30 days • 12 months ± 45 days • 18 months ± 45 days • 24 months ± 60 days

The CE Mark study commenced in January 2015, in Riga, Latvia (Site 01), where the first two patients were enrolled. As of May 2016, 60 subjects have been treated at 7 sites and have been followed through 6 months. Of the first 60 subjects treated, 35 have completed follow up through 12 months. Enrollment and follow up through 24 months is ongoing.

Baseline demographics and lesion characteristics for the first 60 subjects treated in STP 115 are provided below in **Table 6.** As noted in the inclusion exclusion criteria, the population being treated involves TASC C/D long lesions (avg. = 28.6 cm, 93.3% TASC D) including a large proportion (96.7%) of CTOs.

Table 6: STP 115 - Baseline Demographics and Lesion Characteristics

Baseline Demographics	Treated Subjects N = 60[1]
Age, years[2]	
Mean ± Stdev	64 ± 9
Range (N)	50 – 87 (60)
Male Gender[2], (%, n/N)	83.3% (50/60)
History of Diabetes[2], (%, n/N)	20% (12/60)
History of Smoking[2], (%, n/N)	92% (55/60)
Previous Peripheral Intervention[2], (%, n/N)	33.3% (20/60)
Lesion Characteristics	**Treated Subjects N = 60[1]**
SFA lesion length[3], cm	
Mean ± Stdev	28.6 ± 5.1
Range (N)	13.4 – 43.2 (60)
Chronic total occlusion [3], (%, n/N)	96.7% (58/60)
TASC II lesion type[3], (%, n/N)	
B	1.7% (1/60)
C	5.0% (3/60)
D	93.3% (56/60)
Calcification @ landing zones[3], (%, n/N)	
Mild	56.7% (34/60)
Moderate	28.3% (17/60)
Severe	15.0% (9/60)
Run-off vessels[3], (%, n/N)	
0	1.7% (1/60)
1	15.0% (9/60)
2	36.7% (22/60)
3	46.6% (28/60)
Rutherford Classification[2], (%, n/N)	
0	1.7% (1/60)
1	0
2	0
3	95 % (57/60)
4	1.7% (1/60)
5	1.7% (1/60)
6	0
Ankle- Brachial Index[2],	
Mean ± Stdev	0.65 ± 0.19
Range (N)	0.34 – 1.50 (59)

[1] Denom nators < 60 subjects ref ect m ss ng data.
[2] As reported on S te Case Report Forms.
[3] As assessed by Independent Med ca Rev ew.

Outcomes, including technical success, (**Table 7**), 30 day, 6 and 12 month safety (**Table 8**) and 6 and 12 month patency (**Table 11**) are presented below. The results from the CE Mark study, show low morbidity and high patency rates in TASC D lesions, serve to support the safety profile of the Stent Graft.

Technical Success is provided below in **Table 7**. Technical success is defined as successful delivery of the investigational devices to the identified area and removal of delivery system was achieved in 98.3% of subjects. One subject did not achieve technical success. In this subject, the case was aborted after several unsuccessful attempts to access the vein from the artery proximally due to the severity of the arterial calcification. The subject was discharged without issue and was exited from the study, per study protocol.

Table 7: STP 115 Technical Success

Technical Success	Treated Subjects N = 60
Technical Success[1], (%, n/N)	98.3% (59/60)

[1] Defined as successful delivery of the investigational devices to the identified area and removal of delivery system.

Safety Outcomes

Safety outcomes through 30 days and 6 and 12 months, as adjudicated by Independent Medical Review, are presented below in **Table 8**.

A Major Adverse Event (MAE) is defined as death, target limb amputation and target vessel revascularization (TVR). A Major Adverse Clinical Event (MACE) is defined as death, target limb amputation, TVR, major bleeding (transfusion of > 2 units of blood) and Deep Vein Thrombosis (DVT) on the ipsilateral limb.

Though 30 days, 3.4% subjects (2/59) experienced MAE and MACE. Two subjects underwent TVR, 1 for stent graft thrombosis and 1 for stent graft separation leading to acute limb ischemia.

Through 6 months, 10.2% of subjects (6/59) experienced MAE and MACE. In addition to the 2 subjects who experienced events through 30 days, an additional 4 subjects underwent TVR through 6 months, including 3 subjects for stent graft thrombosis and 1 subject for >50% stenosis of the stent graft. One subject (06 002) withdrew post discharge from the index procedure (no device implanted due to a technical failure) and is excluded from analysis at 30 days and 6 months.

In the 35 subjects with follow up at 12 months, 14.3% of subjects (5/35) experienced MAE, and MACE. In the 5 subjects who experienced MAE/MACE through 12 months, 3 TVR were performed for stent graft edge stenosis > 50% and 2 TVR were performed for stent graft occlusions.

To date, no subjects (0%) have died, had a target limb amputation or DVT of the ipsilateral limb or have experienced procedure related major bleeding requiring transfusion of > 2 units of packed red blood cells (PRBCs).

It should be noted that these outcomes are comparable to those reported in the literature for percutaneous SFA interventions.

Table 8: STP 115 Safety Outcomes

Safety Outcomes	30-Day Treated Subjects N = 59[1]	6-Month Treated Subjects N = 59[1]	12-Month Treated Subjects N =35
Major Adverse Events (MAE)[2], (%, n/N)	3.4% (2/59)	10.2% (6/59)[6]	14.3% (5/35)
Major Adverse Clinical Events (MACE)[3], (%, n/N)	3.4% (2/59)	10.2% (6/59)[6,7]	14.3% (5/35)
Deep Vein Thrombosis (DVT)[4], (%, n/N)	0% (0/59)	0% (0/59)	0% (0/35)
Major Bleeding[5], (%, n/N)	0% (0/59)	0% (0/59)	0% (0/35)

[1] Excludes 1 subject who did not receive an implant and withdrew from the study post-discharge.
[2] Composite endpoint defined as death, target limb amputation and target vessel revascularization as adjudicated by Independent Medical Review.
[3] Composite endpoint defined as death, target limb amputation, TVR, DVT of ipsilateral limb or bleeding event requiring transfusion > 2 units of packed red blood cells as adjudicated by Independent Medical Review.
[4] Defined as a symptomatic blood clot (thrombus) in the ipsilateral limb as adjudicated by Independent Medical Review.
[5] Defined as transfusion of >2 units packed red blood cells (PRBC)) through discharge as adjudicated by Independent Medical Review.
[6] All subjects experienced target vessel revascularizations (TVR).
[7] One subject experienced 2 events (TVR and acute limb ischemia).

Comparison of MAE Rates at 30 days and 12 Months to the Viabahn Stent Graft

MAE, defined similarly to the PQ Bypass study (all cause death, TVR and amputation of index limb) through 30 days and 12 months for the Viabahn Endoprosthesis, as reported in the literature, are presented below in **Table 9** and **Table 10**. Only studies which reported all individual events included in the MAE composite were included, so a sum total MAE rate could be calculated.

MAE rates in studies which reported on the Viabahn stent graft ranged from 0.0% to 11.1% at 30 days and from 32.5% to 50.0% at 12 months.

Table 9: Comparison of PQ Bypass 30 Day MAE Rates to Viabahn 30 Day MAE Rates as Reported in the Literature

Lead Author - Year	30 Day Death (%)	30 Day TLR/TVR (%)	30 Day Amputation (%)	Total 30 Day MAE[1] (%)
Schneider_2011[1]	0.0%	7.4%	3.7%	11.1%
Saxon_2013[2]	0.0%	0.8%	0.0%	0.8%
Lammer_2013[3]	0.0%	1.3%	0.0%	1.3%
Zeller_2014[4]	0.0%	0.0%	0.0%	0.0%
PQ Bypass Study	**0.0% (0/59)**	**3.4% (2/59)**	**0.0% (0/59)**	**3.4% (2/35)**

[1] Total MAE is a sum of the individual events and therefore may slightly overestimate the actual MAE rate, as individual patients may have had multiple MAE.

Table 10: Comparison of PQ Bypass 12 Month MAE Rates to Viabahn 12 Month MAE Rates as Reported in the Literature

Lead Author - Year	12-Month Death (%)	12-Month TLR/TVR (%)	12-Month Amputation (%)	Total 12-Month MAE[1] (%)
McQuade_2010[5]	0.0%	30.0%	2.5%	32.5%
Johnston_2012[6]	17.0%	43.0%	0.0%	50.0%
PQ Bypass Study	**0.0% (0/35)**	**14.3% (5/35)**	**0.0% (0/35)**	**14.3% (5/35)**

[1] Total MAE is a sum of the individual events and therefore may slightly overestimate the actual MAE rate, as

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[1] Schne der JR, Verta MJ, A onzo MJ, Hahn D, Pate NH, K m S. Resu ts w th V abahn-ass sted sub nt ma recana zat on for TASC C and TASC D superf c a femora artery occ us ve d sease. Vasc Endovascu ar Surg. 2011 Ju ;45(5):391-7.

[2] Saxon RR, Chervu A, Jones PA, Bajwa TK, Gab e DR, Soukas PA, Begg RJ, Adams JG, Anse GM, Schne der DB, E ch er CM, Rush MJ. Hepar n-bonded, expanded po ytetraf uoroethy ene- ned stent graft n the treatment of femoropop tea artery d sease: 1-year resu ts of the VIPER (V abahn Endoprosthes s w th Hepar n B oact ve Surface n the Treatment of Superf c a Femora Artery Obstruct ve D sease) tr a . J Vasc Interv Rad o . 2013 Feb;24(2):165-73.

[3] Lammer J, Ze er T, Hausegger KA, Schaefer PJ, Gschwendtner M, Mue er-Hue sbeck S, Rand T, Funov cs M, Wo f F, Rastan A, Gschwandtner M, Puchner S, R st R, Schoder M. Hepar n-bonded covered stents versus bare-meta stents for comp ex femoropop tea artery es ons: the random zed VIASTAR tr a (V abahn endoprosthes s w th PROPATEN b oact ve surface [VIA] versus bare n t no stent n the treatment of ong es ons n superf c a femora artery occ us ve d sease). J Am Co Card o . 2013 Oct 8;62(15):1320-7.

[4] Ze er T, Peeters P, Bos ers M, Lammer J, Brechte K, Sche nert D, Rastan A, Noory E, Beschorner U. Hepar n-bonded stent-graft for the treatment of TASC II C and D femoropop tea es ons: the V abahn-25 cm tr a . J Endovasc Ther. 2014 Dec;21(6):765-74.

[5] McQuade K, Gab e D, Pear G, et a . Four-year random zed prospect ve compar son of percutaneous ePTFE/N t no se f-expand ng stent graft versus prosthet c femora -pop tea bypass n the treatment of superf c a femora artery occ us ve d sease. J vasc Surg. 2010;52:584-91.

[6] Johnston, PC, Vartan an, SM, Runge, SJ et a . R sk factors for c n ca fa ure after stent graft treatment for femoropop tea occ us ve d sease. J Vasv Surg. 2012;56:998-1007.

individual patients may have had multiple MAE.

Patency Outcomes

Six and 12 month primary, primary assisted and secondary patency, as adjudicated by Independent Medical Review, are presented below in**Table 11**.

