SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Venous Stent
Device Trade Name:	VENOUS WALLSTENT
Device Procode:	QAN
Applicant's Name and Address:	Boston Scientific Corporation 300 Boston Scientific Way Marlborough, MA 01752-1234
Date of Panel Recommendation:	None
Premarket Approval Application (PMA) Number:	P980033/S050
Date of FDA Notice of Approval:	March 17, 2020

Premarket Approval Application (PMA) P980033 was approved on November 16, 2001 for the WALLSTENT Endoprosthesis Venous with a central venous (innominate and subclavian veins) indication. The SSED to support the central venous indication is available on the CDRH website and is incorporated by reference here.

This application (P980033/S050) for the VENOUS WALLSTENT adds the indication for the treatment of symptomatic iliofemoral venous outflow obstruction.

II. INDICATIONS FOR USE

The VENOUS WALLSTENT is indicated for improving central venous luminal diameter following unsuccessful angioplasty in patients on chronic hemodialysis with stenosis of the venous outflow tract. Unsuccessful angioplasty is defined as:

- residual stenosis ≥ 30% for a vein ≤ 10mm in diameter or ≥ 50% for a vein > 10 mm in diameter;
- a tear which interrupts the integrity of the intima or lumen;
- abrupt lesion site occlusion, or refractory spasm.

The vessels that can be treated with the VENOUS WALLSTENT are the innominate and subclavian veins, ranging from 8 mm to 15 mm in diameter.

The VENOUS WALLSTENT is also indicated for improving luminal diameter in the iliofemoral veins for the treatment of symptomatic venous outflow obstruction.

III. CONTRAINDICATIONS

The VENOUS WALLSTENT is contraindicated for use in:

- Patients with uncorrected bleeding disorders.
- Patients who cannot receive anticoagulation or antiplatelet aggregation therapy.
- Patients who are judged to have a lesion that prevents complete inflation of a balloon dilatation catheter or proper placement of the stent or the stent delivery system.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the VENOUS WALLSTENT Directions for Use.

V. DEVICE DESCRIPTION

The Boston Scientific VENOUS WALLSTENT is a self-expanding stent composed of biomedical superalloy or a drawn filled biomedical superalloy with a radiopaque core braided in a tubular mesh configuration. The delivery system is composed of co-axial tubes which allow reconstrainment as indicated by the limit marker and has radiopaque marker bands which aid in accurate placement of the stent (**Figure 1**).

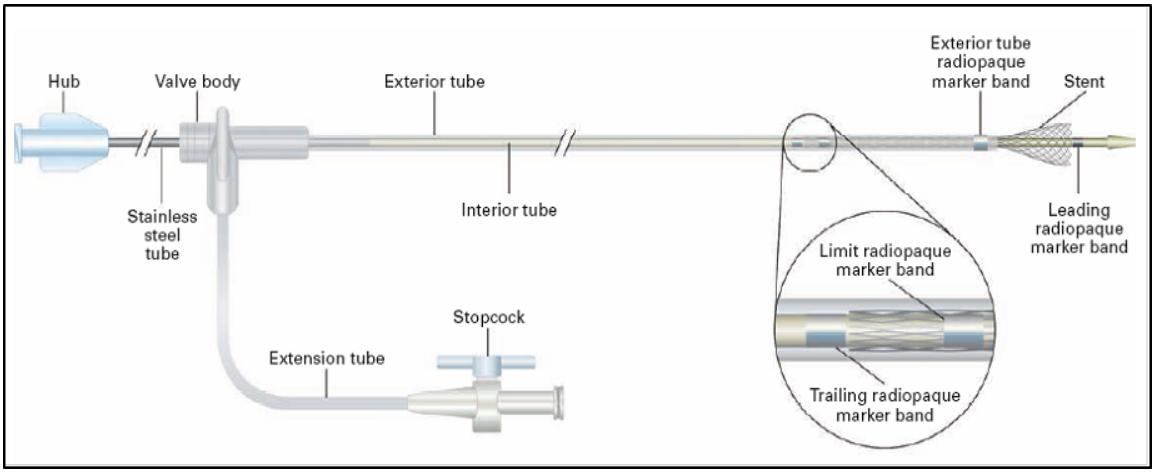

Figure 1: WALLSTENT VENOUS

The iliofemoral VENOUS WALLSTENT is available in the following stent diameters: 12, 14, 16, 18, 20 mm. Delivery catheter shaft outer diameters range from 8 F, 9F and 10F (**Table 1**). The iliofemoral VENOUS WALLSTENT delivery catheter is compatible with 0.035" guidewires and is available in 75 cm length catheters; the 12 mm diameter stents are also available on 135 cm length catheters.

Table 1: Iliofemoral VENOUS WALLSTENT Product Sizes

	Stent Lengths					
Delivery System OD (F)	**Stent Diameter (mm)**	**40 mm**	**55 mm**	**60 mm**	**80 mm**	**90mm**
8	12*	√		√		√
9	14	√		√		√
	16	√		√		√
10	18	√		√		√
	20	√	√		√	

**12 mm stent diameters are offered on both 75 cm and 135 cm length delivery systems. All other sizes are available on 75 cm length only.*

The stent diameter selected should be such that it is larger than the target vessel diameter and longer than the minimum length required to provide adequate lesion coverage. Constricting the stent to a smaller diameter will cause a longer deployed length, depending on the degree of constriction. The variation in stent length as the stent diameter changes is displayed in VENOUS WALLSTENT labelling i.e., Sizing Chart and Directions for Use**.** Deployed lengths reflect expansion to desired vessel diameter.

Stent Description

The VENOUS WALLSTENT is a flexible, compliant, self-expanding stent braided in a one-over/one-under tubular mesh pattern from a biomedical super-alloy wire called Elgiloy (an alloy of cobalt-chromium-nickel-molybdenum-iron) or Elgiloy with a radiopaque tantulum core. The VENOUS WALLSTENT braided stent design forms a matrix of closed segments which are highly dependent upon adjacent segments. External focal forces placed upon the VENOUS WALLSTENT result in full circumferential axial elongation in the region, increasing the overall stent length.

Delivery System Description

The VENOUS WALLSTENT stent delivery system consists of a coaxial tube system with two main tubes: an interior tube and an exterior tube (**Figure 1**) available in 75 cm and 135 cm working lengths. The interior tube extends from the hub to the distal tip forming the central lumen that accommodates a 0.035” guidewire. The interior tube keeps the stent stationary during deployment as the exterior tube is retracted. A stent holding sleeve and stent cup bonded to the interior tube aid in stabilizing the stent. The interior tube has three radiopaque (RO) marker bands; two are situated adjacent to the distal and proximal ends of the stent to aid in deployment accuracy while the limit RO marker band (just distal to the stent holder) is used during the reconstrainment process.

The stainless steel (SS) tube seen in **Figure 1** is concentric to the interior tube and extends from the hub to just distal of the valve body where it is then bonded to the inner member jacket. The SS tube is used for support of the exterior tube during the deployment process.

The exterior tube extends from the valve body to the distal tip of the assembled device. The exterior tube serves to protect and constrain the stent, until it is retracted during stent deployment. There is one RO marker band at the distal end of the exterior tube; reconstrainment is possible up to the point the exterior tube RO marker band is retracted to the limit RO marker band of the interior tube.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several alternatives for prevention or treatment of symptomatic venous outflow obstruction including:

- Preventative measures include life-style changes such as balanced diet, exercise regimen, weight loss, smoking cessation and avoiding prolonged sitting or standing.
- Non-invasive treatment therapies may include compression stockings, pneumatic compression therapy and/or an oral anticoagulation regimen with Vitamin K antagonists (VKA) or direct oral anticoagulation (DOACs).
- Minimally-invasive treatment options may include percutaneous transluminal angioplasty (PTA) or stenting with another stent for which there is an approved indication. Thrombolysis (systemic, catheter-directed or pharmacomechanical) may also be performed adjunctively.
- Open surgical treatments are endophlebectomy, crossover vein bypass and surgical bypass with graft, all with or without A/V fistula.

