SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Stent, Iliac Vein
Device Trade Name:	VICI VENOUS STENT® System
Device Procode:	QAN
Applicant's Name and Address:	Boston Scientific Corporation Three Scimed Place Maple Grove, MN 55311
Date(s) of Panel Recommendation:	None
Premarket Approval Application (PMA) Number:	P180013
Date of FDA Notice of Approval:	5/02/2019

II. INDICATIONS FOR USE

The VICI VENOUS STENT System is intended for improving luminal diameter in the iliofemoral veins for the treatment of symptomatic venous outflow obstruction.

III. CONTRAINDICATIONS

The VICI VENOUS STENT System is contraindicated for use in:

- 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.
- Patients who cannot receive intraprocedural anti-coagulation therapy.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the VICI VENOUS STENT System labeling.

V. DEVICE DESCRIPTION

The VICI VENOUS STENT System is comprised of two components: the implantable endoprosthesis and the stent delivery system. The stent is a laser cut self-expanding stent composed of a nickel titanium alloy (Nitinol). On both the proximal and distal ends of the stent, radiopaque (RO) markers made of tantalum increase visibility of the stent to aid in placement.

The stent is constrained in a 9F (maximum 3mm outside diameter) delivery system (**Figure 1**) available in a 100cm length. The delivery system is a coaxial design with an exterior shaft to protect and constrain the stent prior to deployment. The delivery system is an Over-the-

Wire system compatible with 0.035in (0.89mm) guidewires.

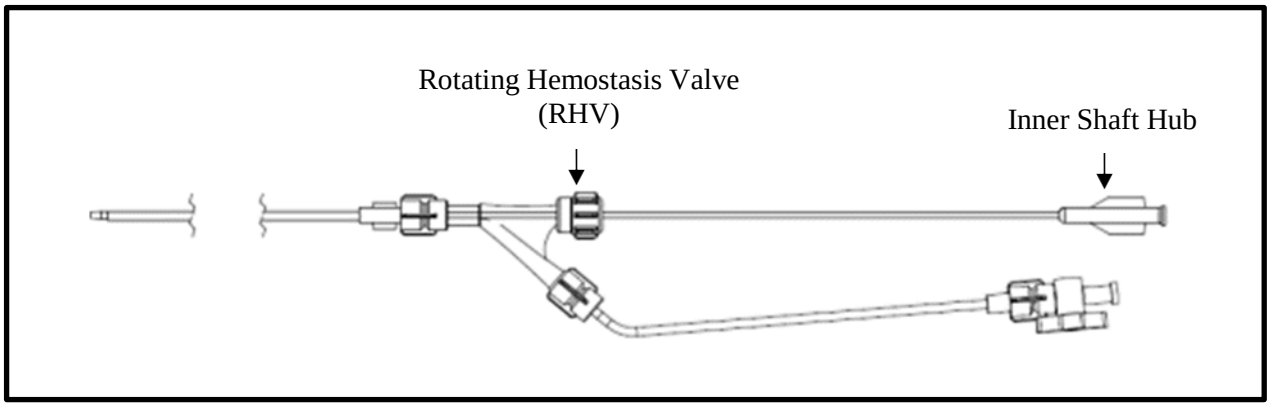


Figure 1: VICI VENOUS STENT Delivery System

The VICI VENOUS STENT is available in a variety of stent diameters and lengths. The VICI VENOUS STENT size matrix is provided in **Table 1.**

Table 1: VICI VENOUS STENT Size Matrix

Stent Diameter	Stent Length		
12 mm	60 mm	90 mm	120 mm
14 mm	60 mm	90 mm	120 mm
16 mm	60 mm	90 mm	120 mm

The VICI VENOUS STENT System delivers the stent in a distal-to- proximal direction with the standard "pin and pull" method. After obtaining access to the vessel, the physician prepares the System by flushing the inner lumen and outer shaft with heparinized saline. When the physician is ready to deploy a stent in a patient, the delivery system is inserted into the vasculature over an 0.035in guidewire that runs through the entire inner lumen of the delivery system. The delivery system is advanced to the location where the stent is to be deployed.