Primary patency is 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), with no clinically driven re intervention within the stented segment. Primary assisted patency is defined as revascularization of non occlusive (<99%) stenosis within the stent graft or immediately above or below the treated arterial segment with less than 50% residual stenosis through follow up. Secondary patency is defined as revascularization of occlusion (100%) within the stent graft or immediately above or below the treated arterial segment with less than 50% residual stenosis through follow up.

Through 6 and 12 months, primary patency was achieved in 84.7% (50/59) and 82.9% (29/35) of subjects. Of the 9 subjects who failed primary patency through 6 months, 7 subjects failed due to stent graft thrombosis and 2 subjects failed due to > 50% stenosis of the stent graft.

Table 11: STP 115 –Primary, Primary Assisted and Secondary Patency at 6 and 12 Months

Primary, Primary-Assisted and Secondary Patency	6 Month Patency Treated Subjects N = 59[1]	12 Month Patency Treated Subjects N =35
Primary Patency, (%, n/N)	84.7% (50/59)	82.9% (29/35)
Primary Assisted Patency, (%, n/N)	88.1% (52/59)	94.3% (33/35)
Secondary Patency, (%, n/N)	93.2% (55/59)	100% (35/35)

[1] Excludes 1 subject who did not receive an implant and withdrew from the study post-discharge.

Of the 9 failures through 6 months, 5 failures were attributed to the suboptimal (low) position of the proximal stent graft.

Table 12 below provides a detailed imaging based analysis which was performed on the 9 primary efficacy endpoint failures through 6 months.

Table 12: STP-115 – Description of 6 Month Primary Patency Failures

Subject ID	Index Procedure Date	Event	Proposed Cause	Associated with landing position of proximal graft?
03-011	26-Aug-15	Thrombos s	L ke y assoc ated w th ow and ng pos t on of prox ma graft.	Yes
06-005	24-Feb-16	Thrombos s	L ke y assoc ated w th ow and ng pos t on of prox ma graft.	Yes

Subject ID	Index Procedure Date	Event	Proposed Cause	Associated with landing position of proximal graft?
04-012	29-Mar-16	Thrombos s	L ke y assoc ated w th ow and ng pos t on of prox ma graft.	Yes
03-014	15-Jan-16	Thrombos s	L ke y assoc ated w th stenos s n outf ow vesse s and unfavorab e SFA/profunda rat o.	No
01-030	2-Mar-16	Thrombos s	L ke y assoc ated w th d ssect on f ap at prox ma edge.	No
16-001	6-Apr-16	Thrombos s	L ke y assoc ated w th poor outf ow and drug reg men.	No
02-001	12-Feb-15	Edge Stenos s	Def n te y assoc ated w th ow and ng pos t on of prox ma graft.	Yes
02-006	15-May-15	Edge Stenos s	Def n te y assoc ated w th ow and ng pos t on of prox ma graft.	Yes
04-009	14-Jan-16	Thrombos s	Poss b y assoc ated w th drug reg men, dehydrat on and outf ow.	No

Shaded rows indicate failures likely attributed to poor placement (too low) of the proximal stent graft.

As sub optimal PQ Bypass stent graft placement is greatly impacted by operator experience with the device and the initial 60 subjects with 6 month (and 35 subjects with 12 month follow up) results represent the initial subjects treated with the PQ Bypass stent graft, PQ Bypass expects patency results to improve as operators gain experience with the device.

As presented below in **Table 13**, primary, primary assisted and secondary patency outcomes were re assessed when failures likely associated with sub optimal proximal stent graft placement (n=5) were excluded. Primary patency at 6 and 12 months increases to 92.6% and 96.7% (29/30), respectively when failures due to sub optimal stent graft placement are excluded.

Table 13: Primary, Primary Assisted and Secondary Patency at 30 Days, 6 Months and 12 Months (Without All Patients with Failures Due to Proximal Positioning[1])

Clinical Success	Patency At 30 Days Treated Subjects N = 54[1]	Patency At 6 Months Treated Subjects N = 54[1]	Patency At 12 Months Treated Subjects N = 30[3]
Primary Patency, (%, n/N)	100% (54/54)	92.6% (50/54)[2]	96.7% (29/30)
Primary Assisted Patency, (%, n/N)	100% (54/54)	92.6% (50/54)	100% (30/30)
Secondary Patency, (%, n/N)	100% (54/54)	94.4% (51/54)	100% (30/30)

[1] Subjects removed from Analysis (n=5): 03-011, 06-005, 04-012, 02-001, 02-006. All failures associated with low proximal landing.

[2] Subject Failure Narratives:

04-009 - Thrombosed at 6 months, successful thrombolysis and surgical embolectomy performed. Re-thrombosis observed post-6 months with no re-intervention. Subject currently LTFU.

03-014 - Thrombosed at 3 months per site. Thrombolysis and fibrinolysis performed, however unsuccessful. Successfully

resolved with fem-fem bypass surgery.

01-030 - Thrombosed at 3 months with thrombosis expanding to side branch at 6 months. No intervention. Patient currently under observation.

16-001 - Thrombosed at 3 months. Subject stopped taking aspirin and plavix 1 week prior to thrombosis. No re-intervention to date.

[3] Subjects Removed from Analysis (n=5): 02-001, 02-006, 10-014, 01-019, 04-006 - All failures associated with low proximal landing.

Comparison of Patency Rates in Long and/or TASC D Lesions

For reference, PQ Bypass 12 month primary patency results were compared to stent and stent graft primary patency outcomes in long lesions as reported by FDA in the Summary of Safety and Effectiveness Data (SSED). As the PQ Bypass study treated long lesions (mean 28.7 cm), only lesion lengths > 15 cm as reported in SSEDs using a Peak Systolic Velocity Ratio (PSVR) of 2.4 or 2.5 were included (patency is defined as PSVR <2.5 in the PQ Bypass Study).

As presented below in **Table 14**, the weighted average 12 month primary patency rate in long lesions treated with stent and stent grafts is 52.7% and ranged from 41.7% (n=72 lesions) to 100% (n=2 lesions). As a reminder, the 12 month primary patency rate in the PQ Bypass study in 35 lesions is 82.9% (29/35).

Table 14: Primary Patency at 12 Months in Long Lesions in Original Recently Approved PMA and a Gore Viabahn PMA Supplement

Device	Device Type	Definition of Long Lesion	Number of Long Lesions with Primary Patency Results	Stent and Stent Graft 12 Month Primary Patency in Long Lesions
P040037 Supplement 060 (25cm Trial) **GORE VIABAHN® Endoprosthesis** **W.L. Gore Associates, Inc.**	Stent Graft	Mean lesion length 26.5 ± 5.3	62	67%
P160004 **GORE TIGRIS Vascular Stent** **W.L. Gore & Associates**	Stent	Lesions > 16 cm	72	41.7%[1]
P140028 **Innova Vascular Self-expanding Stent** **Boston Scientific Corporation**	Stent	18 – 20 cm stents	36	47.2%
P140002 **Misago Peripheral Self-Expanding Stent System**	Stent	Lesions > 15 cm	13	53.8%
P120002 **SMART Control and SMART Vascular Stent System** **Cordis Corporation**	Stent	Lesions > 15 cm	2	100.0%
Weighted Averages in Long Lesions			**185**	**52.7%**

[1] Primary patency of 42.1% reported in 19 lesions > 20 cm.

PQ Bypass 12 month primary patency results were then compared to Viabahn Endoprosthesis

primary patency outcomes in TASC D lesions as reported in the literature. As 97% of the PQ Bypass study subjects had TASC II D lesions, only published literature which reported outcomes of TASC D lesions were included.

As presented below in **Table 15** the weighted average 12 month primary patency rate of TASC D lesions treated with the Viabahn Endoprosthesis, as reported in the literature, was 69.1%. As a reminder, the 12 month primary patency rate in the PQ Bypass study in 35 lesions is 82.7% (29/35).

Table 15: Primary Patency at 12 Months in TASC D Lesions Treated with the Viabahn Endoprosthesis as Reported in the Literature

Lead Author - Year	Number of TASC D Lesions	Viabahn 12 Month Primary Patency TASC D Lesions (%)
Schneider_2011[1]	20	68.0%
Lensvelt_2012[7]	33	69.7%
12M N	**53**	**69.1% (Weighted Average)**

PQ Bypass 12 month primary patency results were then compared to outcomes of surgical bypass with a synthetic graft as reported in the literature. As the PQ Bypass study treated long TASC D lesions (mean 28.7 cm with 97% TASC D), only published literature which reported outcomes of either a) lesions with a mean lesion length > 18 cm or b) a substantial (>50%) proportion of TASC D lesions, were included.

As presented below in **Table 16,** 12 month primary patency rates in long lesions treated with synthetic stent grafts, as reported in the literature, ranged from 76% to 88.0%. As a reminder, the 12 month primary patency rate in the PQ Bypass study in 35 lesions is 82.7% (29/35), which is in line with the patency results of bypass surgery with synthetic grafts.

It should be noted that none of the articles report outcomes for TASC II D lesions separately. Primary patency results for exclusively TASC D lesions are expected to be lower than in articles which combine TASC II A, B, C and D lesions (McQuade et al[5]) or TASC II C and D lesions (Linnakoski et al[8] and Dosluoglu et a[9]). Therefore, the patency rates presented below are assumed to be an overestimation of primary patency rates in exclusively TASC II D lesions.

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[8] L nnakosk H, Uurto I, Suom nen V, Vakh tov D, Sa en us J. Compar son of above-the-knee prosthet c femoro-pop tea bypass versus percutaneous trans um na ang op asty and stent ng for treatment of occ us ve superf c a femora artery d sease. Scand J Surg. 2013;102(4):227-33.

[9] Dos uog u HH, Cherr GS, La P, Harr s LM, Dryjsk ML. Stent ng vs above knee po ytetraf uoroethy ene bypass for TransAt ant c Inter-Soc ety Consensus-II C and D superf c a femora artery d sease. J Vasc Surg. 2008 Nov;48(5):1166-74.

Table 16: Synthetic Surgical Bypass Vascular Graft Lit Search – Effectiveness Outcomes

Lead Author - Year	Synthetic Surgical Bypass 12 Month Primary Patency (%)
Dosluoglu_2008[9]	81.0%
McQuade_2010	76.0%
Linnakoski_2013	88.0%

[1] Estimated from Kaplan-Meier (or Life-Table) curves.

Summary

In summary, MAE rates at 30 days and 12 months for subjects treated in the PQB 4 FP II Study compare favorably to MAE rates for the Viabahn stent graft in long and/or TASC D lesions as reported in published literature (**Table 17** below). Thirty day and 12 month MAE rates for initial subject in the PQ Bypass Study of 3.4% and 14.3% while MAE rates for the Viabahn Endoprosthesis range from 0.0% to 11.1% at 30 days and 32.5% to 50% at 12 months.

Table 17: PQ Bypass 30 Day and 12 Month MAE Rates as Compared to Viabahn as Reported in the Literature

Lead Author - Year	30 Day MAE Rate[1] (%)	12-Month MAE Rate[1] (%)
Schneider_2011	11.1%	N/A
Saxon_2013	0.8%	N/A
Lammer_2013	1.3%	N/A
Zeller_2014	0.0%	N/A
McQuade_2010	N/A	32.5%
Johnston_2012	N/A	50.0%
PQ Bypass Study	**0.0% (0/35)**	**14.3% (5/35)**

[1] Total MAE is a sum of the individual events and therefore may slightly overestimate the actual MAE rate, as individual patients may have had multiple MAE.
N/A = Not applicable.