Each alternative has its own advantages and disadvantages. The physician should fully discuss each alternative with the patient to select the method that meets the patients' expectations and lifestyle.

VII. MARKETING HISTORY

The WALLSTENT Endoprosthesis is currently approved or cleared for indications for use including Central Venous (P980033), TIPS (P930031), Transhepatic Biliary (K152853), and Tracheobronchial (K152842).

Outside of the United States, the WALLSTENT Endoprosthesis is commercialized as WALLSTENT-Uni Endoprosthesis. The WALLSTENT-Uni Endoprosthesis is currently CE marked for the following venous indications: central venous (2002), TIPS (2002), superior vena cava (2002) and iliac vein (2015). Except for labeling and model numbers, the Wallstent-Uni Endoprosthesis are identical to the equivalently sized Wallstent Endoprosthesis commercialized in the United States.

Table 2: WALLSTENT Commercially Available for Venous Use

Argentina	Australia	Austria	Baltics	Belarus
Brazil	Canada	Chile	China	Colombia
Costa Rica	Czech Republic	Ecuador	El Salvador	Finland
France	Germany	Greece	Guatemala	Hong Kong
Hungary	Ireland	Israel	Italy	Kazakhstan
Mexico	Netherlands	Norway	Peru	Philippines
Poland	Portugal	Puerto Rico	Russia	Singapore
Slovakia	South Africa	South Korea	Spain	Sri Lanka
Sweden	Taiwan	Uruguay	United States	Vietnam

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. Allergic reactions (drug, contrast, device or other)

- Angina
- Arteriovenous fistula
- Bleeding
- Cerebrovascular accident/ stroke/ Transient Ischemic Attack
- Death
- Embolism (air, plaque, thrombus, device or other)
- Fever
- Hematoma
- Hemorrhage
- Ischemia
- Hypotension/hypertension
- Myocardial infarction/ ischemia
- Need for urgent intervention or surgery
- Pain
- Pulmonary Embolism

- Renal insufficiency or failure
- Restenosis of stented vessel
- Sepsis/infection
- Stent fracture
- Stent migration
- Stent/vessel occlusion
- Thrombus/thrombosis
- Vasospasm
- Venous congestion
- Vessel injury (perforation, trauma, rupture, dissection, pseudoaneurysm or other)

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

IX. SUMMARY OF NON-CLINICAL STUDIES

A series of non-clinical laboratory studies were performed on the 12 mm - 20 mm diameter VENOUS WALLSTENT. These evaluations included in-vitro functional bench testing. A summary of each of the evaluations is provided below.

A. Biocompatibility Studies

The iliofemoral VENOUS WALLSTENT in its final finished form is identical to the Wallstent Endoprosthesis Venous (P980033) in formulation, processing, sterilization, and geometry and no other chemicals have been added (e.g., plasticizers, fillers, additives, cleaning agents, mold release agents). Supportive biocompatibility data was leveraged from that reviewed under P980033, as summarized below.

Biocompatibility testing was performed in accordance with applicable sections of ISO 10993, "Biological evaluation of medical devices – Part 1: Evaluation and testing". A series of Good Laboratory Practice (GLP) biocompatibility tests were conducted to demonstrate that the components of the Wallstent Endoprosthesis Venous and the stent delivery system are biocompatible. The tests summarized in **Table 3** have been conducted in support of the Wallstent Endoprosthesis Venous and delivery System.

Table 3: Implant & Delivery System biocompatibility testing

Test Name	Test Description	Implant	Delivery System	Results
Cytotoxicity	L929 MEM Elution Test – ISO	X	X	Non-cytotoxic
Sensitization	Kligman Maximization – ISO	X	X	Non-sensitizing
Irritation	Intracutaneous Injection Test – ISO	X	X	Non-irritant
Acute Systemic Toxicity	Systemic Injection Test – ISO	X	X	Non-toxic
Material Mediated Pyrogenicity	Rabbit Pyrogen Test (Material Mediated) – ISO	X[1]	X	Non-pyrogenic
Hemocompatibility	Hemolysis – ASTM Direct and Indirect Contact	X	X	Non-hemolytic
	Complement Activation Assay – ISO Direct Contact	X[1]		Not a complement activator
Implantation	Acute and Chronic Ovine GLP Studies (7, 32, 90, and 180-day)	X		No adverse reaction observed

[1] Elgiloy stent only.

B. In Vitro Engineering Testing

In vitro engineering testing on the VENOUS WALLSTENT Stent System was conducted, as applicable, in accordance with:

- *FDA Guidance for Industry and FDA Staff: Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems, April 18, 2010.*
- *Select Updates for Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems, August 18, 2015.*

The in vitro engineering studies are summarized in **Table 4**. "Pass" denotes that the test results met product specifications and/or the recommendation in the above-referenced guidance documents.

Table 4: Stent and Delivery Catheter Engineering Testing

Test	Test Purpose	Acceptance Criteria	Results
Stent and Delivery System Dimensional and Functional Attributes			
Material Composition	Suitability of material for implant.	Chemical composition of Elgiloy/Elgiloy Tantalum tubing meets chemical composition requirements per ASTM F1058, ASTM B365 and F560.	Pass
Shape Memory and Superelasticity of Intravascular Stents	N/A – The VENOUS WALLSTENT is not manufactured from a shape memory or superelastic material.	N/A	N/A
Stent Corrosion Resistance	To document the potential for fretting, pitting and crevice corrosion of the stent.	No evidence of galvanic or any other form of corrosion observable by SEM at a magnification level up to 3000X.	Pass
Stent Dimensional Verification	To characterize the unconstrained diameter of the stent.	The outside diameter of the stent must have a recovery diameter not less than or greater than 10% of its nominal diameter.	Pass

Test	Test Purpose	Acceptance Criteria	Results
Stent and Delivery System Dimensional and Functional Attributes			
Percent Surface Area	To characterize the metal to lumen ratio of the stent.	All percent stent free surface areas (SFA) lie between 81 % – 84 % across their respective indicated implant diameters. All percent stent surface areas (μ) lie between 16 % – 19 % at their respective indicated implant diameters.	Pass
Foreshortening	To determine dimensional changes that may occur when deploying a stent to aid in proper stent length selection and proper placement within the body.	Percent of stent shortening when expanded to labeled diameter met labelled requirements for stent length.	Pass
Stent Integrity	To verify the stent integrity after expansion to the unconstrained diameter.	All stents to have no structural damage after expansion to the unconstrained diameter.	Pass
Outward Radial Force	To verify and characterize the radial outward force exerted by the self-expanding stent.	Stent to exert sufficient outward radial force to ensure vessel apposition.	Pass
Mechanical Properties – Preprocessing	Suitability of material for implant.	Chemical composition of Elgiloy/Elgiloy Tantalum tubing meets chemical composition requirements per ASTM F1058, ASTM B365 and F560.	Pass
Stress/Strain Analysis/Fatigue Analysis (Finite Element Analysis)	To evaluate the durability and integrity of the stent using Finite Element Analysis (FEA). The FEA analysis simulated physiological conditions in Iliofemoral Venous usage.	The FEA analysis must demonstrate select worst-case combinations of stent sizes for testing in physiologically based fatigue bench tests.	Pass
Accelerated Durability Testing (May Thurner)	To characterize the accelerated durability of overlapping stents after 10-year cyclic and residual fatigue cycling.	Stents shall demonstrate fatigue integrity after 10-year simulated May-Thurner compression fatigue testing.	Pass

