Summary of Safety and Effectiveness Data (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Iliac Stent
Device Trade Name:	Protégé™ GPS Self-Expanding Peripheral Stent System
Device Product Code:	NIO
Applicant Name and Address:	ev3, Inc. 3033 Campus Drive, Suite, #N550 Plymouth, MN 55441
Date of Panel Recommendation:	None
Premarket Approval Application (PMA) Number:	P060001/S020
Date of FDA Notice of Approval:	January 21, 2015
Priority Review:	Not applicable

The original Protégé™ GPS Carotid Stent System PMA (P060001) was approved on January 24, 2007 and is indicated for the treatment of patients at high risk for adverse events from carotid endarterectomy who require percutaneous carotid revascularization and meet the criteria outlined below:

1. Patients with carotid artery stenosis (> 50% for symptomatic patients by ultrasound or angiography or > 70% for asymptomatic patients by ultrasound or angiography) of the common or internal carotid artery, AND
2. Patients must have a reference vessel diameter within the range of 4.5 mm and 9.5 mm at the target lesion.

The SSED to support the indication is available on the CDRH website and is incorporated by reference here. The current supplement (S020) was submitted to expand the indication for the Protégé GPS™ Self- Expanding Peripheral Stent System to include use in common and/or external iliac arteries.

II. INDICATION FOR USE

The Protégé™ GPS Self-Expanding Peripheral Stent System is indicated for improving luminal diameter in patients with atherosclerotic disease of the common and/or external iliac arteries up to and including 100 mm in length, with a reference vessel diameter of 7.5 – 11 mm.

III. CONTRAINDICATIONS

- Patients with known hypersensitivity to nickel-titanium
- Patients in whom anticoagulant and/or antiplatelet therapy is contraindicated
- Patients who are judged to have a lesion that prevents complete inflation of an angioplasty balloon or proper placement of the stent or stent delivery system.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Protégé™ GPS Self-expanding Peripheral Stent System labeling (Instructions for Use).

V. DEVICE DESCRIPTION

The Protégé™ GPS Self-Expanding Peripheral Stent System (Protégé GPS) consists of a self-expanding stent pre-mounted on an over-the-wire stent delivery system. The Protégé GPS stent is a flexible self-expanding Nitinol (nickel-titanium alloy) stent provided in multiple lengths and diameters. **Table 1** lists the available stent diameters and lengths for the Protégé™ GPS Self-expanding Peripheral Stent System.

Table 1: Protégé GPS Stent Diameters and Lengths

		Stent Length (mm)				
		20	**30**	**40**	**60**	**80**
Stent Diameter (mm)	**9**	x	x	x	x	x
	10	x	x	x	x	x
	12	x	x	x	x	x

The stent is laser machined from a continuous non-welded (seamless) piece of Nitinol tubing into an open lattice design. The Protégé GPS stent cell geometry includes two wave peaks between every two connection bridges on the 9 and 10 mm diameter stents, and three wave peaks between every two connection bridges on the 12 mm diameter stents as shown in **Figure 1**. The connection bridges between wave peaks are along the same longitudinal axis. Tantalum radiopaque markers are located on both ends of the stent to aid in visualization.

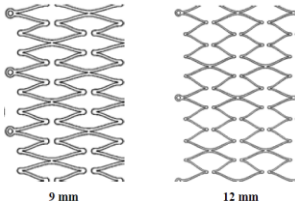

Figure 1: Schematic of Laser Cut Protégé GPS stent geometry

The stent is pre-mounted on a 80 or 120 cm working length 6F, .035" over-the-wire (OTW) stent delivery system that is comprised of multiple components as shown in **Figure 2.**

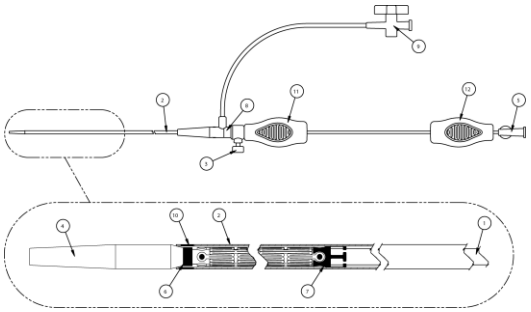

Figure 2 – Schematic of Delivery System

1. Inner Subassembly
2. Outer Subassembly
3. Safety Lock
4. Distal Catheter Tip
5. Proximal Hub
6. Inner Subassembly Distal Marker Band
7. Inner Subassembly Proximal Marker Band/Retainer
8. Manifold Subassembly
9. Stopcock
10. Outer Subassembly Distal Marker Band
11. Distal Grip
12. Proximal Grip

Radiopaque markers on the stent delivery system are intended to aid in the accurate placement of the stent. Deployment is achieved by pulling the distal delivery system handle proximally, which retracts the outer sheath. The delivery system radiopaque stent retainer holds the stent stationary until the outer sheath is fully retracted to facilitate accurate placement. Upon deployment, the stent achieves its pre-determined diameter and exerts a constant, gentle outward force to maintain patency in the target vessel.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Alternative practices and procedures for treatment of atherosclerotic disease of the common and/or external iliac arteries with non-invasive lifestyle modifications including exercise, weight control, cessation of smoking and drug therapy; minimally invasive endovascular intervention with balloon angioplasty, stent placement using other FDA-approved peripheral stents. Each alternative has its own advantages and disadvantages. A patient should fully discuss those alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The Protégé™ GPS Self-Expanding Peripheral Stent System has been commercially available in the European Union (EU) since July, 2002, and the Protégé™ GPS Carotid Stent System has been commercially available in the EU since 2004. Protégé™ GPS and RX Carotid Stent Systems have been commercially available in the US since January 24, 2007, and the Protégé™ GPS Self-Expanding Biliary Stent System has been commercially available in the United States since October 2003.