The 12 month primary patency rate for subjects treated in the PQB 4 FP II Study as compared to long and/or TASC D lesions treated with stents, stent grafts (Viabahn) and bypass surgery with synthetic grafts as reported in either SSEDs or in published literature are presented in

Table 18Table 18 below.

The 12 month primary patency rate in the PQB 4 FP II Study of 82.9% compares favorably to primary patency rates of: a) stent and stent grafts as reported in SSEDs in long (>15 cm) lesions (52.7% weighted average), b) the Viabahn stent graft in TASC D lesions as reported in the literature (69.1% weighted average), and c) synthetic surgical bypass grafts in TASC D lesions as reported in the literature (range from 76% to 88%). The 12 month primary patency rate in the PQB 4 FP II Study of 82.9% was achieved in lesions that were, on average, longer than the average lesion length reported in both SSED and the literature, and included a much higher proportion of TASC D lesions (97%) than reported in both SSEDs and the literature. Hence, favorable 12 month patency rates were achieved in complex femoropopliteal lesions.

Also, improved patency rates are expected as operators gain experience with the device.

Table 18: Comparison Table of 12 Month Primary Patency Rates in Long and/or TASC D Lesions treated

Primary Patency	PQB 4 FP II Study 12 Month Patency N = 35	Stents and Stent Grafts in Long Lesions 12 Month Patency[2]	Viabahn in TASC D Lesions 12 Month Patency[3]	Surgical Bypass in TASC D Lesions 12 Month Patency (Prosthetic)[4]
Primary Patency, (%, n/N)	**82.9%** (29/35)	**52.7%**	**69.1%**	**76.0 - 88.0%**
Primary Patency, (%, n/N) Excluding failures due to sub-optimal proximal graft placement[5]	**96.7%** (29/30)	**N/A -**	**N/A**	**N/A -**

[1] Summary of Safety and Effectiveness Data (US IDE data). Weighted Average of primary patency in long lesions where patency reported using PSVR ≤ 2.4 / 2.5

[2] Weighted average of long lesions (> 15 cm) as reported in the literature.

[3] Weighted average of TASC D lesions as reported in the literature.

[4] Patency ranges based on TASC D lesions as reported in the literature.

[5] Excludes failures associated with low proximal landing including: 02-001, 02-006, 10-014, 01-019, 04-006.

PSVR = Peak Systolic Velocity Ratio.

N/A = Not Applicable.

Conclusion

In conclusion, based on comprehensive literature reviews of both predicate Viabahn Endoprosthesis and synthetic surgical grafts and clinical studies in humans utilizing the PQ Bypass Stent Graft System, the PQ Bypass SGS is safe and effective for its intended use, to place stent grafts in the peripheral vasculature to improve blood flow in patients with peripheral artery disease.

Safety and effectiveness outcomes are consistent with EU cleared devices including the Viabahn Endoprosthesis and synthetic surgical bypass grafts in subjects with long and/or TASC II C and D lesions.

3.0 DEVICE / TECHNOLOGY DESCRIPTION

3.1 Introduction

PQ Bypass designs and manufactures the PQ Bypass Stent Graft System (SGS). The SGS is comprised of a Stent Graft and a Stent Graft Delivery System and is intended to place stent grafts in the peripheral vasculature to improve blood flow.

3.2 Device Characteristics

The PQ Bypass Stent Graft System device characteristics are listed in Fehler! Verweisquelle konnte nicht gefunden werden.

: Device Characteristics

Characteristic	Description
Design	Peripheral stent graft
Radiopaque Markers	No
Implant Materials	Expanded polytetrafluoroethylene (ePTFE) graft, nitinol stent.
Stent Graft Construction	Single nitinol wire shape set in a helical, sinusoidal pattern and encapsulated in expanded Polytetrafluoroethylene (ePTFE) film.
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
Catheter Guidewire Compatibility	0.035”
Catheter Introducer Compatibility	8F
Sizes	
Length	100, 150 & 200 mm
Diameter	5.5, 6 & 6.7 mm
Safety Features	Atraumatic Tip

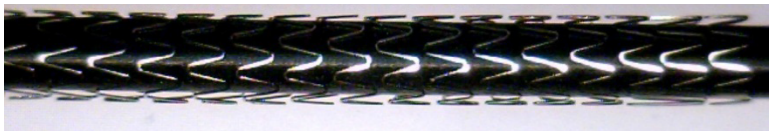
3.3 Stent Graft

The PQ Bypass Stent Graft (SG) is a flexible, self expanding composite structure made of a NiTi wire frame encapsulated in an Expanded Polytetrafluoroethylene (ePTFE) film. The SG is pre loaded on the Stent Graft Delivery System (SGDS). The SG uses a standard crowned wire frame design that exhibits twice the radial strength as commercially available stent grafts with comparable bending capability without kinking **Figure 5**.

Figure 5: PQ Bypass Stent Graft Encapsulated in ePTFE

The SG frame is a nitinol (NiTi) wire formed structure. It is made from a single 0.008" diameter NiTi wire that is shape set and electropolished. The NiTi frame is wrapped in a helical, sinusoidal pattern with seven (7) crowns per revolution. To maintain flexibility when covered, the frame has a compression gap between adjacent helical wraps to achieve the required flexibility. Each crown has a radius with varying crown length based on the diameter of the stent graft.

Figure 6: NiTi Wire Frame (pictured on a process mandrel)



The NiTi wire frame is encapsulated by the ePTFE material. Due to the frame design, the cover could be applied to both the inner and outer lumen and still maintain flexibility and compressibility. The inner and outer lays of the Cover are thermally laminated together.

ePTFE is a commonly used stent graft material and is considered the 'material of choice' for grafts. It is currently used in the Gore Viabahn endovascular stent graft as well as a number of AAA stent grafts:

- Endologix Powerlink/ AFX
- Trivascular – Ovation
- Gore – Excluder

The PQ Bypass supplier of ePTFE is Zeus Industrial Products, Inc. the same supplier as for the Endologix AAA stent grafts. The Stent Graft is available in lengths of 100, 150 and 200 mm (**Table 19** and **Table 20**).

Table 19: Sizing – Vessel Diameter

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	100, 150, 200	5
6.0	5.4-6.0	100, 150, 200	6
6.7	6.1-6.7	100, 150, 200	7

Table 20: Stent Graft Catalogue Numbers

Catalog Number	Description
SGS-5.5X100	Stent Graft System – 5.5 mm X 100 mm
SGS-5.5X150	Stent Graft System – 5.5 mm X 150 mm
SGS-5.5X200	Stent Graft System – 5.5 mm X 200 mm
SGS-6X100	Stent Graft System – 6 mm X 100 mm
SGS-6X150	Stent Graft System – 6 mm X 150 mm
SGS-6X200	Stent Graft System – 6 mm X 200 mm
SGS-6.7X100	Stent Graft System – 6.7 mm X 100 mm
SGS-6.7X150	Stent Graft System – 6.7 mm X 150 mm
SGS-6.7X200	Stent Graft System – 6.7 mm X 200 mm

PQ Bypass ensures that the raw materials used to manufacture the implant components of the PQ Bypass Stent Graft System conform to applicable standards and/or PQ Bypass material specifications via raw material certifications, certificates of conformance, and evidence of material testing provided by approved PQ Bypass suppliers who manufacture the components. The implantable raw material properties are listed in **Table 21.**

Table 21: Implantable Raw Material Properties

Description	Material Type	Raw Material Properties	
Wire Frame	Nitinol	Af Temperature:	14±4°C
		Upper Plateau Stress:	≥483 MPa
		Lower Plateau Stress:	≥ 138 MPa
		Permanent Set after 8% Strain:	≤ 0.5%
		Ultimate Tensile Strength:	≥1000 MPa
		Elongation at Ultimate Tensile Strength:	≥10%
Stent Graft Cover	ePTFE	Permanent Set After 8% Strain:	≤ 0.3%
		Ultimate Tensile Strength:	≥1100 MPa
		Elongation at Ultimate Tensile Strength:	≥10%

Description	Material Type	Raw Material Properties	
		Upper Plateau Stress:	≥483 MPa
		Lower Plateau Stress:	≥ 138 MPa
		Permanent Set after 8% Strain:	≤ 0.5%
		Ultimate Tensile Strength:	≥1000 MPa
		Elongation at Ultimate Tensile Strength:	≥10%
Stent Graft Cover End Wrap	Fluorinated ethylene propylene (FEP)		

3.4 Delivery Catheter

The Stent Graft Delivery System (SGDS) is an 8 F. system. It is compatible with a 0.035" guidewire and has a 135 cm working length. The handle of the delivery system consists of an internal pulley mechanism activated through turning an external knob. The handle also features the fluid flush insertion point for the inner lumen. The SGDS is a familiar design, which uses an outer sheath to maintain the SG in a compressed state. Once at the target site, the user can slide the outer sheath proximally by turning the knob to expose the SG, which is self expanding. The SGDS has radiopaque markers on both the proximal and distal ends of the SG landing zone (area where SG is located), as well as a marker band on the outer sheath to allow visualization of the sheath during deployment. The SGDS is shown below.

Figure 7: PQ Bypass Stent Graft Delivery System

The outer sheath of the SGDS consists of PTFE liner, braid, and pebax layers laminated together. The proximal area of the outer sheath (area behind the SG) consists of a second layer of extrusion to reduce stretching during SG deployment.

The inner shaft of the SGDS consists of a polyimide guidewire lumen, which has a Pebax section where the SG is compressed to minimize movement during deployment. Proximal to this section, the inner shaft has a proximal stop bushing, followed by a solid wound coil that runs the entire length of the inner shaft to the handle. The proximal stop bushing reacts to the compressive load on the inner shaft created during stent graft deployment. The coil

reacts to this same load, but transfers it to the handle section, which is rigid.

The outermost sheath of the SGDS, or the tri axial layer, isolates the outer shaft from friction induced by the valve of the introducer sheath, the vessel walls, and other sources of interference. This allows the outer shaft to be retracted with a lower deployment force, and for the SG to be deployed more accurately.

3.5 Mechanism of Action

The PQ Bypass Stent Graft System delivers an individual Stent Graft via a manual catheter delivery system.

3.6 Device Materials

The PQ Bypass Stent Graft System is constructed using known manufacturing processes and materials commonly used in the medical device industry (**Table 228**). The materials used to manufacture the PQ Bypass Stent Graft System were chosen, in part, for their long history of use in medical applications and specifically their use in cardiovascular applications. Use of these materials in limited and permanent exposure applications are well characterized, have a long history of use in the medical community, and their strength, robustness, and durability are well characterized. There are no device materials intended to come into contact with the user as the user is gloved while handling the device. The PQ Bypass Stent Graft System component materials and patient contact designations are presented in **Table 22**. Comprehensive biocompatibility testing has been completed in accordance with ISO10993 1 and FDA's Blue Book Memorandum.

