

SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Endovascular Prosthesis

Device Trade Name: GORE® VIABAHN® Endoprosthesis
GORE® VIABAHN® Endoprosthesis with Heparin Bioactive Surface

Device Procode: NIP

Applicant's Name and Address: W.L. Gore & Associates, Inc.
3250 West Kiltie Lane
Flagstaff, AZ 86005

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P040037/S060

Date of FDA Notice of Approval: September 19, 2014

REGULATORY HISTORY

The original indications statements for the subject GORE® VIABAHN® Endoprosthesis as well as the major changes to those statements are provided in the text below.

The original PMA P040037, GORE® VIABAHN® Endoprosthesis, was approved on June 14, 2005 with an indication statement as follows:

The GORE® VIABAHN® Endoprosthesis is indicated for improving blood flow in patients with symptomatic peripheral arterial disease in superficial femoral artery lesions with reference vessel diameters ranging from 4.8 to 7.5 mm.

The SSED to support the indication is available on the CDRH website and is incorporated by reference here: http://www.accessdata.fda.gov/cdrh_docs/pdf4/P040037b.pdf

PMA supplement P040037/S004 (GORE® VIABAHN® Endoprosthesis with Heparin Bioactive Surface) was approved on July 31, 2007 to add device configurations containing a Heparin Bioactive Surface.

PMA supplement P040037/S007 was approved on August 14, 2008 where the indication statement was modified to add an Indication for treatment of iliac artery lesions and read:

The GORE VIABAHN® Endoprosthesis is indicated for improving blood flow in patients with symptomatic peripheral arterial disease in superficial femoral artery lesions with reference vessel diameters ranging from 4.0 - 7.5 mm.

The GORE VIABAHN® Endoprosthesis is indicated for improving blood flow in patients with symptomatic peripheral arterial disease in iliac artery lesions with reference vessel diameters ranging from 4.0 - 12 mm.

The SSED to support the indication is available on the CDRH website and is incorporated by reference here: http://www.accessdata.fda.gov/cdrh_docs/pdf4/P040037S007b.pdf

PMA supplement P040037/S050 was approved on October 18, 2013 for the addition of a 25cm length for the 5-8mm diameter endoprostheses and where the indication statement was modified to specify lesion lengths and read:

The GORE® VIABAHN® Endoprosthesis is indicated for improving blood flow in patients with symptomatic peripheral arterial disease in superficial femoral artery lesions up to 230mm in length with reference vessel diameters ranging from 4.0 – 7.5mm.

The GORE® VIABAHN® Endoprosthesis is indicated for improving blood flow in patients with symptomatic peripheral arterial disease in iliac artery lesions up to 80mm in length with reference vessel diameters ranging from 4.0 – 12mm.

PMA P130006 was approved on December 5, 2013 for the addition of an indication to treat stenosis or thrombotic occlusion in AV access grafts. The additional indication reads:

The GORE® VIABAHN® Endoprosthesis is indicated for the treatment of stenosis or thrombotic occlusion at the venous anastomosis of synthetic arteriovenous (AV) access grafts.

The SSED to support the indication is available on the CDRH website and is incorporated by reference here: http://www.accessdata.fda.gov/cdrh_docs/pdf13/P130006b.pdf

The current supplement was submitted to expand the Indication for Use within the superficial femoral artery to increase the maximum treatable lesion length from 230mm to 270mm and to include in-stent restenotic (ISR) lesions up to 270mm in length with reference vessel diameters ranging from 4.0 – 6.5 mm.

II. INDICATIONS FOR USE

The GORE® VIABAHN® Endoprosthesis is indicated for improving blood flow in patients with symptomatic peripheral arterial disease in superficial femoral artery de novo and restenotic lesions up to 270 mm in length with reference vessel diameters ranging from 4.0 – 7.5 mm.

The GORE® VIABAHN® Endoprosthesis is indicated for improving blood flow in patients with symptomatic peripheral arterial disease in superficial femoral artery in-stent restenotic lesions up to 270 mm in length with reference vessel diameters ranging from 4.0 – 6.5 mm.

III. CONTRAINDICATIONS

The GORE® VIABAHN® Endoprosthesis and GORE® VIABAHN® Endoprosthesis with Heparin Bioactive Surface are contraindicated for non-compliant lesions where full expansion of an angioplasty balloon catheter was not achieved during pre-dilatation, or where lesions cannot be dilated sufficiently to allow passage of the delivery system.

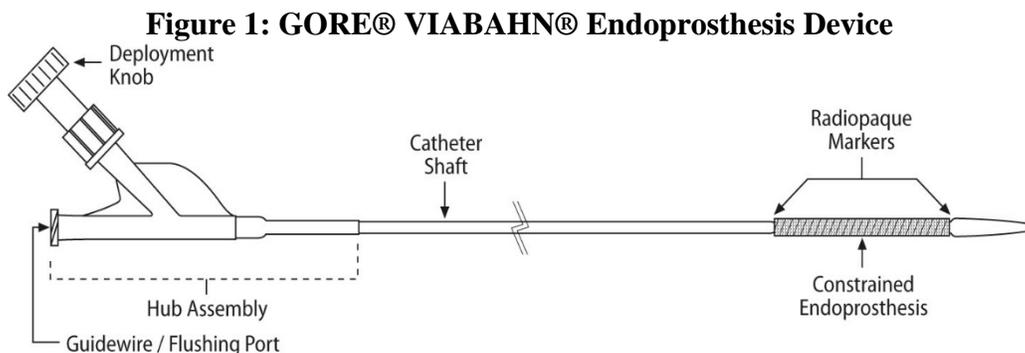
Do not use the GORE® VIABAHN® Endoprosthesis with Heparin Bioactive Surface in patients with known hypersensitivity to heparin, including those patients who have had a previous incidence of Heparin-Induced Thrombocytopenia (HIT) Type II.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the GORE® VIABAHN® Endoprosthesis and the GORE® VIABAHN® Endoprosthesis with Heparin Bioactive Surface labeling.

V. DEVICE DESCRIPTION

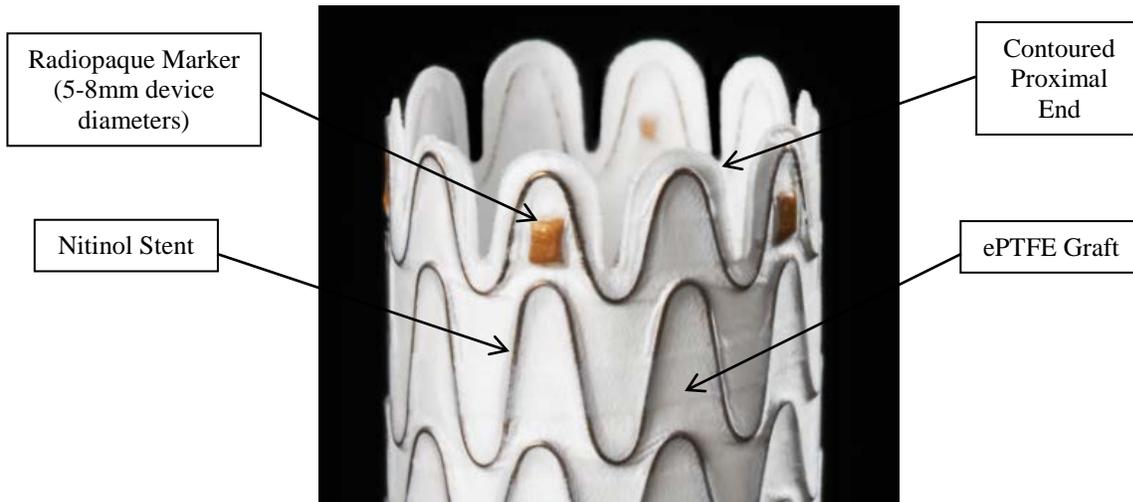
The GORE® VIABAHN® Endoprosthesis is comprised of an implantable endoprosthesis and a delivery catheter (**Figure 1**). The endoprosthesis is also available with the Heparin Bioactive Surface, where the surface of the endoprosthesis is modified with covalently bound, bioactive heparin.