The physician will determine the specific location of the vessel to land the first part of the stent. A radiopaque marker at the distal end of the delivery system aids in visibility during placement and deployment. Under fluoroscopic guidance, the physician will align the distal end of the VICI VENOUS STENT and the selected delivery system with the desired location. The physician deploys the stent by "pinning" the proximal end of the inner catheter (i.e., inner shaft hub) and "pulling" the outer shaft back. This exposes the distal end of the stent and, as the outer shaft is pulled more, the stent length is progressively uncovered until the proximal end of the VICI stent is exposed and opens in the vasculature. As the stent is exposed to body temperature, it expands to appose the vessel wall.

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 VICI VENOUS STENT System was first commercially available in the European Union in January 2014. The countries where the VICI VENOUS STENT System is currently commercially available are listed below. The device has not been withdrawn from marketing for any reason related to its safety or effectiveness.

- Republic of Ireland
- United Kingdom
- France
- Norway
- Sweden
- Denmark
- The Netherlands
- Belgium
- Germany
- Poland
- Slovakia
- Switzerland
- Austria
- Italy
- Spain
- Argentina
- Australia
- New Zealand
- Hong Kong

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g. complications) which may be associated with use of the device:

- Abscess
- Access site complications including: bleeding, pain, tenderness, pseudoaneurysm, hematoma, nerve or vessel damage, or infection
- Allergic or hypersensitivity reactions (drug, contrast, device or other)
- Amputation
- Aneurysm
- Arteriovenous fistula formation and rupture
- Back pain

- Cerebrovascular dysfunction and/or stroke
- Death
- Embolization
- Entanglement of delivery system in deployed stent
- Fever
- GI bleeding
- Hypotension/hypertension
- Myocardial infarction, ischemia, angina, or other cardiovascular disturbance
- Need for urgent intervention or surgery
- Obstruction of venous tributaries
- Organ failure
- Pneumothorax or respiratory distress, pneumonia and/or atelectasis
- Renal failure
- Restenosis
- Sepsis/Infection
- Stent fracture
- Stent migration, misplacement/jumping, or embolization
- Stent occlusion
- Stent thrombosis
- Thrombophlebitis
- Tissue ischemia/necrosis
- Vasospasm
- Vein thrombosis
- Venous congestion
- Venous occlusion
- Vessel injury, examples include dissection, intimal tear, rupture or perforation

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

IX. SUMMARY OF NON-CLINICAL STUDIES

A series of non-clinical laboratory and animal studies related to the product were performed to evaluate the device.

A. Biocompatibility Studies

A series of Good Laboratory Practice (GLP) biocompatibility tests were conducted to demonstrate that the components of the VICI VENOUS STENT and the VICI VENOUS STENT Delivery System are biocompatible.

All biocompatibility testing was conducted in accordance with:

- Guidance for Industry and FDA Staff, Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems Guidance, Document issued on April 18, 2010
- Good Laboratory Practices Regulations (§CFR Part 58)
- Guidance for Industry and Food and Drug Administration Staff,

Use of International Standard ISO 10993-1, "Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process," Document Issued on June 16, 2016

The tests summarized in **Table 2** have been conducted in support of the VICI STENT as recommended for a permanent implantable device contacting circulating blood for >30 days and **Table 3** for the VICI VENOUS STENT Delivery System as recommended for external communicating, circulating blood contact with limited contact duration (< 24 hours).