Test	Test Purpose	Acceptance Criteria	Results
Stent and Delivery System Dimensional and Functional Attributes			
Accelerated Durability Testing (Bend and Localized Crush)	To characterize the accelerated durability of stents after 10-year fatigue cycling with relative Iliofemoral venous physiological motions.	Stents shall demonstrate fatigue integrity after 10-year simulated bend and localized crush fatigue testing.	Pass
Particulate/ Coating Integrity	To characterize the levels of particulate matter generated by the VENOUS WALLSTENT device	Limit for particulates is compared against specifications acceptable for products marketed for peripheral applications.	Pass
Magnetic Resonance Imaging (MRI) Safety and Compatibility	To evaluate the stent for magnetically induced force, magnetically induced torque, image artifact, and radio frequency (RF) induced heating when placed in field strengths of 1.5 and 3.0 Tesla.	The stent must meet the requirements of *Guidance for Industry and FDA Staff: Establishing Safety and Compatibility of Passive Implants in the MR (Magnetic Resonance) Environment*, ASTM F2052, ASTM F2213, ASTM F2182, and ASTM 2119 standards for MR Conditional.	Pass
Radiopacity	To assess the radiopacity of the stent.	The radiopacity of the stent while loaded in the delivery system and post stent deployment must be clinically acceptable.	Pass
Crush Resistance	To demonstrate the ability of the stent to recover its desired size and shape after applying an external load (parallel plates and local compression).	Recovery of the stent diameter post compressive loads (parallel plate and local compression testing).	Pass
Kink Resistance	To characterize the smallest radius of curvature the stent can withstand without kinking.	Kink Resistance of the implanted stent must be clinically acceptable.	Pass
Delivery System Dimensional Verification	To document dimensional characteristics of the delivery system.	The delivery system working length must be ± 1.0cm of the labeled delivery system working length. The delivery system must track and exchange over 0.035” guide wire. The delivery system outer diameter/crossing profile must be within specification for 8 F -10 F.	Pass

Test	Test Purpose	Acceptance Criteria	Results
Stent and Delivery System Dimensional and Functional Attributes			
Delivery, Deployment, and Retraction	To assess the ability of the delivery system to deliver the stent to the intended location and deploy the stent.	The delivery system must demonstrate the ability to be pushed through a representative model at 37 C.	Pass
Catheter Bond Strength	To evaluate the tensile strength of the delivery system bonds.	The delivery system must maintain its integrity during tracking, stent deployment and withdrawal.	Pass
Delivery System Flexibility and Kink Test	To determine the susceptibility of the delivery system to kink.	The delivery system must not kink and maintain guidewire movement when placed in a simulated anatomical model.	Pass

C. Packaging Testing

As the packaging design, design specifications and materials remain unchanged from the Wallstent Endoprosthesis Venous (P980033) and the packaged product has a safe history of use, the existing data was determined to remain applicable to the VENOUS WALLSTENT.

D. Stability/Shelf Life Testing

Functional performance testing was conducted to demonstrate that the VENOUS WALLSTENT and packaging performs within product specifications for a labeled shelf life of 24 months.

E. Sterilization

The VENOUS WALLSTENT is sterilized using ethylene oxide (EO) sterilization. The cycle is validated per ISO 11135-1:2014, "Sterilization of health-care products — Ethylene oxide — Requirements for the development, validation and routine control of a sterilization process for medical devices." Results show that the product satisfies a minimum Sterility Assurance Level (SAL) of 10^{-6}. In addition, the amount of EO residual and bacterial endotoxin was verified to be within acceptable ranges in accordance with ISO 10993-7:2008, "Biological Evaluation of Medical Devices - Part 7: Ethylene Oxide Sterilization Residuals."

X. SUMMARY OF PRIMARY CLINICAL EVIDENCE

The clinical data presented below are intended to support approval for the use of VENOUS WALLSTENT in the treatment of iliofemoral venous outflow obstruction. The primary data source consisted of a review and analysis of clinical literature. Secondary, supporting data was taken from an Investigator Sponsored Research Study at a single site.

Clinical Literature Review and Analysis

The VENOUS WALLSTENT has a considerable history of use in iliac venous stenting. A substantial number of articles have been published documenting this clinical experience, with studies and registries that represent thousands of patients. Literature data is limited by potentially confounding effects of subject and site heterogeneity, the need to isolate the outcomes specific to the VENOUS WALLSTENT when multiple stents were used, and the reduced level of detail available regarding patient outcomes compared to a formal prospective clinical study. However, the VENOUS WALLSTENT was supported by the availability of clinical data representing the outcomes of a substantially larger number of subjects than would be available from a prospective clinical study. The primary strength of this dataset is the large number of subjects available for analysis and the fact that they represent 'real-world' use of the VENOUS WALLSTENT outside of a formal clinical trial with a more limited patient population and expert users. When considered in their totality, it was concluded that the strengths of this approach exceeded the limitations.

A. Literature Summary

This literature review was focused on obtaining relevant clinical data to provide a critical review of the published information relevant to safety and performance of the VENOUS WALLSTENT. A systematic search of the literature was performed using databases representative of the US and OUS literature. The search strategy progressively filtered the literature using a sequence of searches integrated with Boolean logic. The search criteria were used to identify English language articles published on or before April 1, 2019, excluding conference reviews, letters, errata or news. Key words used in the search were targeted to identify specific stents (including the WALLSTENT and competitors) used for venous obstruction or pelvic obstruction (lower extremity, superior vena cava and central venous).

A total of 29 articles were returned from the systematic search. Eight additional articles were included that were not identified by the systematic search described above (references 10, 22, 26, 27, 29-31 and 30 in Table 5). Boston Scientific was aware of these additional articles from previous literature searches using similar methodologies. The addition of these eight articles was acceptable since they had a small effect on the effectiveness outcomes but provided additional reports of adverse events that were informative in evaluating safety. One additional article was included in the literature analysis. This article (reference 38 in Table 5) is a meta-analysis that was included because of its relevance to iliac venous stenting.

A total of 38 articles were included in the literature review. Of the 38 articles, 21 articles included only VENOUS WALLSTENT device use (these articles are shaded in Table 5). A total

of 37 articles included single data sets; article 38 is a meta-analysis. All publications reviewed are provided in **Table** 5.