The Protégé™ GPS Self-Expanding Stent System has remained in continuous distribution since commercial introduction.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

The potential adverse effects (e.g., complications) that may occur and/or require intervention with the use of this device include, but are not limited to:

- Abrupt or sub-acute closure
- Allergic reaction to device materials or procedure medications
- Allergic reaction to Nitinol
- Amputation
- Aneurysm
- Angina
- Arrhythmia
- Arterio-venous fistula
- Artery injury (e.g. dissection, perforation, or rupture)
- Bleeding requiring transfusion
- Bruising
- Contrast medium reaction/renal failure
- Death
- Device breakage
- Edema
- Embolism
- Failure to deploy stent
- Fever
- Gastrointestinal bleeding due to anticoagulation
- Hematoma
- Hypertension/Hypotension
- Infection
- Inflammation
- Intraluminal thrombus
- Myocardial Infarction
- Pain
- Partial stent deployment
- Pseudoaneurysm
- Renal failure
- Renal insufficiency
- Restenosis
- Sepsis
- Shock
- Stent collapse or fracture
- Stent migration
- Stent misplacement
- Stroke
- Surgical or endovascular intervention
- Thrombosis/occlusion of the stent
- Transient Ischemic Attack
- Venous Thromboembolism
- Vessel spasm
- Worsening claudication or rest pain

For the adverse events that occurred in the clinical study, please see **Table 10**.

IX. SUMMARY OF PRE-CLINICAL STUDIES

A. Biocompatibility

Biocompatibility testing for the Protégé™ GPS Self-Expanding Peripheral Stent System was adequately leveraged from the PMA for the Protégé™ GPS Carotid Stent System (P060001) and the PMA for the EverFlex™ Self-Expanding Peripheral Stent System (P110023).

B. Animal Studies

The animal study for the Protégé™ GPS Self-Expanding Peripheral Stent System was adequately leveraged from PMA (P060001) for the Protégé™ GPS Carotid Stent System.

C. *In Vitro* Product Testing

In vitro bench testing to support the Protégé™ GPS Self-Expanding Peripheral Stent System was developed based on the device risk assessment and is consistent with FDA *Non-Clinical Tests and Recommended Labeling of Intravascular Stents and Associated Delivery Systems*, January, 2005 and April 18, 2010. Because the Protégé GPS is a self-expanding stent, tests recommended specifically for balloon-expandable stents were not conducted. A summary of the tests that were previously reviewed in other submissions and deemed relevant and acceptable for the current submission is provided in **Table 3**. A summary of the new tests performed and the associated results provided in S020 is provided in **Table 4**.

Table 3: Summary of In Vitro Product Testing Previously Reviewed

Test	Previously Approved
Material Composition	P110023
Mechanical Properties	P110023
Crush Resistance	P110023
Galvanic Corrosion	P110023
Radial Pulsatile Fatigue	P060001
Radiopacity	P060001
Torque Strength	P110023
Accelerated Aging	P110023, P060001

Table 4: Summary of New In Vitro Product Testing

Test	Clinical or Functional Relevance	Acceptance Criteria	Summary of Results
Stent			
Shape, Memory & Elasticity	The stent must exhibit super elastic properties *in vivo* and expands to its specified size and shape.	9mm: 25 ± 5º C 10mm: 22 ± 5º C 12mm: 19 ± 8º C	Stents were tested and met established specifications for austenitic finish temperature and the stent exhibits expected shape memory properties.
Corrosion Resistance	The stent must resist corrosion following implantation.	To demonstrate a relative comparison of corrosion behavior between Protégé GPS and the commercially available EverFlex peripheral stent.	Protégé GPS showed comparable or better pitting and crevice corrosion resistance to the EverFlex peripheral stent.
Fretting Corrosion	The stent must resist corrosion following implantation due to wear of mated surfaces when overlapped with another stent.	To demonstrate a relative comparison of corrosion behavior between Protégé GPS and the commercially available EverFlex peripheral stent.	Protégé GPS showed comparable or better fretting corrosion resistance to the EverFlex peripheral stent.
Pitting Corrosion	(Stent surface finish is known to affect other material properties	The mean Protégé GPS titanium oxide layer ≥ the	Protégé GPS stent met the established