Table 22: Component Material List

Component Name	Patient Contact	Material
Stent Graft- blood contact permanent implantable devices (>30 days)		
Wire Frame	Direct	Nitinol
Stent Graft Cover	Direct	expanded Polytetrafluroethylene (ePTFE)
Stent Graft Cover End Wrap	Direct	FEP
Delivery Catheter - externally communicating blood contact limited exposure device (<24 hours)		
Inner Shaft*	Direct	Polyimide, 304 Stainless Steel, PTFE, 72D Pebax, 25D Pebax, Loctite 3924, Loctite 4011, 90% PT, 10% IR (Platinum / Iridium)
Outer Shaft*	Direct	72D Pebax, 304 Stainless Steel, PTFE, 90% PT, 10% IR
Tri-Axial Sheath*	Direct	72D Pebax, 304 Stainless Steel, PTFE, 90% PT, 10% IR
Distal Tip*	Direct	63D Pebax
Hypotube	Direct	316 Stainless Steel
SST Coil*	Direct	300 Stainless Steel
Female to Female Luer Lock Connector	Direct	Polypropylene
O Ring	Direct	Nitrile (Buna 70)
Marker Band*	Direct	90% PT, 10% IR
T-plunger Syringe	Direct	Polypropylene
Delivery Catheter – non-patient contacting		

Component Name	Patient Contact	Material
Handle y Catheter	None	ABS Lustran 248FC
Latch, Seal Container, Pulley	None	PC Lexan 124R
Seal	None	VMQ ML-254 Transp
String	None	Polyester
Tri-axial Sheath & Syringe Handle Sleeve, Proximal Syringe Handle	None	Polycarbonate

3.7 Principles of Operation

The PQ Bypass Stent Graft System is intended to improve blood flow in patients with peripheral artery disease.

The device is intended to be introduced percutaneously. Method of vascular access is at the discretion of the attending physician. Once arterial access is achieved, a stiff 0.035" guidewire is inserted and advanced into the femoral under fluoroscopy. An angiographic pigtail catheter is back loaded over the wire and an angiogram is performed in the customary fashion. Diameter measurements of the femoral and/or popliteal vessels are performed to confirm vessel sizing. Once the artery diameters are confirmed the device size best suited for the patient's anatomy is selected.

3.8 User Interface

The PQ Bypass Stent Graft System currently requires one operator to deploy using standard percutaneous techniques. The PQ Bypass Stent Graft System does not interface and/or interact with other devices with the exception of standard ancillaries such as sheaths, guidewires, balloons, etc.

4.0 PROPOSED INTENDED USE

The 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.

5.0 STUDY DESIGN

5.1 Study Design

Prospective, single arm, multi center, international, non randomized, pre market, safety and effectiveness clinical investigation.

5.2 Study Endpoints

Primary Safety Endpoint:

The primary safety endpoint for this study is 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.

Primary Effectiveness Endpoint:

The primary effectiveness endpoint is defined as stent patency as evidenced by a peak systolic velocity ratio (PSVR) < 2.5 from DUS obtained within the 12 month visit window with no clinically driven re intervention within the stented segment.

Secondary Safety Endpoints:

Secondary safety endpoints will be evaluated and include:

1. The combined rate of death at 30 (±7) days, target lesion revascularization (TLR), index limb amputation, and an increase in Rutherford Becker Classification by 2 classes (comparing pre to post procedural assessments) at 12 months.
2. Major adverse vascular event (MAVE) at 30 days, 6 months (180 ± 14 days) and 12 months (360 ± 30 days) defined as stent thrombosis, target limb amputation, clinically apparent distal embolization, defined as causing end organ damage (e.g. lower extremity ulceration, tissue necrosis, or gangrene), procedure related arterial rupture, acute limb ischemia, or bleeding event requiring transfusion.
3. The combined rate of serious procedural adverse events, including death, myocardial infarction, index limb amputation, and access site and treatment site complications requiring surgery, blood transfusion (>2 units of PRBC), or prolonged hospital stay within 30 days of the index procedure.

Secondary Effectiveness Endpoints:

1. Acute technical (lesion) success, procedural success and device success.
2. Ankle Brachial Index (ABI) and Toe Brachial Index (TBI) at 1, 6 and 12 months.
3. Target vessel revascularization (TVR) at 6 and 12 months.
4. Limb ischemia by Rutherford Becker Classification at Baseline, 1, 6, and 12 months.
5. Number of any type of index limb amputations at 6 and 12 months.
6. Absolute Claudication Distance as measured by the Exercise Tolerance Test (TASCII) assessed in 100 subjects at baseline, 1, 6, and 12 months.
7. Target lesion revascularization (TLR) at 1, 6 and 12 months.

8. The rate of primary assisted patency through follow up defined as: revascularization of non occlusive (<99%) stenosis within the stent graft or immediately above or below the treated arterial segment with less than 50% residual stenosis.
9. The rate of secondary patency through follow up defined as: revascularization of occlusion (100%) within the stent graft or immediately above or below the treated arterial segment with less than 50% residual stenosis.

Additional Secondary Endpoints:

The following additional endpoints will also be reported:

1. A combined rate of death at 30 days, or TLR, index limb amputation, and an increase in Rutherford Becker Classification by 2 classes (comparing pre to post procedural assessments) measured at 24 months.
2. Target vessel revascularization (TVR) at 24 months post procedure.
3. Limb ischemia improvement by Rutherford Becker (improvement in scale by ≥ 1) at 24 months.
4. Major Adverse Vascular Event (MAVE) by 24 months, defined as: Stent thrombosis, target limb amputation, or clinically apparent distal embolization, defined as causing end organ damage (e.g. lower extremity ulceration, tissue necrosis, or gangrene).
5. Procedure related arterial rupture, acute limb ischemia, or bleeding event requiring transfusion. Number of any type of index limb amputations at 24 month follow up. Target lesion revascularization (TLR) at 24 months post procedure.

5.3 Study Duration

This study is expected to commence enrollment in the first quarter of 2016. Enrollment of all subjects is expected to be completed in the second quarter of 2016.

5.4 Number of Subjects and Sites

Up to 65subjects may be enrolled. A total of 60 evaluable subjects with a documented untreated, atherosclerotic lesions of the native superficial femoral artery (SFA) or the superficial femoral and proximal popliteal arteries, suitable for treatment with PQ Bypass™ Stent Graft System.

5.5 Inclusion Criteria

The subject must meet all of the following criteria at the time of eligibility:

1. Age ≥ 18 years and of age of legal consent.
2. Women of child bearing potential must have a negative pregnancy test within 7 days prior to the index procedure.
3. Subject has lifestyle limiting claudication or rest pain (Rutherford Becker scale 2 4*) with a resting ABI < 0.9. Resting TBI is utilized only if unable to reliably assess ABI. TBI must be <0.7. These assessments are required for the target limb, but both limbs are preferred.
4. A superficial femoral artery lesion with >50% stenosis or occlusion which requires treatment.

5. Stenotic lesion(s) or occluded length within the same vessel (one long or multiple serial lesions) ≥ 80mm to ≤ 180mm.
6. Reference vessel diameter (RVD) ≥ 5.0mm and ≤ 6.7 mm, angiographically/CTA/MRA defined.
7. Patent popliteal artery 3 cm proximal to tibial plateau
8. At least 1 patent tibial artery to the foot (<50% stenosis)
9. The target lesion(s) can be successfully crossed with a guide wire and dilated.
10. Adequate aortoiliac or common femoral "inflow" is defined as <30% stenosis after either PTA or stenting of the inflow lesion. After treatment of the inflow lesion, the residual pressure gradient across the target lesion will be obtained and if the peak to peak pressure gradient is < 20mmHg, the subject will be included in the study. Subjects enrolled with aortoiliac or common femoral artery lesions resulting in poor inflow, must be treated prior to receiving the study treatment. (Same Day or earlier)
11. If a subject has bilateral obstructive SFA disease, only 1 leg may be treated with the investigational device in the study.
    a. If the study leg is treated first, the contra lateral procedure should not be performed until at least 30 days after the index procedure (staged); and should only be performed with an approved (CE Marked) device.
    b. If the contra lateral leg is treated with an approved (CE Marked) device prior to treatment of the study leg, treatment of the contra lateral leg should be performed at least 15 days prior to the treatment of the study leg.
12. The subject is eligible for standard surgical repair, if necessary.
13. A subject who requires a coronary intervention should have it performed at least 30 days prior or 30 days post the treatment of the target lesion.
14. Subject must provide written informed consent.
15. Subject must be willing to comply with the specified follow up evaluation schedule.

*Note – Patients with stage 2 Rutherford classification can be included when conservative physical and drug therapy have been unsuccessful and documented.

5.6 Exclusion Criteria

The following must NOT be present at the time of subject eligibility:

1. Age greater than 90
2. Thrombophlebitis, within the previous 30 days.
3. Receiving dialysis or immunosuppressant therapy within the previous 30 days.
4. Thrombolysis of the target vessel within 72 hours prior to the index procedure, where complete resolution of the thrombus was not achieved.
5. Stroke within the previous 90 days.
6. Ipsilateral femoral aneurysm or aneurysm in the SFA or popliteal artery.
7. Required stent placement via a popliteal approach.
8. Procedures which are pre determined to require stent in stent placement to obtain patency, such as in stent restenosis.
9. Significant vessel tortuosity or other parameters prohibiting access to the lesion or 90° tortuosity which would prevent delivery of the stent device.
10. Required stent placement within 1 cm of a previously deployed stent.
11. Known allergies to any of the following: aspirin and clopidogrel bisulfate (Plavix®),

ticlopidine (Ticlid ®), and prasugrel (Effient®); heparin; Nitinol (nickel titanium); or contrast agent, that cannot be medically managed.

12. Presence of thrombus prior to crossing the lesion.
13. Known or suspected active infection at the time of the procedure.
14. Use of cryoplasty, laser, or atherectomy devices in the target vessel at the time of index procedure.
15. Restenotic lesion that had previously been treated by atherectomy, laser or cryoplasty within 3 months of the index procedure.
16. History of neutropenia, coagulopathy, or thrombocytopenia that was unexplained or is considered to be at risk for reoccurrence.
17. Known bleeding or hypercoagulability disorder or significant anemia (Hb<8.0) that cannot be corrected.
18. Subject has the following laboratory values: a. platelet count less than 80,000/µL, b. international normalized ratio (INR) greater than 1.5, c. serum creatinine level greater than 2.0 mg/dL.
19. Subject requires general anesthesia for the procedure.
20. Major distal amputation (above the transmetatarsal) in the study or non study limb.
21. Patient has had a revascularization procedure on the target limb within 30 days of the planned index procedure
22. Patient has a planned amputation of the target limb
23. Previous bypass surgery on the target limb
24. Subject is pregnant or plans to become pregnant during the study.
25. Subject has a co morbid illness that may result in a life expectancy of less than 1 year.
26. Subject is participating in an investigational study of a new drug, biologic or device at the time of study screening.

6.0 SUBJECT ENROLLMENT INFORMATION

6.1 Written Informed Consent

Subjects who meet general entry criteria will be asked to sign the study specific Ethics Committee (EC) approved Informed Consent form before any study specific tests or procedures are performed. Study personnel should explain that even if a subject agrees to participate in the study and signs an Informed Consent Form, the subject may not be eligible to participate if he/she fails screening criteria.