Table 2: Summary of Biocompatibility/Toxicity Results for the VICI VENOUS STENT

Test	Test Description	Applicable Standard	Acceptance Criteria	Results /Status
Cytotoxicity	Colony Assay	ISO 10993-5:2009 Tests for Cytotoxicity	The test requirement is met if none of the cultures treated with the test article showed greater than mild reactivity (Grade 2).	Non- Cytotoxic/ **PASS**
Sensitization	Guinea Pig Maximization Test – SC and SO Extracts	ISO 10993-10:2010 Tests for Irritation & Sensitization	The test requirement is met if the skin reaction scores received by the test group are equal or less than the scores received by the negative control group.	Non- sensitizer/ **PASS**
Irritation/ Intracutaneous Toxicity	Intracutaneous Study – SC and SO Extracts	ISO 10993-10:2010 Tests for Irritation & Sensitization	The test requirement is met if the difference between the test article and the control mean score is 1.0 or less (negligible or slight).	Non- irritant/ **PASS**
Systemic Toxicity (Acute)	Systemic Toxicity Study – SC and SO Extracts	ISO 10993-11:2006 Tests for Systemic Toxicity	The test requirement is met if none of the animals injected with the test article extracts show a significantly greater biological reaction than the animals treated with the vehicle control.	Non-toxic/ **PASS**
Material Mediated Pyrogenicity	USP Pyrogen Study – Material Mediated	ISO 10993-11:2006 Tests for Systemic Toxicity	The test requirement is met if no rabbit shows an individual rise in temperature of 0.5°C or more above baseline	Non- pyrogenic/ **PASS**
Hemocompatibility: Hemolysis	ASTM Hemolysis – Direct and Indirect Contact	ISO 10993-4:2002 Tests for Hemocompatibility	The test requirement is met if the hemolytic index of test article/test article extract is 2% or less.	Non- hemolytic/ **PASS**
Hemocompatibility: Complement Activation C3a	Complement Activation Assay – C3a	ISO 10993-4:2002 Tests for Hemocompatibility	The test requirement is met if the C3a concentration from the test article extract is not statistically higher than both the activated NHS	Non- activator/ **PASS**

Test	Test Description	Applicable Standard	Acceptance Criteria	Results /Status
			and negative controls.	
Hemocompatibility: Complement Activation SC5b-9	Complement Activation Assay – SC5b-9	ISO 10993-4:2002 Tests for Hemocompatibility	The test requirement is met if the SC5b-9 concentration from the test article extract is not statistically higher than both the activated NHS and negative controls.	Non- activator/ **PASS**
Genotoxicity: (Bacterial Reverse Mutation Assay)	Bacterial Reverse Mutation Assay – SC and DMSO Extracts	ISO 10993-3:2003 Tests for Genotoxicity, Carcinogenicity & Reproductive Toxicity	The test requirement is met if less than 2-fold increase in the number of mean revertants over the means obtained from the negative control for strains of TA98, TA100 and WP2uvrA, and/or less than 3-fold increase in the number of mean revertants over the means obtained from the negative control for strains TA1535 and TA 1537 are observed in the DMSO and saline extracts.	Non- mutagenic/ **PASS**
Genotoxicity: Chromosomal Aberration (MLA)	Mouse Lymphoma Assay - Serum-Free Culture Medium and DMSO Extracts	ISO 10993-3:2003 Tests for Genotoxicity, Carcinogenicity & Reproductive Toxicity	The test requirement is met if less than two-fold increase in the RPMI0 and DMSO test article extracts are observed in the mean mutant frequency of L5178Y/TK$^{+/-}$ cell line either in the presence or absence of metabolic activation.	Non- mutagenic/ **PASS**
Genotoxicity: (Mouse Peripheral Blood Micronucleus)	Mouse Peripheral Blood Micronucleus Assay – SC and SO Extracts	ISO 10993-3:2003 Tests for Genotoxicity, Carcinogenicity & Reproductive Toxicity	The test requirement is met if the average %MN-RETs obtained for the negative control animals was between 0.1% and 0.5% and the average %MN-RETs for the positive control animals was at least 1.0%.	No increase in mutagenic activity/ **PASS**
Hemocompatibility: Thrombogenicity *(in vivo)*	Acute and Chronic Thromboresistance – Ovine GLP Study	ISO 10993-4:2002 Tests for Hemocompatibility	The test requirement is met if no significant differences in vascular response between test article and control stents in stent-related mortality	No evidence of thrombogenicity detected/ **PASS**