	therefore; the stent surface must be uniformly oxidized.	mean EverFlex titanium oxide layer -10Å and < 200 Å	criteria for pitting corrosion
Dimensional Verification	The stent diameter must be uniform to achieve adequate wall apposition, and stent length must meet specifications to allow proper sizing of target lesion.	<u>Stent Length</u> 9x20: 22.7 ± 1.0 mm 10x80: 82.7 ± 2.0 mm <u>Stent Inner Diameter (ID)</u> 9 mm: 9.1 ± 0.4mm (0.3583 ± 0.0157") 10 mm: 10.15 ± 0.45mm (0.3996 ± 0.0177") 12 mm: 12.0 ± 0.5mm (0.4724 ± 0.0197") <u>Stent Outer Diameter (OD)</u> For information only	The acceptance criteria were met. The stent OD was calculated and results were deemed acceptable.
Percent Surface Area of Stent	The metal coverage of the stent must provide sufficient vessel wall contact to help maintain patency.	For Information Only the Percent Metal Coverage was calculated. 9 mm to 12 mm: 18.4% to 14.1%	The stent metal coverage was calculated and met the established design inputs.
Foreshortening	The stent must exhibit minimal foreshortening to assure accurate stent deployment and predictable deployed stent length for the user.	<u>Change in Length</u>:9x20mm: +6.6%/ -13.2% 9x80mm: +4.8%/ -8.5% 10x20mm: +6.6%/ -13.7% 10x80mm: +4.8%/ -8.5% 12x20mm: +9.5%/ -14.2% 12x80mm: +4.8%/ -8.4%	Stents were tested and met the acceptance criteria.
Stent Integrity	Post deployment the stent must be free of defects or cracks that may affect long-term performance outcomes.	No visible defects or cracks on stent as a cause of deployment.	Stents were tested and met the acceptance criteria.
Radial Outward Force	To characterize the force produced by the stent as a function of diameter and assure the force is acceptable for the intended use.	Radial Resistive Force (RRF) and Chronic Outward Force (COF) in g/mm • Specification – ev3 Everflex (SFA, proximal popliteal) 5-8mm: RRF 5.03-17.01; COF ≥ 3.03 Competitor Stents: • Cordis SMART Stent (Iliac, SFA) • 9mm: RRF - 15.24; COF - 5.05 • 10mm: RRF - 14.31; COF – 3.90 • 12mm: RRF - 9.20; COF - 3.96 • IDEV Supera (SFA, proximal	Stents were tested and their results were compared to that of competitor stents. The force was comparable to competitor stents and was acceptable for the intended use.

		popliteal) • 5mm: RRF - 19.8; COF – 1.1 • Abbott Absolute (Iliac) 6mm: RRF - 3.7; COF – 3.1	
Strain and Fatigue Analysis/Finite Element Analysis (FEA)	To evaluate strains the stent experiences during processing, deployment and *in vivo* conditions. To assure the stent does not experience unreasonable strains for the material or the intended use.	Safety Factor > 1.0	Finite element analysis (FEA) results showed strains reasonable for the material and worst-case Iliac loading (pulsatile) conditions for a ten-year period. The 9, 10, and 12mm stents has a safety factor > 1.0.
MR Compatibility	The stent must not pose additional risk of magnetic field interactions, RF-heating or image artifacts to patient undergoing MR imaging at 1.5 and 3.0 Tesla.	The stent must be MR Conditional (ASTM F2503) with respect to implant radiofrequency (RF) heating, magnetically induced translation or magnetically induced torque upon subjection to 1.5 Tesla or 3 Tesla magnetic field. The MR conditions in which the device was tested are specified in the IFU.	Test results demonstrate the stent does not pose additional risk to patients and may be labeled MR Conditional.
Kink Resistance	The stent must be able to reach a radius of curvature suitable for the intended use without kinking.	For Information Only. Stent kink resistance is defined as the smallest radius of curvature that the stent can withstand without kinking.	Stents were tested and were able to reach a radius suitable for the intended use without kinking.
Catheter Delivery System			
Crossing Profile	To verify the maximum diameter of the stent delivery system and assure compatibility with 6F sheaths.	≤ 0.0805" at the tip, outer sheath marker band, catheter body, tip length	Test results met the acceptance criteria.
Deployment Force	Measure the force required to deploy the stent and verify it meets specifications based on the intended use.	≤ 3.0 lbs	Test results met the acceptance criteria.

Deployment Accuracy	The delivery catheter must deploy the stent with accuracy at the target location based on the intended use.	± 3.0 mm to ± 6.4 mm	Test results demonstrate the stent may be deployed accurately and met the acceptance criteria.
Catheter Bond Strengths			
Distal Tip to Distal Inner Lumen Bond	Verify the delivery catheter bond strengths meet specifications based on the intended use.	≥ 2.0 lbs	Test results met the acceptance criteria.
Distal Inner Tip Tube to Spline			
Spline Tube to Stainless Steel Tube			
Manifold Bond		≥ 5.0 lbs	
Catheter Flexibility	To verify the stent delivery system is able to flex and track around a bend radius based on the intended use.	The stent/catheter must easily pass through the sheath and around the bend radius without kinking.	Test results met the acceptance criteria.

D. Sterilization, Packaging, & Shelf Life

Sterilization

The Protégé™ GPS Self-Expanding Peripheral Stent System sterilization validation was previously approved in P060001.

Packaging Testing

The Protégé™ GPS Self-Expanding Peripheral Stent System package testing was previously approved in P060001.