A Screening/Enrollment Log will be maintained to document select information about candidates who fail to meet the entry criteria.

6.2 Enrollment

Subjects will be considered enrolled into the study once informed consent has been signed and all eligibility criteria confirmed. Investigators will access the target artery using standard percutaneous techniques and devices. Patient eligibility will be confirmed prior to insertion of the study device, based on procedural angiogram, sheath placement and wire placement across lesion followed by dilatation.

6.3 Duration of Subject Participation

Subjects enrolled in the trial will participate for approximately 24 months.

6.4 Withdrawal of Subjects

Each subject may voluntarily withdraw his/her participation from the study at any time. Investigators may discontinue a subject's participation in the study as deemed appropriate per safety measures and/or if the subject's medical condition contraindicates further study participation. All enrolled subjects will undergo the complete study follow up for safety evaluation.

6.5 Lost to Follow-Up

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

- Documentation of three unsuccessful attempts on three different days over a period of three (3) months by the Investigator or his/her designee to contact the subject or next of kin, one of which should be by certified mail with signature confirmation.
- Prior agreement of the Sponsor to remove the subject from the clinical investigation

6.6 Subject Confidentiality

All information concerning subjects in this trial will be considered confidential. Only authorized PQ Bypass personnel and designated consultants and regulatory agencies will

have access to these confidential files. Enrolled subjects will be assigned a unique identifier that will be used to maintain confidentiality of each subject's medical information. Subject names and other protected health information will not be captured on the case report forms. In addition, angiographic and ultrasonic images submitted from the participating site to the Sponsor or angiographic reviewers for analysis should be redacted.

7.0 RISK-BENEFIT ASSESSMENT

7.1 Risks

There are standard risks associated with any interventional procedure or stent graft placement as well as risks specific to the PQ Bypass devices and procedure. Risks associated with any interventional procedure include access site hemorrhage or hematoma, access site pain, acute vessel closure, infection, renal insufficiency/failure due to excessive contrast load, and death.

Possible risks related to the PQ Bypass Stent Graft System include, but are not limited to, the following: thrombosis, stenosis or occlusion, aneurysm or pseudoaneurysm formation, vessel dissection, perforation or wall trauma, embolism, edema or phlebitis), arteriovenous fistula formation, bleeding infection or side branch occlusion. Adverse events are enumerated noted in **Section 12** below.

Additionally, subjects will be exposed to risks associated with conscious sedation, use of radiographic contrast and procedural medications. Subjects will be asked to take anti platelet medication for this study, such as aspirin, Plavix (clopidogrel)). These medications have been approved to reduce the risk of cardiovascular events. An Investigator will discuss with each subject the standard risks associated with these medications.

7.2 Risks Minimization

Risk Management of the PQ Bypass Stent Graft System follows a systematic approach to failure analysis, which includes both identification and mitigation of failure modes per ISO 14971 Medical Devices — Application of Risk Management to Medical Devices. Potential risk or failure mode identification will be assessed through the following tools, all of which are part of design history file:

- Device Characteristics Survey
- Hazard Analysis
- Design Failure Mode Effect Analysis (dFMEA)
- Process Failure Mode Effect Analysis (pFMEA)
- Risk Management Plan/Report

As part of each assessment, risks based on severity and probability are calculated for each potential failure mode. Potential failure modes having risks above a specified limit are mitigated and verified as a result of design changes, continued analyses, testing, and/or monitoring. For the risks that remain, protection appropriate to each risk is provided to minimize the hazard from potential device failures. Any possible adverse effect of the device constitutes an acceptable risk when weighed against the benefits to the subject and the risk is compatible with a high level of protection of health and safety. Results of the risk analysis demonstrate that use of the device as intended does not adversely affect the health or safety of the subject, user, or other person(s).

Additional efforts to minimize risk include the following:

- Clearly defining the subject inclusion/exclusion criteria.
- Selecting only qualified, experienced Investigators trained in the endovascular treatment of vascular disease who have participated in an extensive training program to assure thorough proper technique.
- Careful review of the dimensional specifications of each subject's anatomy and surrounding vasculature, including the peripheral vasculature to ensure that the subject's is anatomically appropriate for treatment with the PQ Bypass Stent Graft and that access can be achieved through the peripheral vasculature.
- Attending to proper vascular access technique to minimize the trauma to vascular structures.
- Ensuring that treatment and follow up of subjects is consistent with standard and current medical practice.
- If the Investigator determines that an adverse event is sufficiently severe to remove the subject from the study, a termination assessment will be performed and PQ Bypass will be notified. The subject will then be given appropriate treatment under medical supervision.

Risk will be mitigated by working with Investigators who are experienced and skilled in endovascular techniques including use of re entry tools and stent graft placement. Additionally, each Investigator will be thoroughly trained on proper device operation prior to device use. Risks will also be minimized in this study by adhering to the inclusion/exclusion criteria. For example, subjects with known allergies or contraindications to study medications (contrast, anti platelet) will be excluded. Risks associated with device malfunctions or failures will be minimized through bench and in vivo animal verification and validation testing prior to use in this study.

7.3 Benefits

Endovascular treatment of peripheral arterial disease (PAD) obviates the need for peripheral surgery and associated complications by using the stent/stent graft as a means of intra arterial revascularization of TASC A C lesions. Endovascular treatment can be performed safely resulting in lower morbidity and lower mortality rates than those of open surgical repair. Benefits include, but are not limited to:

- Absence of surgical incision/cut down
- Faster recovery, shorter hospital stay
- No requirement for general anesthesia in some cases
- Less post procedure pain
- Fewer complications

Subjects included in this study have lesions (TASC B and C) that are commonly treated with conventional endovascular means, including stent grafts. Based on previous treatments using commercially available devices, bench and animal testing and reported outcomes in the ongoing more challenging Bypass approach CE mark study (STP 115), it is expected that the participants in this study will have their lesions successfully treated without the need for

surgery or additional risk relative to other endovascular procedures.

The PQ Bypass Stent Graft System may allow physicians to treat challenging lesions in the femoral artery percutaneously, thereby avoiding the risks and morbidity of more invasive procedures such as surgical bypass or amputation.

8.0 STUDY PROCEDURE

8.1 Vascular Access and Guidewire Delivery

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, sheath placement and wire crossing the lesion.

8.2 Stent Graft Placement

Stent Grafts (SGs) of appropriate dimension are selected based on the instructions provided in the Stent Graft System IFU (**Appendix II**). After placement, the Investigator uses a standard balloon dilation catheter to complete stent deployment, ensuring that the balloon is only inflated within the SGs' lumen.

8.3 Follow-Up

Subjects will return to the study center at 1 month, 6 months, 12 months, and 24 months following the procedure for a follow up evaluation. The subject will undergo lower extremity arterial ultrasounds, and examined for any post procedural complications or adverse events.

9.0 MATERIALS AND METHODS

Safety and performance evaluations will be conducted throughout the study. Such evaluations will be conducted on the case report forms.

9.1 Initial Eligibility

After subjects have signed an informed consent form and before the scheduled interventional procedure, subjects will undergo an initial eligibility evaluation. This evaluation may be conducted from an office visit within the previous 90 days. The evaluation is described in the schedule of events table.

9.2 Baseline Evaluation

After subjects have signed an informed consent form and before the scheduled interventional procedure, subjects will undergo a baseline evaluation. This evaluation may be conducted from an office visit within the previous 30 days. The evaluation is described in the schedule of events table.

9.3 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 evaluation is described in the schedule of events table.

9.4 Discharge Evaluation

The discharge evaluation is described in the schedule of events table. CK at discharge is to be obtained only if subject shows signs or symptoms of cardiac ischemia. CK MB is required if CK is elevated (≥ 2X the laboratory upper limit of normal).

9.5 Follow-Up Evaluation

A follow up evaluation will be conducted at 30 day, 6 months, 12 months and 24 months following the procedure or when a subject withdraws prematurely. The evaluation is described in the schedule of events table.

Patients will be exited from the study after the last trial visit and will undergo further follow up at the discretion of their treating physician per the standard of care. It is however recommended that a doppler ultrasound be performed at least annually post study exit through 5 years (additional 3 years post follow up) for monitoring purposes. A further recommendation is to maintain dual antiplatelet therapy (Aspirin and Plavix) indefinitely. An information sheet will be provided to the patient upon study exit that contains these recommendations for the treating physicians.

Patients will be provided an implant card at the time of hospital discharge that contains the patient´s name, device name, device model number, serial number of the implant,

manufacturer's information, date of implantation, and facility at which the implantation was carried out.

10.0 INVESTIGATIONAL DEVICE DISTRIBUTION AND ACCOUNTABILITY

10.1 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 turned to PQ Bypass in a Device Accountability Log provided by PQ Bypass.

10.2 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 subject enrollment or at the conclusion of the study.

11.0 ENDPOINTS AND STATISTICAL ANALYSIS PLAN

11.1 Endpoints Analyses and Reporting of Results

The study objective is to assess the safety and performance of the PQ Bypass Stent Graft System to access, deliver guidewires and implant stent grafts. The statistical methods for the primary endpoints are pre specified in this analysis plan and cannot be changed at the time of analysis.

All subjects will be followed on an intent to treat basis. The device performance will be assessed based on a per protocol analysis of the primary safety and effectiveness endpoints. An Intent to treat analysis, along with other secondary analyses, will also be completed and reported. Demographic, baseline clinical and disease characteristics, procedural results and primary, secondary and all additional endpoints will be summarized using descriptive statistics. All statistical analyses will be performed using SAS for Windows version 9.1 or higher.

As noted above, up to 65 subjects with a documented untreated, atherosclerotic lesions of the native superficial femoral artery (SFA) or the superficial femoral and proximal popliteal arteries, suitable for treatment with PQ Bypass Stent Graft may be enrolled in the study to ensure an appropriate sample size of 60 evaluable subjects post treatment.

- Safety assessment will be achieved by recording and measuring Major Complication rates/Serious Adverse Event rates associated with the PQ Bypass stent grafts. The primary safety endpoint (MAE) and MAVE will be presented using descriptive statistics at various time intervals. Using the Wilson Method, the one sided upper 95% confidence bound will be calculated and presented.
- The primary performance hypothesis will be tested by calculating the one sided 95% lower confidence limit for the rate of successful performance using the Wilson Method. If the lower limit exceeds the performance goal rate of 70% the null hypothesis will be rejected and the endpoint will be met. In addition to hypothesis testing, descriptive statistics of the primary performance endpoint will include the total number and percentage of patent PQB grafts.
- Descriptive statistics of the primary performance endpoint which includes total number of patent PQ Bypass grafts, percentage of patent PQ Bypass grafts, and the one sided 95% CI of the percentage using the Score approximation will be presented. The lower bound of the one sided 95% CI will be will be calculated and presented.

- The secondary endpoint of primary assisted and secondary patency will be summarized using Kaplan Meier survival analysis. Life tables will be created and a Kaplan Meier survival curve will be presented.

- Other secondary endpoints will be summarized by providing point estimates,

number of subjects, and 95% confidence bounds calculated using the Score approximation.

The primary patency rate of the PQ Bypass Stent Graft is expected to be superior to a historical control rate due to its design in lesion lengths 8 18 TASC B C lesions.