Description of the GORE® VIABAHN® Endoprosthesis

The GORE® VIABAHN® Endoprosthesis is a flexible, self-expanding endoluminal endoprosthesis consisting of an expanded polytetrafluoroethylene (ePTFE) lining with an external nitinol (Nickel-Titanium) support extending along its entire length (**Figure 2**). The nitinol wire is attached to the graft with a tape comprised of ePTFE and fluorinated ethylene propylene (FEP). The 5 to 8mm device diameter configurations also include radiopaque markers at each end of the endoprosthesis. The endoprosthesis radiopaque markers aid in fluoroscopic visualization of the endoprosthesis.

Figure 2: GORE® VIABAHN® Endoprosthesis



Below is a list of the GORE® VIABAHN® Endoprosthesis device configurations.

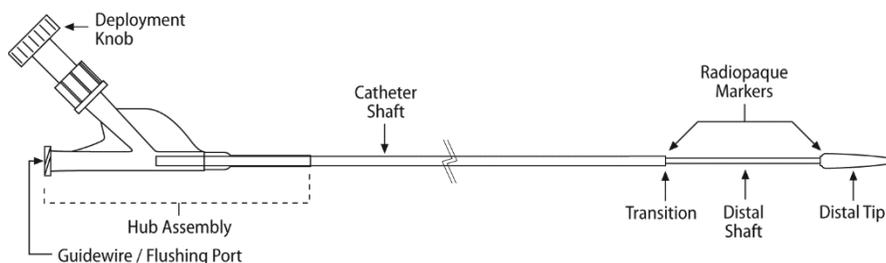
Device Name	Configurations		
	Guidewire Compatibility	Labeled Device Diameters	Labeled Device Lengths
GORE®VIABAHN Endoprosthesis	0.035"	5-13mm	2.5cm-15cm
		5-8mm	25cm
GOREVIABAHN Endoprosthesis with HeparinBioactive Surface ¹	0.035"	5-13mm	2.5cm-15cm
		5-8mm	25cm
GOREVIABAHN Endoprosthesis	0.014"	5-8mm	2.5cm-15cm
	0.018"	5-8mm	25cm
GORE®VIABAHN Endoprosthesis with Heparin Bioactive Surface ¹	0.014" 0.018"	5-8mm	2.5cm-15cm
		5-8mm	25cm

1. The Heparin Bioactive Surface (US tradename) is the same as the PROPATEN Bioactive Surface (OUS tradename).

Description of the GORE® VIABAHN® Endoprosthesis Delivery Catheter

The delivery catheter is composed of a hub assembly, catheter shaft, transition, distal shaft, tip, and radiopaque markers (Figure 3).

Figure 3: GORE® VIABAHN® Endoprosthesis Delivery Catheter



Catheters are compatible with 0.035”, 0.018”, and 0.014” guidewires and are available in working lengths of 75cm (0.035” only) or 120 cm. One radiopaque marker is embedded into the transition at the proximal end of the distal shaft while the other is embedded into the distal tip. The endoprosthesis is constrained to the portion of the delivery catheter between the transition and the distal tip. The catheter radiopaque markers aid in the placement/delivery of the endoprosthesis.

The endoprosthesis is radially constrained on the distal end of the delivery catheter with a multi-filament knitted ePTFE constraint sleeve (Figure 4). The constraint sleeve extends beyond the endoprosthesis to create the deployment line. The endoprosthesis is deployed by pulling on the deployment line, which unravels the constraint sleeve allowing the endoprosthesis to expand radially. The endoprosthesis deploys in a direction from the distal tip of the catheter back in the direction toward the hub assembly (Tip to Hub).

Figure 4: Constrained GORE® VIABAHN® Endoprostheses



The dual lumen tubing forms the majority of the working length of the delivery catheter. The tubing is comprised of two round lumens for the catheter. The flushing or guidewire lumen is continuous with the lumen of the distal shaft. The deployment line lumen contains the deployment line. The proximal end of the dual lumen tubing is attached to the hub assembly.

The dual port hub assembly consists of a guidewire introduction port and a port for the deployment line/deployment knob. The deployment line is routed from the proximal end of

the constrained endoprosthesis through the deployment line lumen of the transition and dual lumen tubing to the deployment line port of the hub assembly where it is attached to the deployment knob. The deployment knob/deployment line assembly allows the physician to actuate deployment of the endoprosthesis.

Heparin Bioactive Surface

The GORE® VIABAHN® Endoprosthesis may be purchased with or without the Heparin Bioactive Surface (also known as Carmeda® Bioactive Surface or CBAS® Surface). The Carmeda® Bioactive Surface consists of heparin molecules that are covalently bonded to the surface by an “end-point attachment” method. USP heparin sodium API of porcine origin is used in the manufacture of the Carmeda® Bioactive Surface. The heparin sodium API has been tested and certified to meet USP/EP requirements. The heparin sodium API is entirely of North American origin and is subsequently derivatized by a proprietary process established by Carmeda AB, Uplands Väsby, Sweden. Heparin bioactivity (ability to bind antithrombin III) is retained in the binding process due to the end-point covalent attachment that does not interfere with the heparin active site.

Principle of Operation

The GORE® VIABAHN® Endoprosthesis functions by creating a stent-supported ePTFE-lined blood conduit. The steps of implanting the GORE® VIABAHN® Endoprosthesis are described briefly below:

The physician gains guidewire access to the target location.

The physician pre-dilates the target lesion by inflating a PTA balloon catheter, and makes angiographic measurements to select the appropriate size endoprosthesis.

The catheter-mounted endoprosthesis is delivered to the target location over the guidewire and positioned at the target lesion.

The endoprosthesis is deployed from the delivery catheter.

The delivery catheter is withdrawn from the patient.

Physician seats the device against the vessel wall by inflating an angioplasty balloon within the endoprosthesis.

When fully deployed and seated, the nitinol frame of the endoprosthesis creates a conduit and supports the target vessel, allowing blood to flow.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Alternative procedures for treatment of in-stent restenosis include use of other commercially available stents (both bare metal stents and drug-eluting stents), percutaneous transluminal angioplasty (PTA), medical management, atherectomy and bypass graft surgery.

VII. MARKETING HISTORY

The GORE® VIABAHN® Endoprosthesis is currently available and marketed for vascular use in several markets worldwide, including the European Union, where the CE mark was obtained in 1996. These countries include the following: Argentina; Australia; Austria; Barbados; Belgium; Bermuda; Bolivia; Brazil; Canada; Chile; China; Colombia; Costa Rica; Dominican Republic; Denmark; El Salvador; Finland; France; Germany; Greece; Guatemala; Hong Kong; Iceland; Indonesia; Ireland; Italy; Luxembourg; Malaysia; Mexico; Monaco; the

Netherlands; New Zealand; Norway; Panama; Paraguay; Peru; the Philippines; Portugal; Singapore; South Africa; South Korea; Spain; Sweden; Switzerland; Taiwan; Thailand; Trinidad / Tobago; Uruguay; Venezuela; Vietnam; United Kingdom.