Shelf-Life Testing

The Protégé™ GPS Self-Expanding Peripheral Stent System was tested following accelerated aging to an equivalent of three-years under a shelf-life protocol. Testing demonstrated that the Protégé™ GPS stent and delivery catheter met the established acceptance criteria, and is in compliance with ASTM F1980 for accelerated aging of medical devices. Based on results from this testing, a three year shelf-life was adequately established for the device.

X. SUMMARY OF PRIMARY CLINICAL STUDY

A. Study Design

The DURABILITY Iliac study was a prospective, multi-center, non-randomized, single arm study to evaluate the EverFlex™ Self-Expanding Peripheral Stent System and the Protégé™ GPS Self-Expanding Peripheral Stent System for the treatment of stenotic, restenotic (from PTA or adjunct therapy, not including stents or stent grafts) or occluded lesions of the common and/or external iliac arteries.

The objective of the study was to confirm the safety and effectiveness of primary stenting. A total of seventy-five (75) subjects were enrolled at thirteen (13) US and two (2) European investigational sites; forty-five (45) of the 75 subjects had Protégé™ GPS stent(s) implanted. Subject follow-up occurred at pre-discharge, 30 days, 9 months, 1, 2 and 3 years post-procedure. The primary outcome for the study was Major Adverse Event (MAE) rate at 9 months. Secondary outcomes were MAE rate at 30 days, primary patency rate at 9 months, change in ankle-brachial index at 30 days and 9 months, device success, change in walking impairment questionnaire score at 30 days and 9 months, and clinically driven target vessel revascularization at 30 days and 9 months.

It is important to note that the applicant previously conducted a study titled the Carotid Revascularization with ev3 Arterial Technology Evolution (CREATE) study. CREATE was a prospective, multi-center, non-randomized trial. The primary objective of the trial was to demonstrate the safety and effectiveness of the Protégé™ GPS stent during percutaneous revascularization of the carotid artery for subjects considered to be at high risk for carotid endarterectomy.

1. Clinical Inclusion and Exclusion Criteria

Subjects enrolled in the DURABILITY Iliac study were required to meet the following general and angiographic **inclusion** criteria. Potential study subjects who meet any of the following general and angiographic **exclusion** criteria were not eligible for enrollment in the study. **Table 5** lists all of the inclusion and exclusion Criteria.

Table 5: Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
1. Has a Rutherford Clinical Category Score of 2, 3 or 4 per clinical description. 2. Is willing to comply with all follow-up evaluations at the specified times. 3. Is ≥ 18 years old. 4. Provides written informed consent prior to any enrollment screening procedures. 5. Target lesion(s) located within the native common and/or external iliac artery: proximal point at or distal to the ostium of the common	1. Previous implantation of stent(s) in the target vessel. 2. Has received endovascular treatment of the target lesion within six months prior to the index procedure. 3. Has a contraindication or known untreatable allergy to antiplatelet therapy, anticoagulants, thrombolytic drugs or any other drug used during the study according to the protocol. 4. Has known hypersensitivity to contrast material

Inclusion Criteria	Exclusion Criteria
iliac artery and distal point at least 1 cm above the inguinal ligament measured by straight anteroposterior (AP) view. 6. Evidence of ≥ 50% stenosis or restenosis (from PTA or adjunct therapy, not including stents or stent grafts), or occlusion of target lesion(s) in the common iliac artery and/or external iliac artery. 7. Length of lesion(s) is ≤ 10 cm as determined by a spatially calibrated internal measurement using a device with known distance between radiopaque markers (e.g. marker catheter, balloon catheter, marker wire) and is amenable to stenting. 8. Target vessel diameter is ≥ 4.5 mm and ≤ 11.0 mm. 9. Evidence of patent common femoral artery and origin of *profunda femoris.* 10. Evidence of at least one patent infrapopliteal artery of the target limb that does not require treatment for significant stenosis (> 50% stenosis or occlusion) during the index procedure.	that cannot be adequately pre-treated. 5. Has known hypersensitivity to nickel-titanium. 6. Has bleeding diathesis, coagulopathy, known hypercoagulable condition, or refuses blood transfusion. 7. Is female currently breastfeeding, pregnant, or of child-bearing potential not using adequate contraceptives measures. 8. Has life expectancy of less than 1 year. 9. Has planned use of cutting balloon, scoring balloon, thrombectomy, atherectomy, brachytherapy, cryotherapy or laser devices to treat the common or external iliac arteries as well as the ipsilateral SFA/proximal popliteal during the index procedure. 10. Has any planned surgical intervention (requiring hospitalization) or endovascular procedure 14 days before or 30 days after the index procedure. 11. Current Participation in an investigational drug or other device study. 12. Previously enrolled in this study. 13. Has known aortic aneurysm(s) > 5 cm. 14. Has one of the following co-morbid conditions: ♦ History of severe liver disease (i.e. ascites, esophageal varices, liver transplant) ♦ Known or suspected active infection ♦ Undergoing hemodialysis for kidney failure ♦ Undergoing immunosuppressant therapy ♦ Elevated creatinine level on most recent test (> 2.5 mg/dl) ♦ New York Heart Association Classification of III or IV with hospitalization for decompensated heart failure within 3 months ♦ Recent (within 30 days) myocardial infarction ♦ Recent (within 30 days) hemorrhagic or ischemic stroke ♦ Acute thrombophlebitis or deep venous thrombosis in the limb to be treated ♦ Any other co-morbid condition that in the judgment of the physician precludes safe percutaneous intervention 15. Guidewire or investigational device catheter cannot cross the target lesion(s) and re-enter true vessel lumen beyond the lesion(s). 16. Aneurysmal target vessel. 17. Presence of an acute intraluminal thrombus of the proposed lesion site. 18. If treatment is required of a non-target lesion distal to the target vessel during the index procedure, the non-target lesion must be successfully treated (residual stenosis < 30%) prior to treatment of the target lesion and:

Inclusion Criteria	Exclusion Criteria
	♦ Be located within the native SFA/proximal popliteal ♦ The distal point must be at least 3 cm above the cortical margin of the femur ♦ The proximal point must be at least 1 cm below the origin of the *profunda femoris* ♦ Total lesion length is ≤ 10 cm 19. Lack of straight-line blood flow to the foot/ankle of the target limb prior to index procedure or inability to achieve straight-line blood flow to the foot/ankle of the target limb through treatment of a non-target lesion in the SFA/proximal popliteal during index procedure prior to enrollment. 20. Perforation, dissection or other injury requiring additional stenting or surgical intervention prior to the start of target lesion treatment.

2. Follow-up Schedule

All subjects were assessed at baseline prior to the study procedure, then again at pre-discharge, 30 days, 9 months, 1, 2 and 3 years post-procedure. **Table** provides a summary of the specific study assessment requirements and timeframes at each stage of the study.

Table 6: Study Assessment Schedule and Requirements

Assessment Schedule (Timeframe Window)	**Baseline (30 days prior, labs 7 days prior to enrollment)**	**Procedure**	**Pre-Discharge (within 7 days post-procedure)**	**30 Days (25-40 Days post-procedure)**	**9 Months (240-300 days post-procedure)**	**1, 2 & 3 Years***
Informed Consent	X					
Medical history	X					
Physical exam	X					
Concomitant medication history	X	X	X	X	X	
Rutherford Clinical Category	X			X	X	
Ankle-brachial index	X			X	X	

Walking Impairment Questionnaire	X			X	X	
Duplex ultrasound					X	
Laboratory tests§	X					
Angiogram		X				
Adverse event evaluation		X	X	X	X	X

*Annual visits could be conducted by telephone; 320-410 (1-Year), 685-775 (2-Year), and 1050-1140 (3-Year) days post-procedure.

§Creatinine and Complete Blood Count

3. Clinical Endpoints

The primary outcome for the DURABILITY Iliac study was the Major Adverse Event (MAE) rate at 9 months, defined as a composite of periprocedural death, in-hospital MI, clinically-driven target lesion revascularization (TLR) and amputation of the treated limb through 9 months post-procedure.

The secondary outcomes for the DURABILITY Iliac study included:

- Major Adverse Event rate at 30 days defined as a composite of periprocedural death, in-hospital MI, clinically-driven target lesion revascularization and amputation of the treated limb through 30 days post-procedure.
- Primary patency rate at 9 months defined as a binary duplex ultrasound ratio ≤ 2.4 at the stented target lesion with no clinically-driven re-intervention within the stented segment.
- Change of Ankle-Brachial Index (ABI) at 30 days and 9 months defined as a change of the ABI compared to baseline in subjects with compressible arteries and baseline ABI < 0.9 through 30 days and 9 months post-procedure.
- Device success, defined as the ability to deploy the stent as intended at the treatment site.
- Change in Walking Impairment Questionnaire (WIQ) score at 30 days and 9 months defined as change in WIQ score compared to baseline through 30 days and 9 months post-procedure.
- Clinically-driven Target Vessel Revascularization (TVR) at 30 days and 9 months defined as any re-intervention or artery bypass graft surgery involving the target vessel in which the subject has a $\geq 50\%$ diameter stenosis (per angiographic core lab assessment) in the presence of recurrent symptoms, or a $\geq 70\%$ stenosis without any symptoms.

B. Accountability of PMA Cohort

A total of 75 subjects signed the informed consent and were enrolled in the DURABILITY Iliac study; 45 of the 75 subjects had Protégé™ GPS stent(s) implanted. All 45/45 (100%) study subjects completed the pre-discharge follow-up visit, 97.8% (44/45) completed the 30-day follow-up visit, and 88.9% (40/45) completed the 9-month follow-up visit.

C. Study Population Demographics and Baseline Parameters

Baseline demographic and clinical characteristics for subjects implanted with Protégé™ GPS stent(s) in the DURABILITY Iliac study are summarized in **Table** .