In order to establish a historical control rate, a literature review was performed on reported patency outcomes for percutaneous treatment of lesions between 8 18 centimeters in length corresponding to TASC II B and C Lesions Results are illustrated in **Figure 8** and **Figure 9** below. References on file at PQ Bypass.

Figure 8: Reported Patency Rates Across TASC II Class A-D Modalities Over Time

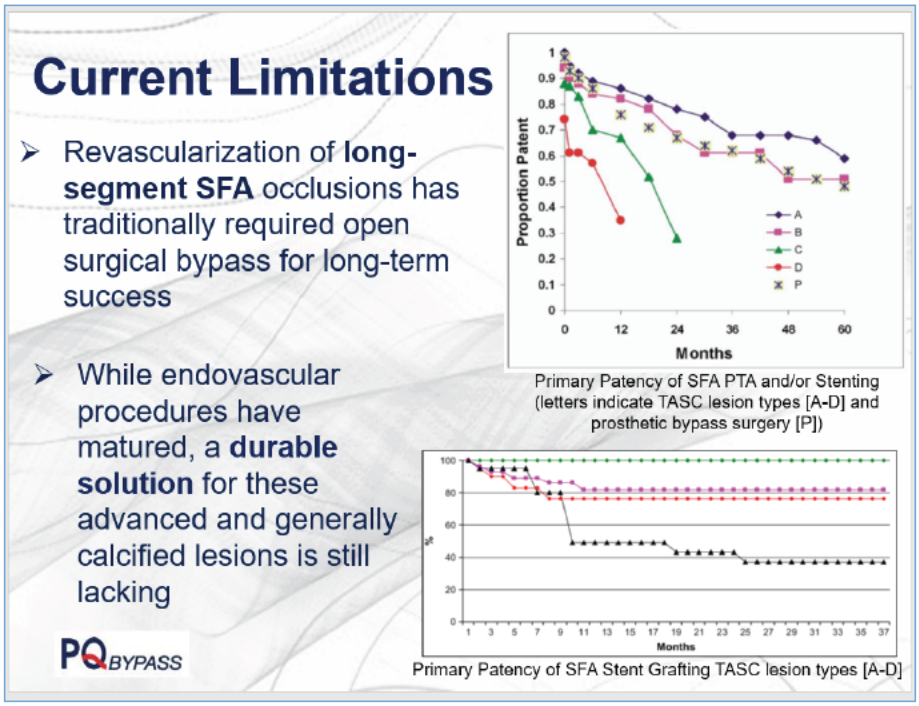
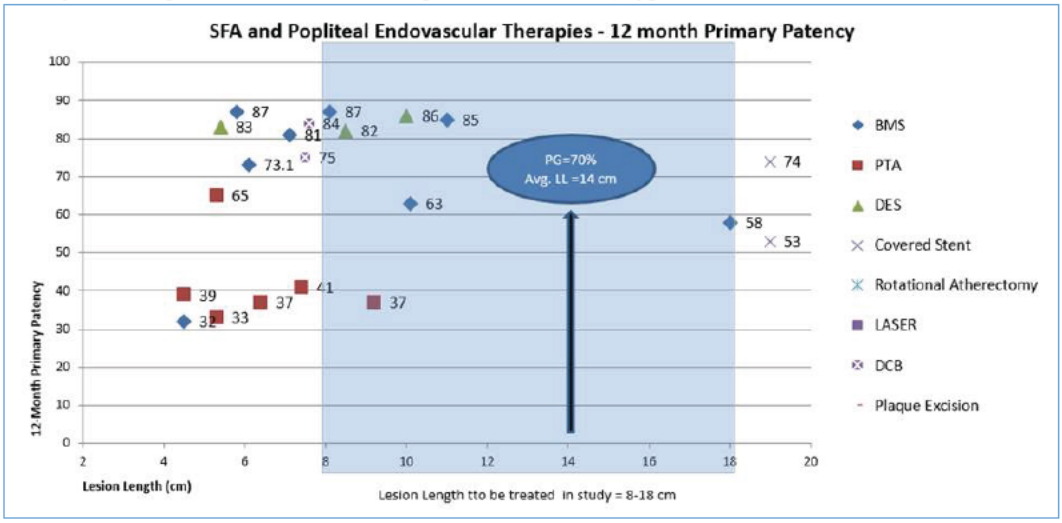


Figure 9: SFA and Popliteal Endovascular Therapies 12-month Primary Patency



References on file

In order to establish a statistical sample size, a delta of 10%, and a one sided α of 0.05 were set to demonstrate superiority of the PQ Bypass Stent Graft relative to the historical control in terms of patency using the following assumptions:

- 80% historical control rate (TASC II B and C lesions) 10% =70%
- 85% PQ Bypass Stent Graft estimated rate

The alternative hypothesis is to be one of superiority against the performance goal of 70%. As such using as historical control rate of 80% and a delta of 10%, the null and alternative hypotheses of the primary performance endpoint can be written as:

$$H0: \pi_{PQB\ performance} \leq \pi_{PG\ performance}$$
$$HA: \pi_{PQB\ performance} > \pi_{PG\ performance}$$

where,

$\pi_{PG\ performance}$ = 80% historical control rate – 10% Delta=70%
$\pi_{PQB\ performance}$ = PQB Systems success rate

The hypotheses for the primary performance endpoint can be rewritten as:

$$H0: \pi PQB\_performance \leq 70\%$$
$$HA: \pi PQB\_performance > 70\%$$

To achieve 80% power using a one sided alpha of 0.05, with a clinically acceptable delta of 10%, a sample size is 50 subjects would be needed to reject the null hypothesis. The required sample size was calculating assuming a true performance rate for PQ Bypass of 85%, using the exact method (ref: Chow S.C. 2003 Sample Size Calculations in Clinical Research.), implemented using the PASS 12 software.

Table 23 : Superiority with PQ Bypass Performance of 85%

	PQ Bypass			
PG	80%	**85%**	90%	95%
70%	119	**50**	26	15
75%	441	103	42	21
80%	-	368	83	32
85%	-	-	283	60

However, due to noise in the literature, the fact that the true performance of the PQ Bypass Stent Graft is unknown at this time, and potential loss to follow up, a larger sample size is required for the Study in order to ensure 50 evaluable subjects taking into account the above assumptions. The lower the true performance rate of the PQ Bypass Stent Graft, the greater the sample size needed to reject the null hypothesis and maintain 80% power. Therefore, up to 65 subjects may be enrolled.

11.2 Primary Safety Endpoint Reporting

The primary safety endpoint is the rate of Major Adverse Events (MAEs) at 30 days. The number and percent of subjects that experience at least one MAE through 30 days post procedure will be reported along with the upper one sided 95% confidence limit. In addition the number and percentage of subjects reporting MAEs and MAVEs will be presented using descriptive statistics at various time intervals, combined and by type of event. The confidence intervals will be calculated using the Wilson method.

11.3 Primary Performance Endpoint Reporting:

The primary performance hypothesis will be tested by calculating the one sided 95% lower confidence limit for the rate of successful performance using the Wilson Method. If the lower limit exceeds the performance goal rate of 70% the null hypothesis will be rejected and the endpoint will be met. In addition to hypothesis testing, descriptive statistics of the primary performance endpoint will include the total number and percentage of patent PQB grafts.

11.4 Secondary Endpoint Analysis:

The secondary endpoint of primary assisted and secondary patency will be summarized using Kaplan Meier survival analysis. Life tables will be created and a Kaplan Meier survival curve will be presented.

The secondary endpoints inclusive of Procedural Success, Clinical Success and Technical Success will be summarized by providing point estimates, number of subjects, and 95% confidence bounds calculated using the Score approximation.

11.5 Demographic, procedural and safety data:

Demographic and baseline clinical and disease characteristics will be summarized in tables. For continuous variables the summary will include number, mean, and standard deviation and 95% confidence intervals. Summaries for categorical variables will include the number and percent of subjects in each category.

11.6 Imputation for Missing Data

Imputations for missing data in (e.g. withdrawn subjects, loss to follow up, missing data) will not be performed. Analyses will be performed with all available data only.

12.0 ADVERSE EVENTS

The occurrence of Adverse Events will be monitored during this study. All Adverse Events will be recorded on the Adverse Event Form at onset and at each follow up visit until resolved. To meet the objectives of this study, the following definitions will apply. (Definitions reference ISO 14155:2011 01). Potential adverse events associated with use of the SGS 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

12.1 Adverse Event (AE)

Adverse Event (AE): Any untoward medical occurrence, unintended disease or injury or any untoward clinical signs (including an abnormal laboratory finding) in subjects, users or other persons whether or not related to the medical device. This includes events related to the 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 subject's usual activity or is transient, resolved without treatment and with no clinical sequelae.
- Moderate: Interferes with the subject's usual activity
- Serious: Any fatal or immediately life threatening clinical experience that requires a subject 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

12.2 Serious Adverse Event (SAE)

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, could have led, or could lead directly or indirectly to death or to a serious deterioration in the health of a subject or user or any other person, without regard to whether the event was caused by a medical product. (§ 2 no. 5 MPSV). The following events (including laboratory results and outcome events) will be considered to be SAEs and must immediately (within 24 hours) be reported to the study Sponsor by telephone, fax and/or email. 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 subject, 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.
- Malignant Tumor (Austrian Medical Device Act, § 3 Abs.16 MPG as amended)

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.

12.3 Unanticipated Adverse Device Effect (UADE)

Unanticipated Serious Adverse Device Effect (USADE): Serious adverse device effect which, by its nature, incidence, severity or outcome has not been identified in the risk analysis report.

Anticipated Serious Adverse Device Effect (ASADE): An effect, which by its nature, incidence, severity or outcome has been identified in the risk analysis report. UADEs must be reported to the study Sponsor by telephone, fax and/or email within 24 hours.

12.4 Reporting of Adverse Events

All incidents will be captured as a part of this clinical study. At each contact with the subject, 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 adverse effect case report form (CRF). All clearly related signs, symptoms, and abnormal diagnostic procedures results should be recorded in the source document. All SAEs, UADEs and

possible device and/or procedure related adverse events must be recorded on the Adverse Event CRF by the Investigator (or his/her designee) and reported to the Sponsor within 24 hours. The report should include: severity, duration, action taken, treatment outcome and relationship to the adverse event to the study device, procedure, concomitant medications, pre existing condition, etc. (i.e., unrelated, relation or relationship unknown).

In the case of serious adverse events (SAE), 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. All SAEs shall be recorded in the CRF and this information shall be faxed to the Study Monitor/PQ Bypass. 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 as described in section 4 which indicate an imminent risk of death, serious injury, or serious illness and that requires prompt remedial action for other patients/subjects, 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.

12.5 Reporting of Device Failures and Malfunctions

All reported device malfunctions or failures of the PQ Bypass Systems are required to be documented in the CRF and must be immediately reported to the study sponsor by telephone, fax and/or within 24 hours. Device failures and malfunctions should also be documented in the subject'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.

12.6 Documentation, evaluation and notification of Serious Adverse Events

The Investigator shall report all serious adverse events (anticipated or unanticipated) to Sponsor or Sponsor's representative within 24 hours upon becoming aware of events. The Sponsor will ensure compliance with all country specific reporting requirements to the appropriate Ethical Committees and Competent Authorities. SAEs should be reported immediately and no later than 7 days from the Sponsor's first knowledge of the event.