Test	Test Description	Applicable Standard	Acceptance Criteria	Results /Status
			or luminal thrombus.	
Implantation	Acute and Chronic Ovine GLP Study	ISO 10993-6:2007 Tests for Local Effects after Implantation	Test is considered negative if the test article did not induce a significantly greater biological reaction than the control article.	No adverse reaction observed/ **PASS**
Sub-Chronic Toxicity	Biological Risk Assessment	ISO 10993-11:2006 Tests for Systemic Toxicity	n/a	Information leveraged from GLP animal studies. See Section IX.G below.
Chronic Toxicity	Biological Risk Assessment	ISO 10993-11:2006 Tests for Systemic Toxicity	n/a	Information leveraged from GLP animal studies. See Section IX.G below.
Genotoxicity/ Carcinogenicity	Biological Risk Assessment	ISO 10993-3:2003 Tests for Genotoxicity, Carcinogenicity & Reproductive Toxicity	n/a	Information leveraged from chemical characterization testing

Table 3: Summary of Biocompatibility/Toxicity Results for the VICI VENOUS STENT Delivery System

Test	Test Description	Test Methodology	Acceptance Criteria	Results/Status
Cytotoxicity	MEM Elution	ISO 10993-5:2009 Tests for Cytotoxicity	The test article meets test requirements if none of the cultures treated with the test article show greater than Mild reactivity (Grade 2).	Non-cytotoxic/ **PASS**
Sensitization	Guinea Pig Maximization Test – SC and SO Extracts	ISO 10993-10:2010 Tests for Irritation & Sensitization	The test requirement is met if the skin reaction scores received by the test group are equal or less than the scores received by the negative control group.	Non-sensitizer/ **PASS**
Irritation/ Intracutaneous Toxicity	Intracutaneous Study – SC and SO Extracts	ISO 10993-10:2010 Tests for Irritation & Sensitization	The test requirement is met if the difference between the test article and the control mean score is 1.0 or less (negligible or slight).	Non-irritant/ **PASS**
Systemic Toxicity (Acute)	Systemic Toxicity Study – SC and SO Extracts	ISO 10993-11:2006 Tests for Systemic Toxicity	The test requirement is met if none of the animals injected with the test article extracts show a significantly greater biological reaction than the animals treated with the vehicle control.	Non-toxic/ **PASS**

Test	Test Description	Test Methodology	Acceptance Criteria	Results/Status
Material Mediated Pyrogenicity	USP Pyrogen Study – Material Mediated	ISO 10993-11:2006 Tests for Systemic Toxicity	The test requirement is met if no rabbit shows an individual rise in temperature of 0.5°C or more above baseline.	Non-pyrogenic/ **PASS**
Hemocompatibility: Hemolysis	ASTM Hemolysis – Direct and Indirect Contact	ISO 10993-4:2002 Tests for Hemocompatibility	The test requirement is met if the hemolytic index of test article/test article extract is 2% or less.	Non-hemolytic/ **PASS**
Hemocompatibility: Complement Activation C3a	Complement Activation Assay – C3a	ISO 10993-4:2002 Tests for Hemocompatibility	The test requirement is met if the C3a concentration from the test article extract is not statistically higher than both the activated NHS and negative controls.	Non-activator/ **PASS**
Hemocompatibility: Complement Activation SC5b-9	Complement Activation Assay – SC5b-9	ISO 10993-4:2002 Tests for Hemocompatibility	The test requirement is met if the SC5b-9 concentration from the test article extract is not statistically higher than both the activated NHS and negative controls.	Low potential activator/ **PASS**
Hemocompatibility: Acute Thromboresistance	Acute Thromboresistance	ISO 10993-4:2002 Tests for Hemocompatibility	The test requirement is met if no significant differences in vascular response between test article and control stents in stent-related mortality or luminal thrombus.	Non-thrombogenic/ **PASS**
Genotoxicity	Biological Risk Assessment	ISO 10993-3:2003 Tests for Genotoxicity, Carcinogenicity & Reproductive Toxicity	n/a	Testing considered not necessary