Table 7: Demographics and Baseline Clinical Characteristics

Subject Characteristics	N=45*
Age (yrs.), Mean± SD (N), [Median] (Min, Max)	62.4 ± 9.2 (45) [62.0] (41.0 , 78.0)
Male	73.3% (33/45)
Race	
Caucasian	91.1% (41/45)
African American	6.7% (3/45)
Asian	0.0% (0/45)
American Indian or Alaska Native	0.0% (0/45)
Native Hawaiian or other Pacific Islander	2.2% (1/45)
Other	0.0% (0/45)
Ethnicity	
Hispanic	2.2% (1/45)
Not Hispanic	97.8% (44/45)
Risk Factors and Medical History	
Diabetes	17.8% (8/45)
Type I	12.5% (1/8)
Type II	87.5% (7/8)
Hyperlipidemia	64.4% (29/45)
Hypertension	68.9% (31/45)
Renal insufficiency	0.0% (0/45)
Current smoker	64.4% (29/45)
Angina	13.3% (6/45)
Arrhythmia	6.7% (3/45)
Congestive Heart Failure (CHF)	6.7% (3/45)
Stroke	4.4% (2/45)
Transient Ischemic Attack (TIA)	4.4% (2/45)
Myocardial Infarction (MI)	24.4% (11/45)
Non-healing ischemic ulcers in the lower extremities	0.0% (0/45)
Amputation of the lower extremities	0.0% (0/45)
Peripheral Intervention**	17.8% (8/45)
Clinical Characteristics	
Rutherford Clinical Category	
2=Moderate claudication	22.2% (10/45)
3=Severe claudication	77.8% (35/45)
4=Ischemic rest pain	0.0% (0/45)
Ankle-Brachial Index (ABI)	0.67 ± 0.19 (45) [0.67] (0.12 , 1.05)

*A total of 45/75 subjects were implanted with the Protege GPS stent(s) in the DURABILITY Iliac study.

**Types of historical peripheral interventions included: PTA, Stenting, Atherectomy or other types of interventions. There was no history of Cryoplasty, Laser interventions or Bypass.

Table 8 presents baseline target lesion characteristics assessed by the angiographic core laboratory for the lesions treated with the Protégé™ GPS stent. The mean pre-procedure percent diameter stenosis was 76.2%, including 23.4% occluded lesions and 25.5% severely calcified lesions.

Table 8: Baseline Target Lesion Characteristics

Lesion Characteristics	N=47 (# of lesions)*
Right Iliac Artery	51.1% (24/47)
Common	75.0% (18/24)
External	25.0% (6/24)
Left Iliac Artery	48.9% (23/47)
Common	73.9% (17/23)
External	26.1% (6/23)
Lesion Morphology	
Distance from Ostium (mm)	25.4 ± 36.8 (47) [0.0] (0.0 , 168.0)
Lesion Length (mm)	47.1 ± 28.3 (47) [32.4] (15.0 , 122.2)
Eccentric Lesion	59.6% (28/47)
Bend	13.4 ± 14.1 (47) [10.0] (0.0 , 80.0)
Thrombus	0.0% (0/47)
Any Calcification	74.5% (35/47)
None/Mild	25.5% (12/47)
Moderate	48.9% (23/47)
Severe	25.5% (12/47)
Ulceration present	27.7% (13/47)
Aneurysm present	8.5% (4/47)
TASC II	
Type A	55.3% (26/47)
Type B	34.0% (16/47)
Type C	6.4% (3/47)
Type D	4.3% (2/47)
Quantitative Angiographic Results	
Pre-procedure Reference Diameter (mm)	8.4 ± 1.4 (47) [8.2] (5.9 , 11.7)
Pre-procedure Minimal Lumen Diameter (mm)	2.0 ± 1.4 (47) [2.3] (0.0 , 5.5)
Pre-procedure % Diameter Stenosis	76.2 ± 15.5 (47) [72.9] (51.6 , 100.0)
Percent Total Occlusions (100% stenosis)	23.4% (11/47)

*A total of 45 subjects with 47 target lesions were implanted with the Protégé™ GPS stent(s). One subject had two target lesions, one treated with the Protégé™ GPS stent and one treated with the EverFlex stent.

D. Confirmatory Results

Primary Outcome

The primary outcome of the study is MAE rate at 9 months (270 days) post-procedure. An MAE was defined as a composite of periprocedural death, in hospital MI, clinically-driven target lesion revascularization, and amputation of treated limb, as adjudicated by the Clinical Event Committee (CEC). The 9-month MAE rate for subjects implanted with the Protégé™ GPS stent was 2.2% (1/45). The Primary Outcome is presented in **Table 9**.

Table 9: Summary of Primary Outcome

9-Month MAE	N=45* %(n/N) [Events]
9-Month MAE	2.2%(1/45)[1]
Periprocedural Death	0.0%(0/45)[0]
In-hospital MI	0.0%(0/45)[0]
Clinically-driven TLR	2.2%(1/45)[1]
Amputation of the Treated limb	0.0%(0/45)[0]

* A total of 45/75 subjects were implanted with the Protégé GPS stent(s) in the DURABILITY Iliac study. Forty (40) out of 45 completed the 9-month follow-up visit - Four subjects exited the study prior to the 9-month visit: One subject was Lost to Follow-up 53 days post-procedure, the second subject withdrew 175 days post-procedure, investigators withdrew the third and fourth subject 296 and 358 days post procedure respectively. One subject missed their 9-month visit; however completed their 1, 2 and 3-Year follow-up visits; therefore all events that would have been reported through the 9-month visit for this subject were reported.