Table 5: Literature Summary Publications

Biblio. Reference[a]	Publication
1	Neglen P, Berry MA, Raju S. Endovascular surgery in the treatment of chronic primary and post-thrombotic iliac vein obstruction. *Eur J Vasc Endovasc Surg.* 2000;20(6):560-571.
2	Neglen P, Raju S. Balloon dilation and stenting of chronic iliac vein obstruction: technical aspects and early clinical outcome. *J Endovasc Ther*. 2000;7(2):79-91.
3	Lamont JP, Pearl GJ, Patetsios P, et al. Prospective evaluation of endoluminal venous stents in the treatment of the May-Thurner syndrome. *Ann Vasc Surg.* 2002;16(1):61-64.
4	Raju S, McAllister S, Neglen P. Recanalization of totally occluded iliac and adjacent venous segments. *J Vasc Surg.* 2002;36(5):903-911.
5	Neglen P, Thrasher TL, Raju S. Venous outflow obstruction: An underestimated contributor to chronic venous disease. *J Vasc Surg.* 2003;38(5):879-885.
6	Kwak HS, Han YM, Lee YS, Jin GY, Chung GH. Stents in common iliac vein obstruction with acute ipsilateral deep venous thrombosis: early and late results. *J Vasc Interv Radiol.* 2005;16(6):815-822.
7	Raju S, Neglen P. High prevalence of nonthrombotic iliac vein lesions in chronic venous disease: a permissive role in pathogenicity. *J Vasc Surg.* 2006;44(1):136-143; discussion 144.
8	Neglen P, Hollis KC, Olivier J, Raju S. Stenting of the venous outflow in chronic venous disease: long-term stent-related outcome, clinical, and hemodynamic result. *J Vasc Surg*. 2007;46(5):979-990.
9	Husmann MJ, Heller G, Kalka C, et al. Stenting of common iliac vein obstructions combined with regional thrombolysis and thrombectomy in acute deep vein thrombosis. *Eur J Vasc Endovasc Surg.* 2007;34(1):87-91.
10	Oguzkurt L, Tercan F, Ozkan U, Gulcan O. Iliac vein compression syndrome: outcome of endovascular treatment with long-term follow-up. *Eur J Radiol.* 2008;68(3):487-492.
11	Raju S, Neglen P. Percutaneous recanalization of total occlusions of the iliac vein. *J Vasc Surg.* 2009;50(2):360-368.
12	Kolbel T, Lindh M, Akesson M, Wasselius J, Gottsater A, Ivancev K. Chronic iliac vein occlusion: midterm results of endovascular recanalization. *J Endovasc Ther.* 2009;16(4):483-491.
13	Hartung O, Loundou AD, Barthelemy P, Arnoux D, Boufi M, Alimi YS. Endovascular management of chronic disabling ilio-caval obstructive lesions: long-term results. *Eur J Vasc Endovasc Surg.* 2009;38(1):118-124.

14	Rosales A, Sandbaek G, Jorgensen JJ. Stenting for chronic post-thrombotic vena cava and iliofemoral venous occlusions: mid-term patency and clinical outcome. *Eur J Vasc Endovasc Surg.* 2010;40(2):234-240.
15	Alimi Y, Hartung O. Endovascular treatment of chronic ilio-caval occlusion. *Italian J Vasc Endovasc Surg.* 2010;17:199-205.
16	Raju S, Darcey R, Neglen P. Unexpected major role for venous stenting in deep reflux disease. *J Vasc Surg.* 2010;51(2):401-408; discussion 408.
17	Gutzeit A, Zollikofer Ch L, Dettling-Pizzolato M, Graf N, Largiader J, Binkert CA. Endovascular stent treatment for symptomatic benign iliofemoral venous occlusive disease: long-term results 1987-2009. *Cardiovasc Intervent Radiol.* 2011;34(3):542-549.
18	Kurklinsky AK, Bjarnason H, Friese JL, et al. Outcomes of venoplasty with stent placement for chronic thrombosis of the iliac and femoral veins: single-center experience. *J Vasc Interv Radiol.* 2012;23(8):1009-1015.
19	Ye K, Lu X, Li W, et al. Long-term outcomes of stent placement for symptomatic nonthrombotic iliac vein compression lesions in chronic venous disease. *J Vasc Interv Radiol.* 2012;23(4):497-502.
20	Nayak L, Hildebolt CF, Vedantham S. Postthrombotic syndrome: feasibility of a strategy of imaging-guided endovascular intervention. *J Vasc Interv Radiol.* 2012;23(9):1165-1173.
21	DeRubertis BG, Alktaifi A, Jimenez JC, Rigberg D, Gelabert H, Lawrence PF. Endovascular management of nonmalignant iliocaval venous lesions. *Ann Vasc Surg.* 2013;27(5):577-586.
22	Hager ES, Yuo T, Tahara R, et al. Outcomes of endovascular intervention for May-Thurner syndrome. *J Vasc Surg Venous Lymphat Disord.* 2013;1(3):270-275.
23	Liu Z, Gao N, Shen L, et al. Endovascular treatment for symptomatic iliac vein compression syndrome: a prospective consecutive series of 48 patients. *Ann Vasc Surg.* 2014;28(3):695-704.
24	Matsuda A, Yamada N, Ogihara Y, et al. Early and long-term outcomes of venous stent implantation for iliac venous stenosis after catheter-directed thrombolysis for acute deep vein thrombosis. *Circ J.* 2014;78(5):1234-1239.
25	Park JY, Ahn JH, Jeon YS, Cho SG, Kim JY, Hong KC. Iliac vein stenting as a durable option for residual stenosis after catheter-directed thrombolysis and angioplasty of iliofemoral deep vein thrombosis secondary to May-Thurner syndrome. *Phlebology.* 2014;29(7):461-470.
26	Caliste XA, Clark AL, Doyle AJ, Cullen JP, Gillespie DL. The incidence of contralateral iliac venous thrombosis after stenting across the iliocaval confluence in patients with acute or chronic venous outflow obstruction. *J Vasc Surg Venous Lymphat Disord.* 2014;2(3):253-259.
27	Blanch Alerany M, Izquierdo Lamoca LM, Ramirez Ortega M, Lago Rivas I, Zotta Desboeufs R, Stefanov Kiuri S. Endovascular treatment of iliofemoral chronic post-thrombotic venous flow obstruction. *J Vasc Surg Venous Lymphat Disord.* 2014;2(1):2-7.

28	Yin M, Shi H, Ye K, et al. Clinical Assessment of Endovascular Stenting Compared with Compression Therapy Alone in Post-thrombotic Patients with Iliofemoral Obstruction. *Eur J Vasc Endovasc Surg.* 2015;50(1):101-107.
29	Raju S, Ward M, Jr., Davis M. Relative importance of iliac vein obstruction in patients with post-thrombotic femoral vein occlusion. *J Vasc Surg Venous Lymphat Disord.* 2015;3(2):161-167.
30	O'Sullivan GJ, Waldron D, Mannion E, Keane M, Donnellan PP. Thrombolysis and iliofemoral vein stent placement in cancer patients with lower extremity swelling attributed to lymphedema. *J Vasc Interv Radiol.* 2015;26(1):39-45.
31	Klitfod L, Just S, Foegh P, Baekgaard N. Excellent long-term results with iliac stenting in local anesthesia for post-thrombotic syndrome. *Acta Radiol Open.* 2015;4(9):2058460115592164.
32	Daugherty SF, Gillespie DL. Venous angioplasty and stenting improve pelvic congestion syndrome caused by venous outflow obstruction. *J Vasc Surg Venous Lymphat Disord.* 2015;3(3):283-289.
33	Ganelin A, Hingorani A, Ascher E, et al. Complications with office-based venoplasties and stenting and their clinical correlation. *J Vasc Surg Venous Lymphat Disord.* 2015;3(4):376-379.
34	Ahmed O, Ng J, Patel M, et al. Endovascular Stent Placement for May-Thurner Syndrome in the Absence of Acute Deep Vein Thrombosis. *J Vasc Interv Radiol.* 2016;27(2):167-173.
35	Khairy SA, Neves RJ, Hartung O, O'Sullivan, GJ. Factors Associated with Contralateral Deep Venous Thrombosis after Iliocaval Venous Stenting. *Eur J Vasc Endovasc Surg* 2017; 54:745-751
36	Rossi FH, Kambara AM, Izukawa NM, et al. Randomized double-blinded study comparing medical treatment versus iliac vein stenting in chronic venous disease. *J Vasc Surg Venous Lymphat Disord.* 2018;6(2):183-191.
37	Gagne PJ, Gagne N, Kucher T, Thompson M, Bentley D. Long-term clinical outcomes and technical factors with the Wallstne for treatment of chronic iliofemoral venous obstruction. *J Vasc Surg Venous Lymphatic Disord*. 2018; 7(1):44-55
38	Razavi MK, Jaff MR, Miller LE. Safety and Effectiveness of Stent Placement for Iliofemoral Venous Outflow Obstruction: Systematic Review and Meta-Analysis. *Circ Cardiovasc Interv.* 2015;8(10):e002772
[a] Shading indicates publications that use VENOUS WALLSTENT exclusively.	