The GORE® VIABAHN® Endoprosthesis has not been withdrawn from marketing for any reason relating to the safety or effectiveness of the device.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

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

• Abrupt stent closure	• Myocardial infarction
• Allergic reaction (contrast medium; drug; stent or filter material)	• Occlusion of SFA/PPA or distal vasculature
• Amputation or limb loss	• Pain (leg or foot)
• Aneurysm or pseudoaneurysm in vessel or at vascular access site	• Pain at catheter insertion site
• Angina or coronary ischemia	• Pulmonary embolism
• Arrhythmia (including premature beats, bradycardia, atrial or ventricular tachycardia, atrial or ventricular fibrillation)	• Renal failure or insufficiency, secondary to contrast medium
• Asystole or bradycardia, requiring placement of a temporary pacemaker	• Restenosis of vessel in stented segment
• Arteriovenous fistula	• Stent malposition, or migration, which may require emergency surgery to remove stent
• Bleeding complications from anticoagulant or antiplatelet medication requiring transfusion or surgical intervention	• Stent strut fracture
• Death	• Stent thrombosis or occlusion
• Detachment of a system component or implantation of an unintended site	• Stroke
• Emboli, distal (for example, air, tissue, plaque, or thrombotic material, or stent)	• Vascular thrombosis or occlusion at puncture site, treatment site, or remote site
• Emergent bypass surgery to perfuse limb	• Vessel dissection, perforation or rupture
• Fever	• Vessel spasm or recoil
• Hematoma at vascular access site, with or without surgical repair	
• Hypotension or hypertension	
• Infection, local or systemic, including bacteremia or septicemia	
• Ischemia requiring intervention (bypass or amputation of toe, foot, or leg)	

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

IX. SUMMARY OF PRECLINICAL STUDIES

This PMA Supplement expands the indication for use in the SFA to include treatment of longer lesions as well as the treatment of in-stent restenosis. There were no modifications made to the device; therefore, the preclinical testing previously conducted remains applicable. The sponsor provided additional in vitro testing specifically to support the addition of the in-stent restenosis indication. In vitro testing was conducted on appropriate

sizes. The testing conducted applied to the range of GORE® VIABAHN® Endoprosthesis stent sizes that are included in the SFA ISR Indication. In vitro testing has been performed according to the recommendations outlined in ISO 25539-1, Cardiovascular implants – Endovascular devices – Part 1: Endovascular prostheses. In vitro testing is summarized in **Table 1** below.

Table 1: In Vitro Test Results for the GORE® VIABAHN® Endoprosthesis

Test	Purpose	Acceptance Criteria	Results
Delivery System Visibility	To confirm that the catheter delivery system may be visualized under fluoroscopy	Catheter must enable Fluoroscopic Visualization	Visibility within a bare nitinol stent was assessed in vitro using a flat detector and an aluminum plate. The endoprosthesis can be visualized within bare nitinol stents, on the catheter prior to deployment, off the catheter after deployment, and in an overlapped configuration.
Endoprosthesis Magnetic Resonance Imaging Compatibility	To evaluate the MRI safety and compatibility of the endoprosthesis	The VIABAHN® endoprosthesis, when placed within a bare nitinol stent, must not present additional patient risk when exposed to static magnetic field strengths of 1.5 and 3.0 Tesla.	MR testing results show that the VIABAHN® endoprosthesis, when placed within a bare nitinol stent, does not present additional hazard or risk to the patient. Additional recommended conditions for MRI scanning are in the IFU. The VIABAHN® endoprosthesis remains “MR Conditional” according to the specific conditions used for testing and may be labeled MR Conditional according to ASTM F2503-13.
Endoprosthesis Visibility	To confirm that the endoprosthesis may be visualized under fluoroscopy	The VIABAHN® endoprosthesis must enable fluoroscopic visualization	Visibility within a bare nitinol stent was assessed in vitro using a flat detector and an aluminum plate. The endoprosthesis can be visualized within bare nitinol stents, on the catheter prior to deployment, off the catheter after deployment, and in an overlapped configuration.
Stress/Strain and Fatigue Analysis	To calculate the maximum principal strains the Nitinol portion of the endoprosthesis when subjected to expected conditions of clinical use	Characterization study	Peak maximum principal mean and alternating strains were calculated for the VIABAHN® device when implanted in a predicate BMS device in a worst-case ISR indication and subjected to in-vivo pulsatile radial loading conditions. The strains were below the endurance limit for the Nitinol material.

Test	Purpose	Acceptance Criteria	Results
Stent to Graft Attachment	To confirm that the device's stent and graft components remain attached under expected conditions of clinical use	The endoprosthesis must exhibit acceptable simulated 10 year fatigue durability, when placed within a bare nitinol stent, in that device function is not compromised.	Potential wear from the bare metal stent was assessed in the Longitudinal Compression durability test. Representative bare metal stents were deployed in mock arteries and then relined with overlapped GORE® VIABAHN® Endoprosthesis devices. Mock arteries were subject to longitudinal compression that approximates the compression in the SFA reported in literature. Devices were tested for a 10 years of simulated use. There was no separation of wire structure from the graft tube.
Corrosion	To confirm that the device demonstrates resistance to fretting and pitting corrosion under expected conditions of clinical use	No Fretting or corrosion that would compromise device function within the 10 year simulated use.	GORE® VIABAHN® Endoprostheses, which had previously undergone longitudinal compression for 10 years of simulated use while deployed inside a self-expanding Nitinol bare metal stent, were subjected to a microscopic examination for evidence of fretting corrosion. There was no evidence of fretting or pitting corrosion.
Durability	To confirm that device integrity is maintained under expected conditions of clinical use	The endoprosthesis must exhibit acceptable simulated 10 year fatigue durability, when placed within a bare nitinol stent, in that device function is not compromised.	Representative bare metal stents were deployed within mock arteries and then relined with overlapped GORE® VIABAHN® Endoprosthesis devices. Mock arteries were subject to longitudinal compression that approximates the compression in the SFA, as reported in literature. Devices were tested for 10 years of simulated use. No fracturing of the wire frame or holes in the graft component were observed. All test acceptance criteria were met.

X. SUMMARY OF PRIMARY CLINICAL STUDIES

The applicant performed two (2) clinical studies to establish a reasonable assurance of safety and effectiveness for the use of the GORE® VIABAHN® Endoprosthesis for improving blood flow in longer SFA lesions and SFA ISR lesions. Characteristics of these studies are listed in **Table 2** below.

Table 2: Clinical Studies

Clinical Study	Study Design	Objective	# of Sites	# of Subjects
25cm Device Study (VBL 10-04)	Prospective, single-arm, multi-center clinical trial	Evaluate the safety and procedural success for implanting the 25cm long VIABAHN® device configuration	7	71 enrolled
In-Stent Restenosis Study (RELINE)	Prospective, randomized, two-arm, multi-center clinical trial	Evaluate the long-term safety and effectiveness of the VIABAHN® device compared to PTA for treatment of SFA in-stent restenosis	7	100 enrolled (47 assigned to VIABAHN®, 53 assigned to PTA)

25cm DEVICE STUDY (VBL 10-04)

A. Study Design

Patients were treated between December 17, 2010 and July 19, 2012. The database for this PMA supplement reflected data collected through October 11, 2013 and included 60 patients still participating in the study. There were 7 investigational sites.

The study was a prospective, multi-center, one-arm clinical study. Seventy-one (71) patients with lesions within the SFA (lesions lengths from 20-40cm) were treated with the GORE® VIABAHN® Endoprosthesis with Heparin Bioactive Surface. This sample size was intended to provide data for at least 50 patients with complete follow-up. A core laboratory was used to assess angiographic imaging, color-flow duplex ultrasound follow-up, and freedom from device fracture. Results were presented with descriptive statistics.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the 25cm Device Study (VBL 10-04) was limited to patients who met the following inclusion criteria:

1. Lifestyle-limiting claudication or rest pain (meeting angiographic entry criteria) affecting a lower extremity (Rutherford Categories 2-4).
2. A written informed consent form, which has been reviewed and approved by the Ethics Committee, has been read, understood and signed by the subject (or their legally authorized representative).
3. At least 21 years of age.
4. Noninvasive lower extremity arterial studies (ankle brachial index, ABI) prior to (within 45 days) or at the time of the study procedure demonstrating resting anklebrachial index (ABI) ≤ 0.9 in the study limb. If ABI > 0.9 , patient is eligible for study if toe-brachial index is ≤ 0.5 .
5. A staged ipsilateral vascular procedure was not completed less than 30 days prior to the study procedure. Resting ABIs were completed prior to the study procedure a minimum of 30 days after the staged vascular procedure.
6. Vascular treatment on the non-study leg for bilateral claudication was not performed less than 30 days prior to study procedure. Resting ABIs on the study limb were completed prior to the study procedure a minimum of 30 days after treatment on the non-study leg.
7. Male, infertile female, or female of child-bearing potential practicing an acceptable method of birth control with a negative pregnancy test within 7 days prior to study procedure.
8. Projected life expectancy of greater than three years.
9. The ability to comply with protocol follow-up requirements and required testing.
10. Angiographic and Lesion Requirements (assessed intraoperatively):
 - 10a. Lesion length of ≥ 20 cm located in the region beginning 1 cm below the origin of the profunda femoris artery and ending 1 cm above the origin of the intercondylar fossa, based on visual estimate.