DURABILITY Iliac Serious Adverse Events

Table 10 provides a summary of the CEC adjudicated serious adverse events (SAEs) for all subjects implanted with the Protégé GPS stent in the DURABILITY Iliac study. They are summarized by MedDRA System/Organ Class and include all reported serious adverse events, regardless of study device, study procedure or study requirement relatedness. The data are presented as a percentage of subjects experiencing an SAE followed by the total number of events in brackets.

Table 10: Summary of Serious Adverse Events

MedDRA System Organ Class	≤ 30 Days %(n/N) [Events]	≤ 9 Months %(n/N) [Events]	≤ 3 Years %(n/N) [Events]
Total*	**15.6% (7/45) [9]**	**35.6% (16/45) [24]**	**40% (18/45) [49]**
Cardiac disorders (Acute myocardial infarction, Angina pectoris, Angina unstable, Atrial fibrillation, Cardiac failure, Coronary artery disease)	2.2% (1/45) [1]	6.7% (3/45) [4]	13.3% (6/45) [12]
Congenital, familial and genetic disorders (Gastrointestinal angiodysplasia hemorrhagic)	0.0% (0/ 45) [0]	2.2% (1/45) [1]	2.2% (1/45) [1]
Gastrointestinal disorders (Colitis ischaemic, Gastrointestinal hemorrhage, Retroperitoneal hemorrhage)	2.2% (1/45) [1]	4.4% (2/45) [2]	6.7% (3/45) [3]
General disorders and administration site conditions (Chest pain, Device occlusion, Thrombosis in device)	0.0% (0/ 45) [0]	2.2% (1/45) [1]	8.9% (4/45) [5]
Infections and infestations Diverticulitis,	0.0% (0/ 45) [0]	4.4% (2/45) [2]	4.4% (2/45) [3]

MedDRA System Organ Class	≤ 30 Days %(n/N) [Events]	≤ 9 Months %(n/N) [Events]	≤ 3 Years %(n/N) [Events]
Pneumonia, Upper respiratory tract infection)			
Injury, poisoning and procedural complications (Arterial restenosis, in-stent arterial restenosis, Incisional hernia, Vascular pseudo-aneurysm)	4.4% (2/45) [2]	11.1% (5/45) [5]	17.8% (8/45) [9]
Neoplasms benign, malignant and unspecified (incl. cysts and polyps) (Lung neoplasm malignant, Prostate cancer)	0.0% (0/ 45) [0]	2.2% (1/45) [1]	4.4% (2/45) [2]
Nervous system disorders (Presyncope)	2.2% (1/45) [1]	2.2% (1/45) [1]	2.2% (1/45) [1]
Renal and urinary disorders (Nephrolithiasis)	0.0% (0/ 45) [0]	0.0% (0/ 45) [0]	2.2% (1/45) [1]
Respiratory, thoracic and mediastinal disorders (Chronic obstructive pulmonary disease)	0.0% (0/ 45) [0]	0.0% (0/ 45) [0]	2.2% (1/45) [1]
Vascular disorders (Arterial stenosis, Artery occlusion, Hypertensive crisis, Iliac artery occlusion, Iliac artery stenosis, Peripheral artery dissection)	8.9% (4/45) [4]	15.6% (7/45) [7]	20% (9/45) [11]

*A total of 45/75 subjects were implanted with the Protégé GPS stent in the DURABILITY Iliac study.

Outcome Summary

Table 11 provides a summary of the primary and secondary Outcome measures for the 45 subjects implanted with the Protégé GPS stent in the DURABILITY Iliac study.

Table 11: Summary of Primary and Secondary Outcomes

Primary Outcome Measures	N=45*
9-Month MAE[1]	2.2%(1/45)[1]
Periprocedural Death	0.0%(0/45)[0]
In-hospital MI	0.0%(0/45)[0]
Clinically-driven TLR	2.2%(1/45)[1]
Amputation of the Treated limb	0.0%(0/45)[0]
Freedom from 9-Month MAE -KM Estimate	97.7%
Secondary Outcome Measures	**N=45***
30-Day MAE[1]	0.0%(0/45)[0]
Periprocedural Death	0.0%(0/45)[0]
In-hospital MI	0.0%(0/45)[0]
Clinically driven TLR	0.0%(0/45)[0]
Amputation of the Treated limb	0.0%(0/45)[0]
Primary Patency Rate at 9 Months - KM Estimate[2]	97.7%
Device Success[3]	100.0% (52/52)**
Freedom from clinically-driven TVR at 30 days -KM Estimate	100.0%
Freedom from clinically-driven TVR at 9 months KM Estimate	97.7%

* A total of 45/75 subjects were implanted with the Protégé GPS stent(s) in the DURABILITY Iliac study. Forty (40) out of 45 completed the 9-month follow-up visit - Four subjects exited the study prior to the 9-month visit: One subject was Lost to Follow-up 53 days post-procedure, the second subject withdrew 175 days post-procedure, investigators withdrew the third and fourth subject 296 and 358 days post procedure respectively. One subject missed their 9-month visit; however completed their 1, 2 and 3-Year follow-up visits; therefore all events that would have been reported through the 9-month visit for this subject were reported.