B. Safety Outcomes

Safety outcomes were evaluated differently by the various studies reported in the literature. For many articles, while Major Adverse Events (MAE) were reported, no prospective definition of MAE was specified. It would be impractical to retrospectively attempt to reconcile the differing definitions of MAE since the underlying patient level data (e.g., imaging) was not available for additional analysis. For the purposes of the literature analysis, MAEs were collated as reported by the individual articles without reconciling the definitions. For the 21 VENOUS WALLSTENT-exclusive studies, representing 2,268 patients, a total of 18 MAEs were reported. Of the 18 MAEs reported,

- 4 were categorized as device- or procedure-related bleeding at target vessel, target lesion, or access site requiring surgical intervention, endovascular intervention, or blood transfusion ≥ 2 units.
- 7 were categorized as device- or procedure-related arterial or venous injury of the target vessel, target lesion, or access site requiring surgical intervention.
- 7 were categorized as device- or procedure-related deep vein thrombosis outside of the target vein segment.

Furthermore, no device or procedure related deaths were reported. A summary of literature-observed Adverse Events (AE), compiled by category, are found in **Table 6** below. In general, the MAEs and AEs are similar to what would be expected for other iliac venous stents and are supportive of the safety of the VENOUS WALLSTENT.

Table 6: Adverse Events found in the published literature by category.

Adverse Event Category	Number of Events	Timing
Overall Event Rate	**307**	
Target vessel revascularization	204	To extent of follow-up
†Other	31	<30 days
Early occlusion of stented area	23	<30 days
Deep vein thrombosis involving the treated limb	17	<30 days
Embolization or migration of stent	11	To extent of follow-up
Deep vein thrombosis involving contralateral limb	7	<30 days
Vascular injury requiring surgical or endovascular intervention	7	<30 days
Major bleeding event (including access site complications and retroperitoneal hematoma)	6	<30 days
Stent fracture	1	To extent of follow-up
Pulmonary embolism	0	<30 days
Major amputation of target limb	0	To extent of follow-up
Device and/or procedure related death	0	To extent of follow-up

Studies including stents other than VENOUS WALLSTENT are excluded. Note for the overall rate that some events are duplicative. For example, an early occlusion of the stented area may also result in a target vessel revascularization event.
†Other: Non-MAEs that do not fit any other category. These include: undefined non-thrombotic complications, minor access site bleeding, contrast extravasation, hematomas at access site, and peripheral sensory nerve lesion.

C. Effectiveness Outcomes

Patency was defined differently by the various studies reported in the literature. Since many studies were not prospective, many did not include specific patient follow-up for assessment of patency, and the determination of patency was not independently adjudicated, there remains uncertainty regarding the accuracy and precision of patency rates reported. Patency rates from the various articles included in the analysis were combined using a weighted average, based on the number of patients in each study. A summary of the weighted average analyses is presented below in **Table 7**. In this table, an additional analysis of weighted averages for all studies, including those that did not exclusively include VENOUS WALLSTENTs , is included for comparative purposes. The weighted mean 1-year primary patency rate for studies exclusively using VENOUS WALLSTENT was 86.6%. The weighted mean 1-year primary patency rate for all studies, including non-VENOUS WALLSTENT exclusive studies, was 86.8%. The weighted primary patency rate reported by studies of the only VENOUS WALLSTENT was similar to those which included other stents, indicating that results from the All Studies column of Table 7 are generally applicable the VENOUS WALLSTENT. For studies using VENOUS WALLSTENT in patients with post thrombotic syndrome (PTS) only, the 1-year primary patency rate was 67.9%, whereas studies that included patients with Non-Thrombotic Iliac Vein Lesions (NIVL) had a 1-year primary patency rate of 90.5%. In general, the 1-year primary patency of the VENOUS WALLSTENT is similar to other iliac venous stents and is therefore supportive of its efficacy.

Table 7: Weighted Mean 1-year primary patency for groups of interest.

	Weighted Mean 1- Year Patency % [95% CI]	
Group Description	**For studies using** VENOUS WALLSTENT **ONLY**	**All Studies**
All studies	**86.6 [77.0, 92.6]**	**86.8 [81.1, 91.0]**
Studies with NIVL patients only	**90.5 [80.3, 95.7]**	**88.4 [82.4, 92.5]**
Studies with PTS patients only	**67.9 [44.4, 84.8]**	**78.5 [62.5, 88.9]**
Studies with mixed NIVL & PTS patient populations	**88.4 [84.5, 91.3]**	**89.3 [87.5, 90.9]**
Retrospective Studies	**84.7 [72.9, 91.9]**	**85.0 [77.5, 90.3]**
Prospective Studies	**92.5 [85.7, 96.2]**	**90.2 [88.2, 91.9]**
USA patient population	**80.2 [54.5, 93.2]**	**84.4 [71.3, 92.2]**
Non-US patient population	**88.8 [84.9, 91.7]**	**88.4 [85.1, 91.0]**
Mean baseline CEAP score ≥4	**84.8 [49.8, 96.9]**	**---**
Mean baseline CEAP score <4	**85.5 [81.1, 89.0]**	**---**

CEAP, clinical-etiologic-anatomic-pathophysiologic. Studies that did not report a 1-year primary patency rate are excluded. Weighted for number of patients in each study. Weighted means were calculated using the Random Effects model.

D. Literature Summary Conclusion

Boston Scientific has compiled an extensive literature summary comprised of 38 peer reviewed articles, of which 21 only used VENOUS WALLSTENT for iliac venous stenting. Analyses to demonstrate the effectiveness and safety of VENOUS WALLSTENT were provided. These analyses provide evidence that similar safety and effectiveness outcomes can be expected for the VENOUS WALLSTENT compared to other iliac venous stents. Therefore, this literature summary is supportive of the conclusion that VENOUS WALLSTENT is safe and effective for the treatment of iliofemoral venous outflow obstruction.

Investigator Sponsored Research Study

E. Study Design

The Investigator Sponsored Research (ISR) study was an observational, single center (US), single investigator, retrospective, non-randomized study to evaluate the procedure, patency rates and clinical outcomes using the VENOUS WALLSTENT system for venous outflow obstruction. The site retrospectively collected and analyzed data from patients operated on between November 1, 2007 and October 31, 2014, follow-up accrued through March 31, 2017.

Since the ISR study only included the experience of a single site it was not sufficient to serve as the primary clinical dataset in support of this PMA. However, the ISR study supported the PMA by providing a greater level of detail regarding patient outcomes than was available in the literature summary.

Patient-level data were available for 67 patients (77 limbs) who presented with venous outflow obstruction and were treated with a total of one-hundred-twenty-six (126) VENOUS WALLSTENT devices. Data were obtained from retrospective chart review.