10b. De novo, post-percutaneous transluminal angioplasty (PTA), or post-atherectomy stenosis (> 50% at some point within the lesion by visual estimate) or occlusion of native SFA.

10c. Origin and proximal 1 cm of SFA are patent, based on visual estimate.

10d. Popliteal artery is patent from 1 cm above the origin of the intercondylar fossa distal to the radiographic knee joint, based on visual estimate.

10e. Reference vessel diameter of 4.0 – 7.5 mm in proximal and distal treatment segments within the SFA, based on visual estimate.

10f. Angiographic evidence, based on visual estimate, of at least one patent tibial artery to the ankle that does not require intervention.

10g. Guidewire has successfully traversed lesion and is within the true lumen of the distal vessel.

Patients were not permitted to enroll in the 25cm Device Study (VBL 10-04) if they met any of the following exclusion criteria:

1. Untreated flow-limiting aortoiliac occlusive disease.
2. Any previous open surgical procedure in the target vessel or previous stent placement in the target vessel.
3. Prior angioplasty on the target lesion performed less than 30 days prior to the study procedure (unless performed at time of study procedure).
4. Prior atherectomy on the target lesion performed less than 6 months prior to the study procedure (unless performed at time of study procedure).
5. Any previous treatment of the target vessel with a drug eluting balloon.
6. Femoral artery or popliteal artery aneurysm.
7. Non-atherosclerotic disease resulting in occlusion (e.g., embolism, Buerger's disease, vasculitis).
8. Tibial artery disease requiring treatment.
9. Prior ipsilateral femoral artery bypass.
10. Severe medical comorbidities (untreated coronary artery disease / congestive heart failure, severe COPD, metastatic malignancy, dementia, etc.) or other medical condition that would preclude post-procedural ambulation.
11. Popliteal artery vascular access at any time during procedure.
12. Antegrade and retrograde vascular access on the same common femoral artery at the time of the SFA intervention.
13. Major distal amputation (above the transmetatarsal) in the study or non-study limb.
14. Septicemia.
15. Any previously known coagulation disorder, including hypercoagulability.
16. Morbid obesity or operative scarring that precludes percutaneous approach (physician's discretion).
17. Contraindication to anticoagulation or antiplatelet therapy.

18. Known allergies to stent/stent-graft components, including heparin sensitivity, allergy, or previous incidence of heparin-induced thrombocytopenia (HIT) type II.
19. History of prior life-threatening reaction to contrast agent.
20. Currently participating in another clinical research trial, unless approved by W. L. Gore & Associates in advance of study enrollment.
21. Subject has one limb currently enrolled in the VBL 10-04 study.
22. Current peritoneal or hemodialysis
23. Patient has a condition (unrelated to the study) that is expected to require indefinite or lifelong anticoagulation.

2. Follow-up Schedule

All patients were scheduled to return for follow-up examinations at 30 days (± 7 days), 1 year (± 45 days), 2 years (± 45 days), and 3 years (± 45 days) postoperatively. All patients received the same follow-up evaluations.

Preoperatively, each patient was assessed against the clinical enrollment criteria prior to the study treatment procedure by a knowledgeable healthcare professional who performed a physical examination of the patient and reviewed the patient's medical records to determine study eligibility. The angiographic inclusion and exclusion criteria were assessed at the time of the study procedure.

Postoperatively, the objective parameters measured during the study included measurement of Ankle Brachial Index (ABI), Color Flow Duplex Ultrasound (CDUS), and plain X-ray as shown in **Table 3** below. Adverse events and complications were recorded at all visits.

Table 3: Schedule of 25cm Device Study Assessments

Event	Screening and Study Enrollment	Procedure	Discharge	30 Days	12, 24, 36 Months
Consent	X				
Inclusion/Exclusion Criteria	X				
Medical History	X				
Laboratory Evaluations: Creatinine, Hemoglobin and Hematocrit, Platelet Count, Pregnancy Testing	X				
Physical Examination	X		X	X	X
Adverse Events		X	X	X	X
Medications	X	X	X	X	X
Rutherford Classification	X				X
Ankle Brachial Index	X		X	X	X
Color Flow Duplex Ultrasound	X			X	X
Angiography		X			
Plain X-Ray				X	X

3. Clinical Endpoints

With regards to safety, the primary safety endpoint is the proportion of subjects who experienced device- or procedure-related serious adverse events within 30 days post-procedure.

With regards to effectiveness, the primary performance success endpoint is successful completion of the assigned treatment and post-deployment stent length (of the first 25 cm GORE VIABAHN Endoprosthesis with HeparinBioactive Surface) being within 10% of pre-deployment stent length. ‘Successful completion of the assigned treatment’ is a composite, defined as the Investigator’s ability to successfully cover the target lesion with the device and result in a post-deployment residual stenosis of <30% within the treated arterial lesion as assessed by the core lab.

B. Accountability of PMA Cohort

At the time of database lock for the PMA submission, of the 71 patients enrolled in the study, 87.3% of the patients (62) remained in the study. At the completion of the 1-year post-operative visit, 81.7% of the patients (58) had attended the follow-up visit and were available for analysis (Table 4).

Table 4: Patient Availability

	30-Days	1-Year
Number of Subjects	N=71	
Subjects Not Withdrawn	66 (93.0%)	62 (87.3%)
Attended Follow-Up Visit	61 (92.4%) [66]	58 (93.5%) [62]

C. Study Population Demographics and Baseline Parameters

The study was conducted in Austria, Belgium, and Germany and the demographics of the study population are typical for an occlusive PAD study performed in the US. Subject demographics are summarized in **Table 5**. Baseline treatment parameters are summarized in **Table 6**.

Table 5: Patient Demographics

Demographic Variable	25 cm GORE® VIABAHN® Device (n=71)
Age (years), Mean ± SD	66.7 ± 8.34
Males	50 (70.4%)
History of Smoking	58 (81.7%)
History of MI	11 (15.5%)
History of Diabetes Mellitus	23 (32.4%)

Table 6: Baseline Treatment Parameters

Baseline Parameter	25 cm GORE® VIABAHN® Device (n=71)
RVD (mm), Mean ± SD	5.3 ± 0.96
ABI, Mean ± SD	0.53 ± 0.19
Lesion Length (cm), Mean ± SD (range)	26.5 ± 5.31 (20.0 - 40.0)
Percent Diameter Stenosis (%), Mean ± SD	74.8 ± 11.30
Chronic Total Occlusion	65 (92.9%)

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety for the 1 month evaluation included 71 enrolled patients. The key safety outcomes for this study at 1 month and 12 months are presented below in **Tables 7** and **8**. At 1 month, 19.7% of patients (14) had experienced at least 1 adverse event. A total of 3 patients died within the first 12 months of the study. One patient died 10 days after the index procedure due to influenza, one patient died 146 days after the index procedure due to heart failure, and one patient died 205 days after the index procedure due to respiratory failure.