** A total of 45 subjects with 47 target lesions were implanted with the Protégé GPS stent using 51 Protégé GPS stents and one EverFlex stent. Thirty-eight subjects had a single Protégé GPS stent implanted in one target lesion. Five subjects had two Protégé GPS stents implanted in one target lesion. One subject had two target lesions, each treated with one Protégé GPS stent, and one subject had two target lesions, one treated with the Protégé GPS stent and one treated with the EverFlex stent.

1. Numbers are % (n/N) [Events]
2. Primary patency rate defined as a binary duplex ultrasound ratio ≤ 2.4 at the stented target lesion with no clinically-driven re-intervention within the stented segment
3. Device success was defined as the ability to deploy the stent as intended at the treatment site. The denominator includes number of stents implanted.

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 any clinical investigator, financial interests, and arrangement of any clinical investigator conducting clinical studies covered by the regulation. The confirmatory clinical study included fifty-five (55) investigators of which none were full-time or part-time employees of the sponsor and two (2) of the 55 investigators 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: two (2) investigators
- Proprietary interest in the product tested held by the investigator: None
- Significant equity interest held by investigator in sponsor of covered study: None

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

XI. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

No supplemental clinical data was available or needed.

XII. PANEL MEETING RECOMMENDATION

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 Systems Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Safety & Effective Conclusions

The applicant previously conducted a study titled the **C**arotid **R**evascularization with **e**v3 **A**rterial **T**echnology **E**volution (CREATE) study. CREATE provided data to support the safety and effectiveness of the Protégé™ GPS Self-Expanding Stent System in the carotid artery for subjects considered to be at high risk for carotid endarterectomy.

The carotid artery is a more rigorous artery for stenting than an iliac artery based on the level of pulsation experienced in the carotid artery. In performing percent compliance calculations for carotid and femoral arteries, Pelton, et al [1] reported a much higher level for carotid arteries than for femoral arteries (6.07% versus 3.47%). Another comparison presented in the literature [2] shows that percent compliance will decrease going distally along the arterial tree. However, adjacent segments (like the Common Femoral and Common Internal Iliac arteries) do not have statistically significant changes in elastic properties. Therefore, the iliac arteries will be much more similar to the femoral arteries in percent compliance than they are with the carotid arteries. Given the established safety and effectiveness of the Protégé™ GPS Self-Expanding Stent System in the carotid arteries with the CREATE study, the DURABILITY Iliac study was successfully completed to confirm safety and effectiveness of the Protégé™ GPS Self-Expanding Peripheral Stent System in the iliac arteries. Primary patency was 97.7% at 9 months and no MAE were reported. The mean ABI improved at 9 months and the WIQ also showed improvement in walking performance at 9 months. The DURABILITY Iliac multi-center confirmatory clinical study results demonstrates that the Protégé™ GPS Self-Expanding Peripheral Stent System is safe and effective for the treatment of atherosclerotic disease of the common and/or external iliac arteries.

B. Benefit Risk Conclusions

Results of the pre-clinical studies were appropriately leveraged from the original PMA to support the safety and performance of the device in the iliac environment considering the carotid arteries represent a more challenging anatomy than iliac arteries.[1,2] Patient follow-up from both the pivotal (P060001) and confirmatory clinical study (P060001/S020) was satisfactory with limited missing data. The probable benefit of the Protégé™ GPS Self-Expanding Peripheral Stent System in the ability to improve luminal diameter outweighs the probable risks associated with use of the device. Additional factors to be considered in determining probable risks and benefit for the Protégé™ GPS Self-Expanding Peripheral Stent System include:

- Patient follow-up was satisfactory. The serious adverse events (SAEs) were limited and the events were comparable to SAEs of similar devices.
- Most patients with the disease have symptoms only, but some patients may have tissue or limb loss. The disease is chronic and affects the mobility of the patient and the quality of life. It is treatable but not curable.

- There are alternative treatments available, but this treatment is perceived as less invasive than open surgery and more effective than percutaneous transluminal angioplasty. This treatment is highly valued by patients and preferred to the alternatives because it improves their quality of life without the need for open surgery.

In conclusion, given the available information obtained from both the CREATE pivotal study and the DURABILITY Iliac confirmatory study, the data suggests that the probable benefits of the Protégé™ GPS Self-Expanding Peripheral Stent System, for the indicated use, outweighs the probable risks.

C. Overall Conclusions

The results from the confirmatory study provides reasonable assurance that the device is safe and effective 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).

XIV. CDRH DECISION

CDRH issued an approval order on January 21, 2015.

XV. APPROVAL SPECIFICATION

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.

XVI. REFERENCES

[1] A.R. Pelton, et al (2008). Fatigue and Durability of Nitinol Stents. J Mech Behavior Biomed Mater, 1, 153-164.

[2] L.I. Stratouly, et. al (1987). The Use of Ultrasound Imaging in the In Vivo Determination of Normal Human Arterial Compliance. Proceedings of the 13th Annual Northeast Bioengineering Conference, pp. 435-437, Philadelphia, PA, U.S., March 1987, Defense Technical Information Center, Fort Belvoir.