Table 4 includes the standard of care treatment schedule at the site, including examination and clinical observations.

Clinical Inclusion and Exclusion Criteria

Subjects were included in the study if they met the inclusion criteria.

- Patients older than 18 years of age with signs and symptoms consistent with chronic venous hypertension in the legs, not ascribed to superficial venous insufficiency, who underwent placement of an iliofemoral VENOUS WALLSTENT.
- CEAP 3-6.

Subjects were ineligible to participate in the study if they met the exclusion criteria.

- Patients with acute or subacute DVT (less than 8 weeks).
- Patients who had stents placed for chronic outflow obstruction from chronic DVT and who terminated their anticoagulation independent of medical advice.
- Iliofemoral obstruction due to neoplasm.

1. Follow-Up Schedule

The follow-up schedule reflects the standard of care treatment schedule at the site, including examination and clinical observations at 1 month, 6 months, 12 months and then annually.

Table 8: ISR Study Schedule

	Pre-Procedure	Index Procedure	30 Day	6 Months	12 Months	24 Months	36 Months
History	X						
VCSS & CEAP	X		X	X	X	X	X
Ultrasound	X		X	X	X	X	X
Clinical Assessment	X	X	X	X	X	X	X
Complications/ Adverse Events		X	X	X	X	X	X
Venogram		X					
IVUS		X					

2. Clinical Endpoints

There were 3 clinical endpoints within the ISR study:

- Safety: Narratives of site reported complications. As part of the regulatory review, a qualitative assessment of major adverse events (MAE) was performed, where the following definition of MAE was retrospectively applied to the ISR dataset:
    - Device or procedure-related death;
    - Major bleeding event defined as device or procedure-related bleeding at the target vessel and/or the target lesion or at the access site requiring surgical or endovascular intervention or blood transfusion ≥2 units;
    - Device or procedure-related arterial or venous injury occurring in the target vessel segment and/or target lesion location or at the access site requiring surgical or endovascular intervention;
    - Device or procedure related acute DVT;
    - Clinically significant pulmonary embolism defined as being symptomatic with chest pain, hemoptysis, dyspnea, hypoxia etc. AND be documented on CT; or
    - Embolization of stent.
- Effectiveness: Patency (primary, assisted primary, and secondary) was defined as flow or no flow (open or closed stent). Additional post hoc analysis was performed to evaluate patency via ultrasound, using a <50% diameter stenosis threshold for patency.
- Clinical Improvement: Significant clinical improvement was defined as a Venous Clinical Severity Score (VCSS) score change of ≥4 points.

F. Accountability of ISR Study Cohort

Data presented within this report includes data collected at the baseline visit, primary procedural visit, secondary procedural visit (if applicable) and at each subject's last follow- up visit prior to March 31, 2017.

The mean follow-up length is 50 (0.25-100) months (n=77 limbs). All patients had at least one clinical follow-up visit; 2 patients had no follow-up imaging. Compression therapy noncompliance post-stent was noted in 31/67 (46%) patients, with 23 of these patients having ongoing symptoms (VCSS >4). Eight patients died during follow-up. Per the investigator, 5 deaths were from causes unrelated to venous disease and the stent/procedure and 3 deaths were of unknown cause. An additional 12 patients were lost to follow-up.

G. Study Population Demographics and Baseline Characteristics

Table 9 provides a review of baseline demographics and clinical characteristics of the subjects enrolled into the ISR study. The age of the subjects enrolled spanned from 47 to 83 years. The site enrolled 30 (45%) female subjects and 37 (55 %) male subjects. More patients with non-thrombotic disease (50%) were treated than post-thrombotic disease (35%). These demographics are representative of the population treated with iliac venous stents.

Table 9: ISR Study - Baseline Demographics and Clinical Characteristics

Demographic Data	Median (range) or no. (%)
Age, years	63 (47-83)
Female	30/67 (45%)
DVT	27/67 (40%)
Hyperthrombophilia	2/67 (3%)
Phlebitis	6/54 (11%)
Diabetes	16/65 (25%)
HTN	29/61 (48%)
Smoking (current or prior)	32/65 (49%)
Compression therapy	19/67 (28%)
No. receiving bilateral treatment	10/67 (15%)
Post-thrombotic	35/77 (45%)
Non-thrombotic	42/77 (55%)
No. treated left limbs	48/77 (62%)
No. treated right limbs	29/77 (38%)
CEAP classification	
3	25/77 (33%)
4	16/77 (21%)
5	8/77 (10%)
6	28/77 (36%)
VCSS Score	9 (3-23)
Vessels occluded as determined by IVUS and/or venography[a]	13/77 (17%)

CEAP, clinical-etiologic-anatomic-pathophysiologic; *DVT*, deep vein thrombosis; *HTN*, hypertension; *IVUS*, intravascular ultrasound; *VCSS*, venous clinical severity score.
Continuous variables are reported as median (range) and categorical variables are reported as number (percentage).
[a] Because there was no protocol-driven definition for occlusion, multiple imaging modalities were used for determination (e.g., DUS, venography and IVUS)

Placement of one or more stent was permitted within the anatomical boundaries of the common femoral vein and the inferior vena cava. The procedural characteristics are summarized in **Table 10**.

Table 10: ISR Data - Procedural Characteristics

	Median (range) or no. (%)
Access vessel[a]	
FV	40/78 (51%)
CFV	14/78 (18%)
PV	24/78 (31%)
No. stents	126
Left limb stents	80/126 (63%)
Right limb stents	46/126 (37%)
Number of patients with unilateral stents	57
Number of patients with bilateral stents	10
No. stents per patient (mean)	1.9
Stent location	
Isolated CIV	18/77 (23%)
Isolated EIV	11/77 (14%)
Isolated CFV	1/77 (1%)
CIV/EIV	28/77 (36%)
EIV/CFV	6/77 (8%)
IVC/CIV/EIV	3/77 (4%)
CIV/EIV/CFV	7/77 (9%)
IVC/CIV/EIV/CFV	3/77 (4%)
Lesion[b] traversing >1 segment	47/77 (61%)
Lesion[b] extending into the CFV	17/77 (22%)
Lesion[b] extending into the IVC	6/77 (8%)
Post-dilatation[c]	75/75 (100%)

CFV, common femoral vein; *CIV*, common iliac vein; *EIV*, external iliac vein; *FV*, femoral vein; *IVC*, inferior vena cava; *PV*, popliteal vein.
Continuous variables are reported as median (range) and categorical variables are reported as number (percentage).
[a] Seventy-eight (78) access vessels were required (10 bilateral patients and 1 patient requiring multiple access vessels).
[b] Lesion was subjectively determined by operator without specific criteria.
[c] Two patients are missing post-dilatation data; however, physician standard of care was to always balloon following stent placement.

A total of 126 VENOUS WALLSTENTs were used within the ISR study, as shown in **Table 11**. Some patients had multiple stents placed.

Table 11: ISR Study - Stent Sizes Used

	Stent Length (mm)					
Stent Diameter (mm)	**40**	**55**	**60**	**80**	**90**	**Total**
12	3	0	2	1	0	6
14	4	0	6	0	18	28
16	1	1	19	0	25	46
18	0	0	11	0	14	25
20	0	2	0	6	0	8
Other[1]						13
Total	8	3	38	7	57	**126**

[1]Other includes stent sizes used that were outside of the stent matrix for the proposed indication expansion or the size was unknown (2).