Table 7: Primary Safety Endpoint

	Total
Number of Subjects	N=71
Successfully Completed Primary Safety Endpoint	N=65
Yes	63 (96.9%)
No	2 (3.1%)

Adverse effects that occurred in the PMA clinical study:

Table 8: Device- and Procedure-Related Serious Adverse Events

SERIOUS ADVERSE EVENTS		
	30 Days	12 Months
Number of Subjects Available	N=71	N=71
Number experiencing any event(s)	2 (2.8%) [2]	17 (23.9%) [20]
Thrombosis in device	0 (0.0%) [0]	10 (14.1%) [10]
Infection	0 (0.0%) [0]	1 (1.4%) [1]
In-stent arterial restenosis	0 (0.0%) [0]	5 (7.0%) [6]
Arterial injury	2 (2.8%) [2]	2 (2.8%) [2]
Intermittent claudication	0 (0.0%) [0]	1 (1.4%) [1]

2. Effectiveness Results

The analysis of effectiveness was based on 60 evaluable patients at the 1-month time point. Additional secondary effectiveness outcomes were evaluated at the 1-year time point. Key effectiveness outcomes are presented in **Tables 9 to 11**.

Table 9: Primary Performance Success Endpoint

	Total
Number of Subjects	N=71
Successfully Completed Primary Performance Endpoint	N=60
Yes	46 (76.7%)
No	14 (23.3%)

Table 10: Primary Performance Success Endpoint Details

	Total
Number of Subjects	N=71
Stent Length Within 10% of Pre-deployment	N=58
Yes	58 (100.0%)
No	0 (0.0%)
Post-deployment – Pre-deployment Length (cm)	N=58
Mean (Std Dev)	-0.37 (0.49)
Median	-0.34
Min-Max	-2.02 - 0.77
Covered Target Lesion	N=71
Yes	71 (100.0%)
No	0 (0.0%)
Post-deployment Residual Stenosis < 30%	N=69
Yes	55 (79.7%)
No	14 (20.3%)

Table 11: Primary Patency

	30 Days (Subjects at start / Events / Censored)	12 Months (Subjects at start / Events / Censored)
Primary Patency	97.0%* (71 / 2 / 7)	67.0%* (62 / 18 / 8)
Primary Patency in lesions ≤ 23cm	92.9% (29 / 2 / 2)	57.8% (25 / 9 / 2)
Primary Patency in lesions > 23cm	100.0% (42 / 0 / 5)	73.8% (37 / 9 / 6)
Primary Patency in lesions ≤ 27cm	94.6% (40 / 2 / 5)	63.5% (33 / 10 / 5)
Primary Patency in lesions > 27cm	100% (31 / 0 / 2)	70.4% (29 / 8 / 3)

*Kaplan-Meier estimate

3. Subgroup Analyses

Gender was a demographic characteristic measured in the 25cm Device study. Analysis has been performed to assess the impact on 1-year primary patency for gender.

The genders experienced similar results in the Primary Performance Success endpoint. Primary Performance Success was 76.5% (13/17) among females and 76.7% (33/43) for males. In 100% of cases, the investigators were able to successfully cover the lesion, and in all cases the post-deployment stent length was within 10% of the pre-deployment stent length, regardless of gender. In all cases where the 25 cm VIABAHN did not meet the Primary Performance Success endpoint, it was due to a post-deployment residual stenosis measured by the core lab >30% and ≤50%.

The genders experienced similar results in the Primary Safety endpoint. Among females, 95.2% (20/21) did not have either a device- or procedure-related adverse event within 30 days of procedure, as compared to 93.5% (43/46) of males. These comparisons are summarized in **Table 12** below.

Table 12: Subgroup Analysis by Gender

	Females	Males
Number of Subjects	N=21	N=50
Successfully Completed Primary Performance Endpoint	N=17	N=43
Yes	13 (76.5%)	33 (76.7%)
No	4 (23.5%)	10 (23.3%)
Successfully Completed Primary Safety Endpoint	N=21	N=44
Yes	20 (95.2%)	43 (97.7%)
No	1 (4.8%)	1 (2.3%)

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The 25cm Device clinical study included 59 investigators of which none were full-time or part-time employees of the sponsor. One (1) investigator had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: None
- Significant payment of other sorts: one (1) Investigator
- Proprietary interest in the product tested held by the investigator: None
- Significant equity interest held by investigator in sponsor of covered study: None

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. The information provided does not raise any questions about the reliability of the data.

In-Stent Restenosis Study (RELINe)

A. Study Design

Patients were treated between June 2010 and February 2012. The database for this PMA supplement reflected data collected through the one-year follow-up and included follow-up data for 88 patients at one year. There were 7 investigational sites, located in Belgium and Germany.

The study was a prospective, multi-center, randomized clinical study. One hundred (100) patients with lesions within previously implanted stents in the SFA (lesions lengths from 4-27cm) were randomized to treatment with either the GORE® VIABAHN® Endoprosthesis with Heparin Bioactive Surface or a standard PTA balloon (also called “Plain Old Balloon Angioplasty”, or POBA). PTA balloons are a legally marketed alternative with similar indications for use. The RELINe study was a single-blinded trial; subjects were blinded to their treatment assignment and the study site personnel were trained not to disclose the treatment assignment to the subject. Subject blinding was maintained until the 24-month follow-up visit for all subjects was completed.

An independent core laboratory was contracted to provide objective analysis of all study imaging (Angiography, Duplex Ultrasound, X-Ray). An independent physician adjudicated the coding of serious adverse events.

Based on literature values, the estimated 1-year primary patency was assumed to be 20% for POBA and 60% for the GORE® VIABAHN® Endoprosthesis with Heparin Bioactive Surface. Assuming that the difference in the treatment modalities in this study would be similar to the reported values, a sample size of 28 subjects in each arm was required to show a statistical difference between the arms, using a one-sided Z test with unpooled variance (Type 1 error rate, $\alpha = 0.05$ and power = 0.95). The number of

subjects was increased to 40 to account for roughly 30% noncompliance to clinical follow-up, mortality, and unevaluable data. The protocol was later revised to allow for enrollment to continue until 80 subjects meeting all general and angiographic requirements was achieved. This resulted in 100 patients being enrolled for the intent-to-treat analysis.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the RELINE trial was limited to patients who met the following inclusion criteria:

1. Patient presenting with lifestyle-limiting claudication, rest pain or minor tissue loss (Rutherford Categories 2-5)
2. Patient is willing to comply with specified follow-up evaluations at the specified times
3. Patient is at least 18 years of age
4. Patient understands the nature of the procedure and provides written informed consent, prior to enrollment in the study
5. Patient has a projected life-expectancy of at least 24 months
6. Patient has non-invasive lower extremity arterial studies (resting or exercise) demonstrating ankle-brachial index ≤ 0.8
7. Patient is eligible for treatment with the GORE® VIABAHN® Endoprosthesis (W. L. Gore)
8. Male, infertile female, or female of child bearing potential practicing an acceptable method of birth control with a negative pregnancy test within seven days prior to study procedure

Angiographic and Lesion Requirements (assessed intraoperatively)

1. Restenotic or reoccluded lesion located in a stent which was previously implanted (>30 days) in the superficial femoral artery, suitable for endovascular therapy
2. Total target lesion length between 4 and 27cm (comprising in-stent restenosis and adjacent stenotic disease)
3. Minimum of 1.0cm of healthy vessel (non-stenotic) both proximal and distal to the treatment area
4. Popliteal artery is patent at the intercondylar fossa of the femur to popliteal bifurcation
5. Target vessel diameter visually estimated to be >4 mm and <7.6 mm at the proximal and distal treatment segments within the SFA
6. Guidewire and delivery system successfully traversed lesion
7. There is angiographic evidence of at least one-vessel-runoff to the foot, that does not require intervention ($<50\%$ stenotic)

Patients were not permitted to enroll in the RELINE trial if they met any of the following exclusion criteria:

1. Untreated flow-limiting aortoiliac occlusive disease.

2. Presence of a chronic total occlusion, i.e. a complete occlusion of the failed bare stent that cannot be reopened with thrombolysis or does not allow easy passage of the guidewire by the physician
3. Any previous surgery in the target vessel
4. Severe ipsilateral common/deep femoral disease requiring surgical reintervention
5. Perioperative unsuccessful ipsilateral percutaneous vascular procedure to treat inflow disease just prior to enrollment
6. Femoral artery or popliteal artery aneurysm located in the target vessel
7. Non-atherosclerotic disease resulting in occlusion (e.g., embolism, Buerger's disease, vasculitis)
8. No patent tibial arteries (>50% stenosis)
9. Prior ipsilateral femoral artery bypass
10. Severe medical comorbidities (untreated CAD/CHF, severe COPD, metastatic malignancy, dementia, etc.) or other medical condition that would preclude compliance with the study protocol or 2-year life expectancy
11. Serum creatinine >2.5mg/dL within 45 days prior to study procedure unless the subject is currently on dialysis
12. Major distal amputation (above the transmetatarsal) in the study or non-study limb
13. Septicemia or bacteremia
14. Any previously known coagulation disorder, including hypercoagulability
15. Contraindication to anticoagulation or antiplatelet therapy
16. Known allergies to stent or stent-graft components (Nickel-titanium or ePTFE)
17. Known allergy to contrast media that cannot be adequately pre-medicated prior to study procedure
18. Patient with known hypersensitivity to heparin, including those patients who have had a previous incidence of heparin-induced thrombocytopenia (HIT) type II
19. Currently participating in another clinical research trial, unless approved by W. L. Gore in advance of study
20. Angiographic evidence of intra-arterial thrombus or atheroembolism from inflow treatment
21. Any planned surgical intervention/procedure within 30 days of the study procedure
22. Target lesion access not performed by transfemoral approach

2. Follow-up Schedule

All patients were scheduled to return for follow-up examinations at 1 day (+ 7 days), 30 days (\pm 7 days), 6 months (180 ± 30 days), 1 year (365 ± 30 days), and 2 years (730 ± 45 days). The schedule of required follow-up examinations is presented in **Table 13**. All patients received the same follow-up evaluations.

Table 13: Schedule of RELINE Study Assessments

Event	Screening	Pre-Procedure	Procedure	Day 1	30 Days	6 Months	12 Months	24 Months
Informed Consent	X							
Inclusion/Exclusion Criteria	X							
Medical History		X						
Medications		X		X	X	X	X	X
Rutherford Classification		X		X	X	X	X	X
Physical Examination		X		X	X	X	X	X
Randomization (VIABAHN VS. POBA)			X					
Adverse Events			X	X	X	X	X	X
Color Flow Duplex Ultrasound		X ¹			X	X	X	X
Angiography			X				X	
Biplanar X-Ray							X	

1- If indicated by investigator, CFDU may be obtained.

3. Clinical Endpoints

With regards to safety, the primary safety endpoint is the proportion of subjects who have experienced device-related serious adverse events (SAEs) within 30 days post-procedure.

With regards to effectiveness, the primary efficacy endpoint is Primary Patency at 12 months, defined as no evidence of restenosis or occlusion within the originally treated lesion based on color-flow duplex ultrasound (CFDU) measuring a Peak Systolic Velocity Ratio (PSVR) of ≤ 2.5 without target lesion revascularization (TLR).

The hypothesis was that the use of the GORE® VIABAHN® Endoprosthesis with Heparin Bioactive Surface would result in a greater primary patency of treated SFA ISR when compared to treatment with POBA. The study was considered a success if this hypothesis was statistically met.

B. Accountability of PMA Cohort

After the 1-year follow-up, of the 100 patients enrolled in the PMA study, 91% (91) patients were available for analysis. Of the 100 enrolled subjects, 6 (6%) subjects died while participating in the RELINE study as of the 1-year window (procedure to day 410). All 6 subject deaths were reported as “Unrelated” to the study or control device. All subject deaths were also reported as “Unrelated” to the study procedure. Of the 47 subjects randomized to the study group, 3 (6.4%) deaths were reported. The reported

cause of death for these 3 subjects was “unknown” (3). Of the 53 subjects randomized to the control group, 3 (5.7%) deaths were reported. The reported cause of death for these 3 subjects was “general deterioration and general weakness” (1), “kidney failure” (1) and “unknown” (1). A total of 3 (3%) subjects were lost to follow-up prior to the 12 month visit. One (1%) subject randomized to the study group did not return for follow-up after day 24. Two (2%) subjects in the control group did not return for follow-up after days 1 and 123.

The intent-to-treat analysis includes all patients randomized in the study. Bail-out at the index procedure is counted as TLR and patency loss at day 0.

The per-protocol analysis excludes 17 patents (8 VIABAHN and 9 POBA) based on inclusion/exclusion criteria and procedural violations identified by the lead investigator. Bail-out at the index procedure is counted as TLR and patency loss at day 0.

The as-treated analysis excludes the same patients as the per-protocol analysis; additionally, all patients receiving bailout at the index procedure are excluded from the analysis (8 additional POBA patients).

Accountability is summarized in **Table 14** below.

Table 14: Patient Availability

	30-Days		12 Months	
	VIABAHN	POBA	VIABAHN	POBA
Number of Subjects	N=47	N=53	N=47	N=53
Subjects Not Available for Follow-up ¹	1 (2.1%)	2 (3.8%)	4 (8.5%)	5 (9.4%)

¹Subjects counted are those deceased before the respective follow-up visit window or with last known follow-up before the respective follow-up visit window.

C. Study Population Demographics and Baseline Parameters

The study was conducted in Belgium and Germany and the demographics of the study population are typical for an occlusive PAD study performed in the US. Population demographics are shown in **Table 15** below. The baseline parameters, including clinical category (Rutherford Category) and lesion characteristics, are shown in **Table 16** below.

Table 15: Population Demographics

	VIABAHN	POBA
Number of Subjects	47	53
Age at Procedure in years, Mean (Std Dev)	67.3 (9.86)	69.3(9.72)
Male	34 (72.3%)	35(66.0%)
Smoking History	31 (66.0%)	40 (75.5%)
History of Hypertension	33 (70.2%)	34 (64.2%)
History of Diabetes	18 (38.3%)	19 (35.8%)
History of Renal Insufficiency	3 (6.4%)	4(7.5%)
Obesity	12 (25.5%)	13(24.5%)
History of Hypercholesterolemia	20 (42.6%)	35(66.0%)

Table 16: Baseline Treatment Parameters

	VIABAHN	POBA
Number of Subjects	47	53
Baseline Rutherford Category		
Category 2	16 (34.0%)	7(13.2%)
Category 3	24 (51.1%)	35(66.0%)
Category 4	4(8.5%)	3(5.7%)
Category 5	3(6.4%)	8(15.1%)
Lesion Length (cm), Mean ± Std Dev (range)	16.8 ± 7.47 (3.0 – 33.0)	19.1 ± 7.53 (3.0 – 37.0)
Occlusion	9 (19.1%)	15(28.3%)

D. Safety and Effectiveness Results**1. Safety Results**

The analysis of safety was based on the intent-to-treat cohort of 100 patients (47 randomized to the GORE® VIABAHN® Endoprosthesis with Heparin Bioactive Surface and 53 randomized to POBA) and is summarized in **Table 17** below. One subject from each treatment group was lost to follow-up prior to the end of the 30-day window. One (2.2%) subject randomized to the study device experienced a device-related serious adverse event within 30 days post-procedure. The following serious device-related adverse event was reported for the VIABAHN® device group:

-Occlusion of the study lesion (Day 29)

Three (5.8%) subjects randomized to the POBA control group experienced a serious device-related adverse event within 30 days post-procedure. The following three serious device-related adverse events were reported for the control group:

-Peripheral embolization (Day 0)

-Reocclusion of target lesion (Day 1)

-Subacute limb ischemia (Day 1)

Table 17: Primary Safety Endpoint – Proportion of Subjects experiencing Serious Device-related Adverse Events within 30-days Post-Procedure

	GORE® VIABAHN® Device	POBA	P-value
Free from Serious Device-Related AEs at 30 Days ^{1, 2}	97.8% (45/46)	94.2% (49/52)	0.620

1 - P-value obtained with Fisher's Exact Test (Successes/Subjects with known status).