13.0 MONITORING

13.1 Selection and Qualification of Monitors (ISO 14155)

Monitors will be appointed by the sponsor. Monitors will be trained with scientific and/or clinical knowledge and the sponsor will document his/her qualifications. The Monitor will be familiar with the investigational product, protocol, consent form and any other written information given to the participant, sponsor's SOPs, and GCP and the relevant regulatory requirements.

13.2 Assessment of the Investigation Site (ISO 14155)

The monitor shall assess each investigation site to verify that the principal investigator has:

a) adequate qualifications;

b) adequate resources, including facilities, laboratories, equipment and a qualified investigation site team;

c) access to an adequate number of subjects.

13.3 Site Initiation (ISO 14155)

The monitor shall initiate each investigation site to ensure that the principal investigator and investigation site team:

a) have received and understood the requirements and contents of

1) CIP,
2) IB,
3) the informed consent form,
4) CRFs,
5) the instructions for use,
6) any written clinical investigation agreements, as appropriate,

b) have access to an adequate number of investigational devices,

c) have been trained in the use of the investigational device, and

d) are familiar with the responsibilities of the principal investigator

13.4 Interim Monitoring Visit (ISO 14155)

The monitor shall perform routine on site monitoring visits to verify that

a) compliance with the CIP, any subsequent amendment(s), this International Standard and regulatory requirements is maintained; deviations shall be discussed with the principal investigator(s) or authorized designee, documented and reported to the sponsor,

b) only authorized individuals are participating in the clinical investigation,

c) the investigational device is being used according to the CIP or instructions for use and that, where modifications are required to the device, its method of use or the CIP,

these are reported to the sponsor,

d) investigation site resources, including laboratories, equipment and the investigation site team, remain adequate throughout the duration of the clinical investigation,

e) the principal investigator continues to have access to an adequate number of subjects and investigational devices,

f) signed and dated informed consent forms have been obtained from each subject at the point of enrolment or before any clinical investigation related procedures are undertaken,

g) source documents and other clinical investigation records are accurate, complete, up to date, stored and maintained appropriately,

h) CRFs and queries are complete, recorded in a timely manner, and consistent with source documents,

i) appropriate corrections, additions or deletions are made to the CRFs , dated, explained if necessary and initialed by the principal investigator or by his/her authorized designee; the monitor shall not make corrections, additions or deletions to the CRFs,

j) all adverse events and device deficiencies are reported to the sponsor, and all serious adverse events and device deficiencies that could have led to a serious adverse device effect are reported to the sponsor without unjustified delay,

k) all serious adverse events and deviations are reported to the EC, if required,

l) the storage and investigational device accountability are correct and the traceability process is being followed,

m) all other required reports, notifications, applications, submissions and correspondence are maintained in the investigator's files and are accurate, complete, timely, legible, dated and identify the clinical investigation,

n) maintenance and calibration of the equipment relevant to the assessment of the clinical investigation is appropriately performed and documented, where applicable,

o) current laboratory normal values, laboratory certifications, accreditations, or other validations are present in the investigator's file, if required,

p) subject withdrawal has been documented; the monitor shall discuss this with the principal investigator or his/her authorized designee,

q) subject non compliance with the requirements stated in the informed consent has been documented; the monitor shall discuss this with the principal investigator or his/her authorized designee,

r) the principal investigator and investigation site team are informed and knowledgeable of all relevant document updates concerning the clinical investigation, and

s) any corrective and preventive actions, as needed, have been implemented and are effective.

13.5 Close-Out Visit (ISO 14155)

A close out visit will be conducted to ensure that the principal investigator’s records are complete, all documents needed for the sponsor’s files are retrieved, remaining clinical investigation materials are disposed of, previously identified issues have been resolved and all parties are notified. The visit will occur after the last subject’s case report forms have been

completed, study has been closed with reviewing IRB/IEC and all regulatory issues have been addressed.

13.6 Monitoring Reports (ISO 14155)

All monitoring activities shall be documented in a written report to the sponsor and shall include:

a) the date, investigation site identification, name of the monitor and name of the principal investigator or other individuals contacted, and

b) a summary of what the monitor reviewed and his/her observation(s) with regard to the completion of previous action items, significant findings, facts, deviations, conclusions, and recommended actions to be taken to secure compliance.

A copy of the monitoring report or a summary of key findings shall be shared with the principal investigator in writing.

14.0 STUDY ADMINISTRATION

PQ Bypass will make necessary efforts to ensure that this study is conducted in compliance with Good Clinical Practices (GCPs) and all applicable regulatory requirements.

14.1 Source Documentation

The Investigator must maintain detailed source documents on all trial subjects who are enrolled in the trial or who undergo screening. Source documents include subject medical records, hospital charts, clinic charts, Investigator's subject trial files, as well as the results of diagnostic tests (e.g., laboratory tests).

The following minimum information should be recorded in the subject's medical records:

- The date the subject entered the trial and the subject number
- The trial protocol number and the name of the Sponsor
- The date that informed consent was obtained
- Evidence that the subject meets trial eligibility requirements (e.g., medical history, trial procedures and/or evaluations)
- The dates of all trial related subject visits
- Evidence that required procedures and/or evaluations were completed
- Use of any concurrent medications
- Documentation of specific device used, if any
- Occurrence and status of any Adverse Events
- The date the subject exited the trial, and a notation as to whether the subject completed the trial or was discontinued, including the reason for discontinuation

14.2 Clinical Data Management

Software

This study will utilize electronic data capture (EDC), allowing the data to be entired directly into the computerized system by the clinical site personnel. The Medrio electronic data capture software will be used. This software was developed and validated by Medrio Incorporated. The specific study set up within the software will be the subject of user acceptance testing and is not released for use in the study until it has successfully passed this testing.

Security

Hosting is provided by Medrio Inc. and the data entered on the electronic case report forms (eCRFs) along with applicable metadata is transmitted using 128 bit SSL and 1024 bit RSA public keys. The server on which the data will be stored resides within a secure data center with security guards, electronic access controls and digital video monitoring as well as cisco firewalls and advanced intrusion detection/prevention systems. Access to the study EDC system will be limited to authorized users with permission levels granted based on the user's role in the study. Each user is given a unique user ID and generate their own private

password.

Query Management

Queries are generated and managed within the EDC system. Data checks, including those that detect missing or inconsistency entries, will be programmed into the system and will automatically be generated upon data entry. Manual queries may also be generated by the monitors, CRAs or data management personnel as necessary. Sites can respond to an automatic system generated query by making an update to the data and/or providing a textual response to the query. Query responses are reviewed and closed out by the monitor, CRA or data management personnel.

Database Closure and Export for Analysis

The primary clinical study report will be generated once all necessary patients have reached the primary efficacy follow up of 12 months. A database snapshot will be taken at this time for analysis. Data will be reviewed per the data snapshot checklist that will list the data cleaning activities required. All data is exported into SAS format for analysis by the study statistician and to be archived. Once all follow up has been completed and the database closure checklist completed, the EDC system study data and metadata will be exported and archived. All CRF data will be exported into SAS format for analysis and archive.

14.3 Criteria for Terminating Study

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 subjects. Investigators and associated EC 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 subjects enrolled in the study
- A decision on the part of PQ Bypass to suspend or discontinue development of the device

14.3 Criteria for Suspending/Terminating a Study Center

PQ Bypass reserves the right to stop the screening of subjects at a study center at any time after the study initiation visit if no subjects have been enrolled or if the center has multiple or severe protocol violations without justification or fails to follow remedial actions.

Possible reasons for suspending/terminating a study center include, but are not limited to:

- Repeated failure to complete case report forms prior to scheduled monitoring visits
- Failure to obtain written Informed Consent
- Failure to report SAEs/UADEs to PQ Bypass within 24 hours of knowledge
- Loss of (or unaccounted for) investigational product inventory

14.4 Data Safety Monitoring Board (DSMB)

A Data Safety Monitoring Board (DSMB) consisting of non Investigator experts, will review safety data from the study and establish stopping rules for early termination of the trial. The composition of the DSMB will include at least one statistician and at least two clinicians with expertise in the treatment interventional peripheral disease. Names of the actual members will not be announced. The frequency of the DSMB meetings will be determined in conjunction with the Sponsor. However, the DSMB may call a meeting at any time if there is reason to suspect safety is an issue.

The DSMB will make recommendations based upon the safety analysis of adverse events, protocol deviations, and device failures. The DSMB will function in accordance with SOPs and applicable regulatory guidelines.

The DSMB chairperson will notify PQ Bypass by confidential memo, of any safety or compliance issues. They will also provide confidential recommendations, when necessary, of study termination based upon the safety stopping rules determined at study onset, or because a clinically significant result was identified in safety analyses of the data. All DSMB reports will remain strictly confidential, but will be made available to regulatory authorities upon request.

15.0 PROTOCOL DEVIATIONS

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

Investigators shall be required to obtain prior approval from PQ Bypass Clinical Director before knowingly deviating from the protocol, except where necessary to protect the life or physical well being of a subject 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., subject 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 subject in an emergency. Subject specific deviations will be reported on the Protocol Deviation case report form. Non subject 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.

16.0 REGULATORY CONSIDERATIONS

16.1 Maintaining Records

The Sponsor will maintain copies of correspondence, data, shipment of devices, serious adverse device effects and other records related to the clinical trial.

16.2 Data Storage and Confidentiality

Study information will be kept in HIPAA compliant files or in secure databases with access protected by password. Neither subject names or other identifying information will be released from the site, nor will any identifying information be used in any published reports that are developed as a result of this study. De identified copies of relevant source documents for each study visit with privacy protected copies of electronic image files for X rays, DUS and CTA will be stored in secured files at PQ Bypass or at a validated data warehousing vendor.

16.3 Site Record Retention Policy

The Sponsor and clinical sites will maintain all records pertaining to this study for a period of seven years following the date on which the investigation is terminated or completed, or the date that the records are no longer required for purposes of supporting a regulatory submission. If the reviewing Ethics Committee or Competent Authority retention policy is longer than seven years, record retention will be mandated under those respective policies. Record retention dates will be provided to all concerned by the Sponsor.

16.4 Ethics Committee (EC) and Competent Authority (CA) Approval

The trial will only be started in a center after written approval of the protocol and Patient Informed Consent has been obtained from the appropriate Ethics Committee. Any amendment to the final protocol and informed consent should be submitted to the Ethics Committee.

Regulatory approvals must be obtained prior to enrolment of the first patient. The Sponsor will arrange EC and CA approvals for the study. The Sponsor or its designated CRO (HealthLink) will require a copy of any EC and CA correspondence, as well as the final approval letter from the EC and CA, where applicable.

No changes in the Clinical Investigation procedures will be effected without mutual agreement of the Principal Investigator and the Sponsor. The agreement of the changes must be documented by signing the corresponding Clinical Investigation Plan amendments.

All changes require notification to the EC/IRB and the CA (when appropriate), or approval where requested by local regulations. Substantial changes may require approval from the EC/IRB and the CA prior to implementation.