H. Safety and Effectiveness Results

1. Safety Results

Site Reported Complications

Per investigator assessment of early adverse events (i.e., < 30 days), 3 occlusion events were reported in 3 patients. Over the initial 12-month follow up period, 3 additional patients required reintervention and additional patients (variably followed) required intervention after 12 months. Note that jailing of the anatomical CIV occurred in 5 subjects where 3 were revascularized, 1 died and 1 was followed clinically. Fourteen subjects (21%) had new or recurrent ulceration during follow-up; a further 3 subjects (5%) had other leg wound issues. Of 14 subjects with recurrent ulceration, 3 were related to an acute DVT episode (1 of which was subsequent to right CIV jailing). Recurrent ulcers or sores were observed in 3 of 5 subjects (60%) with jailed CIVs. Eight patients (12%) required vascular reintervention over follow-up (range, 0.5 – 92 months), with 1 early reintervention. Five of 8 interventions were to maintain stent patency. Details on all reinterventions are presented in **Table 12**. Reinterventions consisted of placement of additional VENOUS WALLSTENT devices in all but one case. In general, these events types are similar to other iliac venous stents and are therefore supportive of the safety of the VENOUS WALLSTENT.

Table 12: Summary of Complications

	Time from Index Procedure	Description
< 30 Days	7 days	82-year-old female with chronic post-thrombotic scar (popliteal vein to common iliac vein [CIV]), was implanted with two stents in the CIV and external iliac vein, which closed at 1 week. The patient refused reintervention and died of unknown causes remote to the intervention.
	14 days	50-year-old male with bilateral post-thrombotic occlusive scar (inferior vena cava [IVC] to CFVs bilaterally). The patient received four stents in each limb, with all eight stents closing at 2 weeks. Further revascularization was not attempted.
	20 days	59-year-old male with protein C deficiency and right leg post-thrombotic stenosis and scarring (popliteal vein-CIV), two stents were implanted from the CIV to the CFV. The stents were occluded 2 weeks later. The patient declined reintervention and was lost to follow-up after 4 weeks.
	0.5 Months	54-year-old male with acute DVT of contralateral (right) limb and subsequent jailing of right CIV. Right stent implantation, angioplasty.
<12 months	4 Months	69-year-old female developed an acute DVT in left limb; stents showed non-occlusive thrombus. Thrombolysis and additional left stent placed.
	5 Months	65-year-old female with an ipsilateral (left) leg ulcer never healed. Left fem-pop arterial bypass with ipsilateral GSV.
> 12 months	17 Months	62-year-old male with onset of new symptoms, morbid obesity; compression observed in EIV. Additional ipsilateral (left) stent placed.
	30 Months	76-year-old-male original stent stenosed and fractured, likely due to ending stent at inguinal ligament and tissue fibrosis from radiation treatment in pelvis for prostate cancer[a]. Two additional ipsilateral (left) stents placed.
	50 Months	60-year-old male original stent patent but exhibited narrowing and proximal scarring; compression noted proximal to the stent. Two additional ipsilateral (right) stents placed.
	72 Months	61-year-old male with right CIV jailed due to left stent implanted high in IVC. Contralateral (right) stent placed through ipsilateral (left) stent to return flow.
	92 Months	68-year-old male with left stents compressing right limb (also previously stented), jailing right CIV. Two additional right stents placed.

CIV, Common iliac vein; DVT, deep vein thrombosis; EIV, external iliac vein; fem-pop, femoral-popliteal; GSV, great saphenous vein; IVC, inferior vena cava.
All additional stents implanted were VENOUS WALLSTENT .
[a] The fracture was at the caudal end of the stent under the inguinal ligament

.

Table 13 includes all adverse events that were collected in the study.

Table 13: Site-Reported Adverse Events

Event	Year <1		Year 1-2		Year 2-3		Year 3-4		Year 4-5		Year >5	
	# of Events	N=67	# of Events	N=57*	# of Events	N=49*	# of Events	N=44*	# of Events	N=33*	# of Events	N=28*
Bleeding	1	1.5%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Cancer	0	0.0%	0	0.0%	0	0.0%	2	4.5%	0	0.0%	0	0.0%
Congestive Heart Failure/Acute Respiratory Failure/Pneumonia	0	0.0%	1	1.8%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Congestive Heart Failure/Respiratory Failure	0	0.0%	0	0.0%	0	0.0%	0	0.0%	1	3.0%	0	0.0%
DVT	2	3.0%	1	1.8%	1	2.0%	1	2.3%	1	3.0%	1	3.6%
Death**	1	1.5%	1	1.8%	0	0.0%	1	2.3%	3	9.1%	2	7.1%
Edema	1	1.5%	0	0.0%	0	0.0%	1	2.3%	0	0.0%	2	7.1%
Obstructed Bloodflow	0	0.0%	1	1.8%	0	0.0%	0	0.0%	0	0.0%	1	3.6%
Restenosis	0	0.0%	0	0.0%	1	2.0%	0	0.0%	1	3.0%	0	0.0%
Sepsis	0	0.0%	0	0.0%	0	0.0%	0	0.0%	1	3.0%	0	0.0%
Stent Thrombosis	3	4.5%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Tumor	1	1.5%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Ulcer	3	4.5%	2	3.5%	4	8.2%	1	2.3%	2	6.1%	4	14.3%
Varicose Veins	0	0.0%	1	1.8%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Total	**12**	**-**	**7**	**-**	**6**	**-**	**6**	**-**	**9**	**-**	**10**	**-**

*Excludes patients that exited study before start of window

** In four (4) patients, the cause of death or the event leading up to the death was also reported as an adverse event

Post-hoc qualitative MAE assessment

The 30-day MAE event rate was 6% (4/67). As shown in Table 14, four patients had five events. One (1) patient had an acute DVT in the contralateral limb (right) and subsequent jailing of the right CIV. This resulted in a target vessel revascularization for this patient. Three (3) patients experienced stent closure. All three patients had a history of DVT, with residual post-thrombotic disease. No re-interventions were performed. No other events that meet these criteria were observed. After retrospective review, stent thrombosis, or DVT, was the only event type reported. The observed MAEs are similar to those expected for iliac venous stenting and are supportive of the safety of the VENOUS WALLSTENT.

Table 154 ISR Study – Major Adverse Events at 30 Days

Major Adverse Event Criteria	**Rate n/N (%)**
Major Adverse Events within 30 days[a]	4/67 (6.0%) [1.7, 14.6]
Device or procedure-related death	0/67 (0.0 %)
Target vessel revascularization	1/67 (1.5%)
Major amputation of target limb	0/67 (0.0 %)
Stent thrombosis or Device- or procedure-related DVT	4/67 (6.0%)
Vascular reinjury requiring surgical/endovascular intervention[b]	0/67 (0.0 %)
Major bleeding event[c]	0/67 (0.0 %)
Pulmonary embolism[d]	0/67 (0.0 %)
Embolization within stent	0/67 (0.0 %)

DVT – Deep vein thrombosis; CI – Confidence Interval, two-sided Clopper-Pearson exact method

[a] Subjects with ≥ 1 event
[b]Device or procedure-related arterial or venous injury occurring in the target vessel segment and/or target lesion location or at the access site requiring surgical or endovascular intervention.
[c]Device or procedure-related bleeding at the target vessel and/or the target lesion or at the access site requiring surgical or endovascular intervention or blood transfusion ≥2 units.
[d] Clinically significant pulmonary embolism defined as being symptomatic with chest pain, hemoptysis, dyspnea, hypoxia etc. and documented on CT.

2. Effectiveness Results

The results of the primary effectiveness analyses are provided in **Table 15**.