2 - Format utilized: Percentage of subjects with attribute (Subjects having attribute/Subjects with known status).

Adverse effects that occurred in the PMA clinical study:

The rate of incidence of various device- or procedure-related serious adverse events are shown in **Table 18** below.

Table 18: Device- and Procedure-Related Serious Adverse Events Reported through 30 days and 12 months

SERIOUS ADVERSE EVENTS				
	GORE® VIABAHN® Device		POBA	
	30 Days	12 Months	30 Days	12 Months
Number of Subjects Available	47	47	53	53
Device occlusion	1 (2.1%) [1]	1 (2.1%) [2]	0 (0.0%) [0]	2 (3.8%) [2]
Device related infection	0 (0.0%) [0]	0 (0.0%) [0]	1 (1.9%) [1]	1 (1.9%) [1]
Fasciotomy	0 (0.0%) [0]	0 (0.0%) [0]	0 (0.0%) [0]	1 (1.9%) [1]
Femoral artery occlusion	0 (0.0%) [0]	3 (6.4%) [3]	0 (0.0%) [0]	1 (1.9%) [1]
Peripheral artery aneurysm	0 (0.0%) [0]	1 (2.1%) [1]	0 (0.0%) [0]	0 (0.0%) [0]
Peripheral artery restenosis	0 (0.0%) [0]	2 (4.3%) [2]	1 (1.9%) [1]	5 (9.4%) [5]
Peripheral artery stenosis	0 (0.0%) [0]	0 (0.0%) [0]	0 (0.0%) [0]	1 (1.9%) [1]
Peripheral artery thrombosis	0 (0.0%) [0]	0 (0.0%) [0]	1 (1.9%) [1]	1 (1.9%) [1]
Peripheral embolism	0 (0.0%) [0]	0 (0.0%) [0]	1 (1.9%) [1]	1 (1.9%) [1]
Peripheral ischaemia	0 (0.0%) [0]	0 (0.0%) [0]	0 (0.0%) [0]	1 (1.9%) [1]
Reocclusion	0 (0.0%) [0]	0 (0.0%) [0]	1 (1.9%) [1]	1 (1.9%) [1]

Device- or procedure-related adverse events were those that resulted from the design or use of the study device or the index procedure.

Subject counts at the top of each column are the number of subjects within the study at the beginning of that interval and are the denominator used in calculating percentages in that column.

Time intervals for estimates: 30 Days (Procedure through 30 days), 12 Months (Procedure through 410 days).

Entries represent MedDRA System Preferred Term. Cells are formatted to display: number of subjects experiencing the event (percentage of subjects experiencing the event) [number of events experienced].

The only device or procedure-related SAEs occurring at a rate of greater than 2% were related to restenosis or reocclusion, whether in the device or target vessel. This is expected for an occlusive PAD trial, and the test device did not show a greater rate of these SAE's than the control arm (in fact, these trended lower for the test device arm, which is expected given the effectiveness endpoints). Other restenoses and reocclusions occurred, but were mainly considered disease-related.

It should be noted that the safety of the device for the SFA ISR indication was not based on this sample alone, but rather on all of the information available for the device to date. The safety data from this study were for confirmatory purposes.

2. Effectiveness Results

The analysis of effectiveness was based on the 91 patients having known 12-month status. Primary and secondary effectiveness endpoints are presented in **Table 19** below.

Table 19: Summary of Effectiveness Endpoints

	GORE® VIABAHN® Device	POBA	P-value
Primary Endpoints			
Primary Patency at 12 months (intent-to-treat analysis ³) ¹	72.5% (47/12/5)	24.2% (53/38/4)	<0.001
Primary Patency at 12 months (per-protocol analysis ⁴) ¹	74.8% (39/9/5)	28.0% (44/31/2)	
Primary Patency at 12 months (as-treated analysis ⁵) ¹	74.8% (39/9/5)	37.0% (36/22/2)	
Secondary Endpoints			
Technical Success ^{2, 3}	97.8% (45/46)	78.4% (40/51)	
Clinical Success at 12 months ^{2, 3}	92.3% (36/39)	88.9% (40/45)	
Stent Fracture at 12 months ^{2, 3}	0% (0/25)	NA	
Kaplan-Meier Analysis	Point Estimate (Subjects at start / Events / Censored)	Point Estimate (Subjects at start / Events / Censored)	
- Primary Patency in lesions ≤ 23 cm at 12 months ^{1, 3}	69.7% (38/11/3)	27.0% (33/22/4)	
- Primary Patency in lesions > 23 cm at 12 months ^{1, 3}	85.7% (9/1/2)	23.5% (17/13/0)	
Primary Assisted Patency at 12 months ^{1, 3}	77.2% (47/10/5)	62.1% (53/19/7)	
Secondary Patency at 12 months ^{1, 3}	93.2% (47/3/6)	76.6% (53/12/7)	
Quantitative Angiographic Patency at 12 months ^{1, 3}	81.3% (16/3/0)	67.1% (20/6/2)	
Freedom from TLR at 12 months ^{1, 3}	81.2% (47/8/6)	40.6% (53/30/6)	

1 - 12-month estimate and p-value obtained with Kaplan-Meier estimator and the log-rank test utilizing the format: Point Estimate (Subjects at start/Events/Censored).

2 - Format utilized: Percentage of subjects with attribute (Subjects having attribute/Subjects with known status).

3 - Intent-to-treat analysis includes all patients randomized in the study. Bail-out at the index procedure is counted as TLR at day 0.

4 - Per-protocol analysis excludes 17 patients (8 GORE® VIABAHN® Device group and 9 POBA) based on inclusion/exclusion criteria and procedural violations identified by the lead investigator. Bail-out at the index procedure is counted as TLR at day 0.

5 - As-treated analysis excludes the same patients as the per-protocol analysis; additionally, all patients receiving bailout at the index procedure are excluded from the analysis (9 additional POBA patients).

In the RELINE study, the primary endpoint showed superiority of the test arm (the GORE® VIABAHN® Endoprosthesis with Heparin Bioactive Surface) over the control arm (POBA).

It should be noted that the performance of the device for the SFA ISR indication was not based on this sample alone, but rather on all of the information available for the device to date. The effectiveness data from this study were for confirmatory purposes.

3. Subgroup Analyses

Gender was a demographic characteristic measured in the ISR (RELINE) study. Analysis has been performed to assess the impact on 1-year primary patency for gender.

Kaplan-Meier analysis was performed separately for each gender. The p-value obtained through the log-rank method was <0.001 for each case, showing a significant difference between the VIABAHN® device and POBA survival curves regardless of gender. At 365 days, the primary patency of the VIABAHN® device was estimated to be 83.9% for females (**Table 20** below) and 68.1% for males (**Table 21** below). The primary patency of POBA was estimated to be 14.8% for females and 28.1% for males.