Substantial changes are changes which could:

- have an effect on the safety of the clinical investigation participants,

- influence the interpretation of the documents on which the conduct of the clinical investigation is based, or
- influence the other requirements assessed by the ethics committee.

17.0 INVESTIGATOR RESPONSIBILITIES, RECORDS AND REPORTS

17.1 Investigator Responsibilities

The Investigator is responsible for ensuring that this trial is conducted according to this protocol and that signed Informed Consent is obtained from each subject prior to his or her inclusion in this trial.

It is the Investigator's responsibility to ensure that all staff assisting with this trial have the appropriate qualifications and are fully instructed on the trial procedures and respect subject confidentiality, as specified in the Investigator Agreement with the Sponsor.

The Investigator is responsible for ensuring that the conduct of the trial conforms to the EC and CA requirements and provides all necessary communication with the EC and CA including, but not limited to, annual trial reports and required adverse event notifications.

17.2 Investigator Records

Case Report Forms

The standardized Case Report Forms (CRFs) will be used to collect complete and accurate records of the clinical data from the trial according to the International Conference on Harmonization (ICH)/WHO Good Clinical Practice (GCP) standards. The Investigator is responsible for collecting and accurately recording the data generated for this trial.

Screening Log

Investigators will maintain a screening log that will record the date of informed consent, the date of screening, the enrollment status (enrolled/excluded) and the reason for exclusion for all screen failures.

17.3 Investigator Report

The final clinical report will be prepared and provided to each Principal Investigator for submission to their respective IEC after conclusion of the trial.

18.0 PUBLICATIONS

The PQ Bypass 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 Investigative 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 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.

19.0 DEFINITIONS

Acute Technical Success

See Technical Success

Adverse Device Effect

An adverse event related to the use of an investigational medical device. This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device. This definition also includes any event resulting from use error or from intentional misuse of the investigational medical device.

Adverse Event (AE)

Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device or index procedure. Adverse events are captured throughout the course of the study.

Allergic Reaction to contrast, polyester, nickel compound of the device and/or anesthesia

An overreaction of the body's immune system to a component of an investigational device (e.g., nitinol metal, polyester, plastics), contrast agents and/or anesthesia medication given to the subject for completion of a study related procedure (e.g., MSCT, angiogram, investigational device), which requires medical intervention to treat the allergic reaction.

Anesthesia Type

Type of anesthesia administered. Categorized as either general, local, or epidural/spinal.

Anticipated Adverse Device Effect (AADE)

An expected effect associated with endovascular treatment of the SFA and may occur during the procedure or during the course of the study. These anticipated effects have been previously identified in the risk analysis report.

Blood Loss

- **Blood loss ≥ 1000 mL** – Defined as any blood loss ≥ 1000 mL.
- **Estimated Procedural Blood Loss -** Defined as the total estimated blood loss (mL) during the index procedure. Includes blood loss resulting from adjunctive procedures performed during the index procedure.

Contrast Volume

Total volume of contrast (mL) administered during the index procedure. Includes contrast administered for adjunctive procedures performed during the index procedure.

Death

Death is divided into two categories and will be reported anytime in a subject's study participation.

- **Device or procedure related death -** Death related to the Study Device or to any procedure (index or subsequent) intended to treat the target vessel.

- **Non-device or procedure related death –** Death NOT related to any procedure (index or subsequent) intended to treat the target vessel or death not related to the Study Device.

Device Deficiency

Inadequacy of the Study Device with respect to its identity, quality, durability, reliability, safety or performance. Device deficiencies include malfunctions, use errors, and inadequate labeling.

Device Time

Number of minutes from initial Study Device insertion to final Study Device removal. It does not include time needed to perform adjunctive procedures.

Explant

Removal of the Study Device implant for any reason.

Estimated Procedural Blood Loss

See Blood Loss

Fluoroscopy Time

Total fluoroscopy time (minutes) used during the index procedure and includes time utilized for adjunctive procedures performed during the index procedure.

Intensive Care Unit Time

See post procedure ICU time

Life Expectancy > 1 Year

The duration of time the test subject is expected survive post procedure. Subjects must not have a concurrent medical condition that would cause expected survival to be less than one year.

Longer-Term Technical Success (1-year)

See Technical Success

Major Adverse Event (MAE)

Composite endpoint of the following: defined as all death, TLR or any amputation of the index limb to 30 days (±7 days). See individual events for detailed definitions.

Myocardial Infarction (MI) [10]

Typical chest pain and either a Q wave or non Q wave MI as described below.

- **Q-Wave Myocardial Infarction –** Development of new, pathological Q waves in two or more contiguous leads V1 V3 or Q Wave ≥ 3 ms in width in leads I, II, aVL, AVF, V4, V5 or V6 and ≥ 1 mm in depth on at least two serial ECGs.
- **Non-Q-Wave Myocardial Infarction –** (1) Non procedural (pre procedural or > 30 days post index procedure, endovascular or surgical intervention) – CK MB elevation ≥ 2 times the

[10] Myocardial infarction redefined--a consensus document of The Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction. Eur Heart J. 2000 Sep;21(18):1502-13. Review.

upper limit of normal in the absence of new pathological Q waves, (2) post index procedure or endovascular re intervention (≤ 30 days) – CK MB elevation ≥ 3 times the upper limit of normal in the absence of new pathological Q waves, or (3) post Surgical intervention (< 30 days) – CK MB elevation ≥ 5 times the upper limit of normal in the absence of new pathological Q waves.

Post-Procedure ICU Time

Number of hours a patient is in an intensive care unit prior to discharge or moving to a step down or standard care unit.

Primary Assisted Patency

Patency following endovascular re intervention at the target vessel site in case of symptomatic restenosis.

Primary Patency

No significant reduction of flow detectable by Duplex ultrasound (DUS) through the index lesion. Significant reduction of flow was determined as binary restenosis, defined as a peak systolic velocity ratio (PSVR) ≥2.5 as measured by DUS.

Post-Procedure Length of Hospital Stay

Number of days from the end of the procedure until the patient is discharged from the hospital. This does not include time spent in a skilled care facility.

Procedure Time

Number of minutes needed to perform the index procedure from time of initial vessel cut down time to time of final guidewire removal. Also referred to as skin to skin time.

Renal Failure

Need for dialysis or a laboratory finding of serum creatinine > 3.5 mg/dL.

Respiratory Failure

The need for mechanical ventilation beyond the first 24 hours post index procedure (and/or re intervention) or the need for re intubation or ventilator support after the first 24 hours (unless the subject was ventilator dependent pre procedure).

Secondary intervention

Any visit to the operating room or catheterization laboratory subsequent to the PQ Bypass Stent Graft implant procedure to treat an adverse event related to the disease, the index procedure or the study device.

Secondary Patency

Patency of the target lesion after treatment of a (re)occlusion of the index lesion.

Serious Adverse Event (SAE)

Any undesirable event occurring which led, could have led or might lead either directly or indirectly to the death or serious deterioration in the health of a subject, user or another person, regardless of whether the event was caused by the medical device.

Stroke or Transient Ischemic Attack (TIA)

- **Stroke -** A new neurological deficit lasting more than 24 hours, or lasting 24 hours or less with a brain imaging study showing infarction.

- **TIA -** A neurological deficit lasting less than 24 hours and, if an imaging study is performed, shows no evidence of infarction. These events may occur anytime throughout a subject's study participation and may or may not require intervention.

Stent Graft Occlusion

Complete blockage of blood flow through the Stent Graft as determined by traditional imaging (e.g. DUS, CTA, MRA or Angiography).

Stent Graft Placement Accuracy

Estimated distance (mm) from the operator's intended target as compared to the actual position placed as assessed via angiography during the index procedure.

Target Lesion Revascularization (TLR)

A re intervention of the index lesion site.

Target Vessel Revascularization (TVR)

Treatment of another lesion at the target vessel site but no the index lesion itself.

Technical Success, Acute

Successful delivery of PQ Bypass Stent Graft System to the identified area and successful removal of delivery system.

Unanticipated Adverse Device Effect (UADE)

An adverse device effect which by its nature, incidence, severity or outcome has not been identified in the risk analysis report.

Vascular Access Type

Method of entry into the vascular system. Categorized as either surgical cut down or percutaneous.

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APPENDIX I: SAMPLE INFORMED CONSENT (ENGLISH VERSION)

(Attached as separate document)

APPENDIX II: INSTRUCTIONS FOR USE

(Attached as separate documents)

APPENDIX III: SERIOUS ADVERSE EVENT REPORTING PROCEDURES

The correct reporting procedures of SAEs to the BfArM can be found at the following website:

http://www.bfarm.de/EN/MedicalDevices/clinTrials/_node.html

The Ordinance on the Recording, Evaluation, and Prevention of Risks Associated with Medical Devices (Ordinance on Medical Devices Vigilance, "Medizinprodukte Sicherheitsplanverordnung", MPSV) of 24 June 2002 (Federal Law Gazette (BGBl. I 2002), p. 2131 no. 40), was amended by Article 4 of the Ordinance on the Making Available of Medical Devices and amending the Regulations governing Medical Devices of 25 July 2014 (Federal Law Gazette (BGBl. I 2014), p. 1227, no. 35). The following notification obligations for SAE reporting have applied since 29 July 2014: Investigators have to report all SAEs to the sponsor immediately. The sponsor of a clinical trial of a medical device that is conducted in Germany (and other countries) has to report SAEs to BfArM immediately or quarterly, depending on the following conditions.

Condition for reporting to BfArM	**Country of occurence**	**Timeline for reporting to BfArM**	**Form**
A causal relationship between the SAE and the investigational medical device, a comparator device, diagnostic or therapeutic procedures performed as part of the clinical trial or other conditions of the trial conduct **cannot be excluded**	Germany	Immediately	Single report German SAE Report Form [redacted]
	All other countries where the clinical trial is performed	Immediately	Summary table MEDDEV 2.7/3 SAE report table All SAEs shall be documented using the same Excel file, in a cumulative manner, using the same Excel sheet. [redacted]
A causal relationship between the SAE and the investigational medical device, a comparator device, diagnostic or therapeutic procedures performed as part of the clinical trial or other conditions of the trial conduct **can be excluded**	All	Quarterly	Summary table MEDDEV 2.7/3 SAE report table Please complete the MEDDEV Excel sheet as outlined above. [redacted]
All SAEs	All	Quarterly	SAE summary evaluation Evaluation Annex 3.1 complication rate

			[redacted] Please observe our notes on completing the SAE summary evaluation

Regardless of the criteria mentioned in the table, the sponsor must report all SAEs occurring in Germany to the competent authorities of other contractual states of the Agreement on the European Economic Area immediately if the clinical trial is also being performed in those countries.

Important information for SAE summary evaluations

The evaluation should be sent concurrently with the next SAE summary table (MEDDEV 2.7/3 SAE report table) and should be updated every 3 months. For further information please observe our notes on completing the SAE summary evaluation.

Important information for completing the MEDDEV SAE Report Table

The MEDDEV table is to be completed consecutively. Please always fill in the complete information for each case. New findings / updates to already reported events with relevance for the assessment may be added at any time. Please indicate your entry as "modified" in such cases.

In the columns for dates please only enter pure dates in the "dd/mm/yyyy" format according to the MEDDEV specifications. Please avoid empty cells in cases where such information is available (e. g. in the column "Description of Event").