Ninety-seven percent (65/67) (97%) of subjects had available imaging follow-up (median, 50 months). At 12 months, primary, primary-assisted, and secondary patency were 93%, 95%, and 95%, respectively where patency was defined as flow or no flow (open or closed stent). Patency rates were also assessed in the post-thrombotic (PT) and non-thrombotic (NT) limb subsets (n=33 and n=42, respectively). Patency rates at 12 months were lower in the PT subset, with primary patency of 85% and primary-assisted and secondary patency of 88%. Primary-assisted and secondary patency remained the same through 72-month follow-up, while primary patency decreased to 75%. In non-thrombotic limbs, 12-month primary, assisted-primary, and secondary patency rates were 100%. Secondary and assisted-primary patency remained at 100% through 72 months. Primary patency was 97% at 72 months.

Table 165: Effectiveness Analysis - Patency Rates

	12 Months (all; NT[1]; PT[2])	24 Months (all; NT; PT)	36 Months (all; NT; PT)	72 Months (all; NT; PT)
Primary Patency	93.2%;100.0%;84.8%	91.7%;100.0%;84.8%	89.9%;97.4%;81.2%	87.4%;97.4%;74.9%
Primary Assisted Patency	94.6%;100.0%;87.9%	94.6%;100.0%;87.9%	94.6%;100.0%;87.9%	94.6%;100.0%;87.9%
Secondary Patency	94.6%;100.0%;87.9%	94.6%;100.0%;87.9%	94.6%;100.0%;87.9%	94.6%;100.0%;87.9%
[1]Non-thrombotic, [2]Post-thrombotic				

3. Additional Clinical Results

Additional clinical effectiveness measures included clinical improvement determined by change in VCSS score.

The median VCSS score change at 12-month follow-up was 5 points improvement (range, 0-17 points improvement). This suggests that a clinically meaningful improvement was typically seen with improvement in multiple VCSS criteria. **Table 16** shows the VCSS scores throughout the ISR study.

Table 17: Clinical Outcomes – Clinical Improvement (VCSS)

Parameter	Baseline N=77	12 Months N=52[a]	24 Months N=29[b]	36 Months N=32[c]	Last Follow-up N=77[d]
VCSS score	9 (3-23)	3 (0-16)	4 (0-16)	4.5 (0-17)	4 (0-17)
VCSS score change		5 (0-14)	4 (-1-12)	5 (0-13)	5 (0-14)

Continuous variables are reported as median (range). Categorical variables are reported as number (%).
a Median follow-up of the 52 limbs (46 patients) at this interval was 12 months (range, 0.25-20 months).
b Median follow-up of the 29 limbs (25 patients) in this window was 24 months (range, 18-29 months).
c Median follow-up of the 32 limbs (29 patients) in this window was 36 months (range, 32-42 months).
d The final follow-up assessment for each patient occurred at a median 26 months (range, 0.25-42 months).
Thirty-six limbs in 32 patients had multiple VCSS assessments in follow-up.

I. 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 ISR study included one investigator of which none were full-time or part-time employees of the sponsor and none 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: 0
- Significant payment of other sorts: 0
- Proprietary interest in the product tested held by the investigator: 0
- Significant equity interest held by investigator in sponsor of covered study: 0

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. Statistical analyses were conducted by FDA to determine whether the financial interests/arrangements had any impact on the clinical study outcome. 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)(3) 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 functional and engineering testing conducted on the VICI VENOUS STENT System demonstrated that the performance characteristics met the defined product specifications. The test results obtained from the sterilization testing demonstrated that the product can be adequately sterilized and is acceptable for clinical use. The shelf life testing has established acceptable performance for a labeled shelf life up to 2 years.

A dedicated prospective clinical trial of the VENOUS WALLSTENT was not conducted in order to support FDA approval of the use of the VENOUS WALLSTENT in patients with symptomatic iliofemoral venous outflow obstruction. However, the WALLSTENT was approved in 2001 and has been used extensively off-label for the treatment of this disease as evidenced by use in over 4500 patients worldwide. A combination of literature data and patient-level data from a single-center (US), single-operator retrospective study (ISR study) were used to support device effectiveness.

The primary measure of device effectiveness was venous patency one-year post-procedure. There were variable definitions of patency including different methods of assessment. Also, because many studies were not prospective, many did not include specific patient follow-up for assessment of patency, and the determination of patency was not independently adjudicated, there remains uncertainty regarding the accuracy and precision of patency rates reported. Nonetheless, one-year patency rates from 21 studies (2,268 patients) that included exclusive use of the VENOUS WALLSTENT were reported. Here, the weighted mean 1-year patency rate was 86.6%. As expected, patients with PTS had a lower patency rate (67.9%) than that of patients with NIVL (90.5%). In the ISR study, one-year patency was assessed in 67 patients with reported rates of 93.2% overall and 100% and 84.8% in the PT and NT groups, respectively. When considered as a whole, the available literature summary and ISR study data demonstrate that similar 1-year primary patency outcomes can be expected for the VENOUS WALLSTENT as for other iliac venous stents in the treatment of symptomatic iliac vein obstructions.

Device effectiveness was also supported by patient level data from the ISR study that demonstrated clinical improvement in symptoms (i.e., VCSS score).

B. Safety Conclusions

The collective physico-chemical, biocompatibility/toxicity and animal/biological testing data conducted for the VENOUS WALLSTENT demonstrated that the device is biocompatible, non-toxic and safely tolerated in a chronic animal implant study.

The primary measure of device safety was the occurrence of Major Adverse Events. As noted above, the literature assessment did not have uniform assessments or definitions such that the incidence of adverse events is variably reported (and perhaps underreported in cases where prospective follow-up or oversight was absent). Nonetheless, the collective information demonstrated that the most common adverse event was clearly target vessel revascularization. Issues related to stent occlusion and thrombosis (i.e., deep vein thrombosis of the treated limb or contralateral limb) were also among the more frequently reported

adverse events. Less frequently, events related to the device (e.g., migration, fracture) or procedure (major bleeding) were also reported. The ISR study included evaluation of Major Adverse Events at 30 days which were reported in 7.5% of patients overall and included stent thrombosis or device- or procedure-related DVT (6.0%) and target vessel revascularization (1%). The types of Major Adverse Events was similar to that expected for iliac venous stenting and was supportive of the safety of the VENOUS WALLSETNT for the proposed indication.

C. Benefit-Risk Conclusion

The probable benefits of the device are based on data collected from a literature analysis and a single-center single-operator retrospective study (ISR study). The probable benefits of the VENOUS WALLSTENT System include improving or restoring blood flow in patients with iliofemoral venous disease to improve the patient symptoms. The probable risks of the device are also based on data collected from the literature and the ISR study, as described above, and the frequency and types of the adverse events reported are in alignment with what might be expected in the studied patient population and therapeutic area. In conclusion, given the available information above, the data support that the probable benefits outweigh the probable risks for using the device to improve luminal diameter in patients with symptomatic iliofemoral venous outflow obstruction.

Patient Perspectives

This submission did not include specific information on patient perspectives for this device.

Pediatric Extrapolation

In this premarket application, existing clinical data was not leveraged to support approval of a pediatric patient population.

D. Overall Conclusions

The clinical and non-clinical data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. The results show that the VENOUS WALLSTENT provides clinical benefits that are comparable to what has been reported in the published literature and confirm that the device is appropriate for the treatment of obstructions and occlusions in the venous vasculature when used in accordance with the labeling and Directions for Use (DFU).

XIII. CDRH DECISION

CDRH issued an approval order on March 17, 2020.

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.