Table 20: 1-Year Primary Patency by Treatment Group, Female Gender

Time Post Treatment (Days)	N at Risk at Start of Interval	N Events During Interval *	N Censored During Interval *	% Subjects Patent	95% Confidence Interval
Group: VIABAHN					
0	13	0 (0)	0 (0)	100%	(100.0%, 100.0%)
(0-30]	13	1 (1)	0 (0)	92.3%	(56.6%, 98.9%)
(30-183]	12	0 (1)	1 (1)	92.3%	(56.6%, 98.9%)
(183-365]	11	1 (2)	0 (1)	83.9%	(49.4%, 95.7%)
Group: POBA					
0	18	4 (4)	0 (0)	77.8%	(51.1%, 91.0%)
(0-30]	14	1 (5)	1 (1)	72.2%	(45.6%, 87.4%)
(30-183]	12	3 (8)	2 (3)	51.7%	(25.6%, 72.6%)
(183-365]	7	5 (13)	0 (3)	14.8%	(2.5%, 37.3%)
Logrank p-value: p=<.001					
* Number in parenthesis represents cumulative events or censored observations through end of interval					

Table 21: 1-Year Primary Patency by Treatment Group, Male Gender

Time Post Treatment (Days)	N at Risk at Start of Interval	N Events During Interval *	N Censored During Interval *	% Subjects Patent	95% Confidence Interval
Group: VIABAHN					
0	34	0 (0)	0 (0)	100%	(100.0%, 100.0%)
(0-30]	34	1 (1)	1 (1)	97.0%	(80.4%, 99.6%)
(30-183]	32	1 (2)	0 (1)	93.9%	(77.9%, 98.4%)
(183-365]	31	8 (10)	3 (4)	68.1%	(48.7%, 81.4%)
Group: POBA					
0	35	6 (6)	0 (0)	82.9%	(65.8%, 91.9%)
(0-30]	29	2 (8)	0 (0)	77.1%	(59.5%, 87.9%)
(30-183]	27	6 (14)	0 (0)	60.0%	(42.0%, 74.0%)
(183-365]	21	11 (25)	1 (1)	28.1%	(14.4%, 43.5%)
Logrank p-value: p=<.001					
* Number in parenthesis represents cumulative events or censored observations through end of interval					

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The RELINE clinical study included 11 investigators of which none were full-time or part-time employees of the sponsor and one (1) investigator who had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: None
- Significant payment of other sorts: one (1) Investigator
- Proprietary interest in the product tested held by the investigator: None
- Significant equity interest held by investigator in sponsor of covered study: None

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. The information provided does not raise any questions about the reliability of the data.

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

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory System Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The sponsor provided data from the 25cm Study and the RELINE Study in order to support the safety and effectiveness of the expanded indication which includes SFA lesions up to 270mm in length as well as in-stent restenotic lesions. The sponsor evaluated patency as the assessment for effectiveness in both studies. For the 25cm Study, the patency rate is 67% at 12 months which demonstrates that there is not a substantial reduction in patency for lesions up to 270mm when using this device. For the RELINE Study, the test arm performed significantly better than the control arm demonstrating the improved patency over balloon angioplasty when treating in-stent restenosis. For the ITT group, primary patency was 72.5% for the VIABAHN® group vs. 24.2% for the POBA group ($p < 0.001$).

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory and/or animal studies as well as data collected in clinical studies conducted to support PMA approval as described above.

The primary safety endpoint was defined as serious device- or procedure-related adverse events occurring within 30 days of the procedure for both the 25cm Study and the RELINE Study.

In the 25cm Study, a total of 14 device- or procedure-related adverse events were reported on 14 subjects (19.7%) within the first 30 days of the procedure. The type and frequency of events were within what is expected for these types of studies. In the RELINE Study, freedom from serious device-related adverse events within 30 days post-procedure was 97.8% for the study arm and 94.2% for the control arm. These rates demonstrate that the test device has equivalent safety to the control, and thus met the primary safety endpoint.

C. Benefit-Risk Conclusions

The probable benefits of the device are also based on data collected in clinical studies conducted to support PMA approval as described above. The probable benefit of the GORE® VIABAHN® Endoprosthesis of improving the patient symptoms and quality of life outweigh the probable risks associated with the use of the device.

Treatment of In-Stent-Restenosis is challenging and treatment with the alternative approved therapy, Plain Old Balloon Angioplasty (POBA), has traditionally yielded high rates of restenosis recurrence after treatment. Because treatment of ISR with the GORE® VIABAHN® Endoprosthesis device yielded a substantial improvement in patency at 12 months, it offers benefit over current therapy. This benefit is expected to outweigh the potential risks associated with placement of permanent implants, including risks for long term adverse events or issues with device durability (e.g., fracture).

In conclusion, given the available information above, the data support that for treatment of in-stent restenosis and lesions up to 270mm in the SFA, the probable benefits outweigh the probable risks.

D. Overall Conclusions

The clinical and non-clinical data in this application provide a reasonable assurance that the device is safe and effective when used in accordance with the indications for use. The results of the 25cm study demonstrate safety and efficacy for lesions up to 270mm when using this device. The results of the RELINE study demonstrate safety and efficacy for use of this device for treatment of in-stent restenosis. Therefore, it is reasonable to conclude that the benefits of use of the device for the target population outweigh the risk of illness or injury when used as indicated in accordance with the labeling and Instructions for Use (IFU).

XIII. CDRH DECISION

CDRH issued an approval order **September 19, 2014.**

A post-approval study involving use of the device according to its newly approved indication is required to obtain data related to the applicability of the clinical study data to the real-world patient population, detection of rare adverse events, and outcomes in clinically meaningful patient sub-populations. The results of these studies will also be evaluated to determine whether any changes should be made to the device labeling to ensure that the information available to physicians is complete, appropriate, and up-to-date.

The final conditions of approval cited in the approval order are described below.

1. W.L. Gore and Associates has agreed to continued follow-up of patients enrolled in the prospective, randomized, multicenter, GORE VIABAHN Endoprosthesis with Heparin Bioactive Surface versus Plain Old Balloon Angioplasty (POBA) in the treatment of in-stent restenosis of the Superficial Femoral Artery (SFA) or RELINE Trial. All 88 remaining patients at 12 months, from the original 100 randomized patients, will be followed out to 24 months post-implant.

The primary endpoint of primary patency [defined as no evidence of restenosis or occlusion within the originally treated lesion based on color-flow duplex ultrasound (CFDU) measuring a peak systolic velocity ratio (PSVR) of ≤ 2.5 without target lesion revascularization (TLR)] at 24 months will be estimated using Kaplan-Meier time-to-event analysis. The secondary endpoints to be assessed through Kaplan-Meier time-to-event analysis are primary assisted patency, secondary patency, and freedom from TLR at 24 months. Clinical success at 24 months will be tested for treatment differences using the Fisher's exact test. Serious adverse events at 24 months will be categorized and presented as frequency and proportions.

2. W.L. Gore and Associates has agreed to assess the incidence of stent fracture and evaluate the long-term performance of the GORE VIABAHN Endoprosthesis and GORE VIABAHN Endoprosthesis with Heparin Bioactive Surface. This will be a prospective, multicenter single-arm study of newly enrolled patients treated with the GORE

VIABAHN Endoprosthesis with Heparin Bioactive Surface device for in-stent restenosis of the SFA. Patients will be followed at 30 days and annually through 36 months.

A sample size of 108 new enrollment patients, with a minimum of 81 US and a maximum of 27 outside of the US (OUS) patients, will be enrolled across a minimum of 15 US sites and up to 5 OUS sites. Patients in Rutherford categories 2 to 5 will be enrolled to provide evidence at various clinical stages of the disease.

The primary effectiveness endpoint is primary patency at 12 months. The primary safety endpoint is device- and procedure-related serious adverse events within 30 days of the procedure. All primary endpoints will be descriptively reported.

The secondary endpoints of primary patency, primary assisted patency, secondary patency, freedom from TLR, and freedom from major amputation will be assessed at 12, 24 and 36 months and estimated by Kaplan Meier methods. Adverse events will be presented as counts and proportions at 30 days, 12 months, 24 months, and 36 months. In addition, the occurrence of stent fracture will be assessed annually post-implant through 36 months by a Core Lab, classified according to stent integrity grading scale (Class 0 to V) as performed for the RELINE Trial, except angiography will not be performed for additional categorization.

The total of 108 subjects is expected to provide an evaluable sample size of 86 subjects at 1-year after 20% lost to follow-up. With 71% assumed patency for the VIABAHN device, this sample size will provide a 95% confidence interval of 60.2% to 80.3% yielding a precision of 20.1%.

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

XIV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.