B. Physico-Chemical Testing

Physico-chemical testing on the VICI VENOUS STENT was conducted, as applicable, in accordance with:

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

Physico-chemical testing on the VICI VENOUS STENT was performed, including the following tests:

- Nickel Ion Release
- Chemical Characterization
  - Exhaustive Extraction: water/hexane/ethanol
  - Inductively Coupled Plasma (ICP)/Mass Spectroscopy (MS): water
  - Ion Chromatography (IC): water

- Gas Chromatography (GC)/Mass Spectroscopy (MS): water/hexane/ethanol
- Fourier Transform Infrared Spectroscopy (FTIR): water/hexane/ethanol
- Ultra Performance Liquid Chromatography/Mass Spectroscopy (UPLC-MS): water/hexane/ethanol

1. Nickel Ion Release Results

In accordance with FDA Guidance Document "Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems" dated April 18, 2010, the assessment of nickel ion release from Nitinol devices is recommended. However, there is no recognized standard that specifies the maximum permissible nickel ion leaching. The acceptance criteria for this study was therefore based on a literature review. The data were analyzed based on the F.W. Sunderman 1983 article (F.W. Sunderman, Potential Toxicity from Nickel Contamination of Intravenous Fluids, Annals of Clinical and Laboratory Science, vol 13 (1), 1-4). Test articles were prepared in accordance with ISO 10993-15 "Biological Evaluation of Medical Devices – Part 15: Identification and quantification of degradation products from metals and alloys."

The nickel ion release was observed at Day 1 and Day 60. Results from the nickel ion release test demonstrated that the amount of nickel released was below the 35 µg per day acceptance criteria recommended by Sundemann.

2. Chemical Characterization Results

The chemical characterization results are provided in **Table 4.** The results from these tests were all acceptable.

Table 4: VICI VENOUS STENT Chemical Characterization Results

Effect	Results
Exhaustive Extraction – water	Total non-volatile residue was determined to be <0.5 mg.
Exhaustive Extraction – ethanol	Total non-volatile residue was determined to be <0.5 mg.
Exhaustive Extraction – hexane	Total non-volatile residue was determined to be <0.5 mg.
FTIR – water	There were no major bands detected
FTIR – ethanol	There were no major bands detected
FTIR – hexane	There were no major bands detected
ICP/MS – water	There was one element detected in the extract
UPLC-MS – water	No compounds were observed greater than the 0.017 µg/cm^2
UPLC-MS – hexane	No compounds were observed greater than the 0.034 µg/cm^2
UPLC-MS – ethanol	No compounds were observed greater than the 0.017 µg/cm^2
GC/MS – water	There were no semi-volatile organic compounds detected.
GC/MS – hexane	There were no semi-volatile organic compounds detected.
GC/MS – ethanol	There were no semi-volatile organic compounds detected.

C. Functional and Engineering Testing

Functional and engineering testing on the VICI VENOUS STENT and the VICI VENOUS STENT System was conducted, as applicable, in accordance with:

- Guidance for Industry and FDA Staff, Non-Clinical Engineering Tests

and Recommended Labeling for Intravascular Stents and Associated Delivery Systems Guidance, April 18, 2010

- Guidance for Industry and FDA Staff, Select Updates for Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems, Document issued on August 18, 2015
- ISO 25539-2:2012 Cardiovascular devices -- Part 2: Vascular Stents

These studies are summarized in **Tables 5-8**. "Pass" denotes that the test results met product specifications and/or the recommendation in the above-referenced guidance documents.

Table 5: Summary of Functional and Engineering Test Results for the VICI VENOUS STENT, T=0

Test Name	Purpose/Objective	Samples Tested	Specification/Acceptance Criteria	Results
Stent Visual Inspections	To evaluate the stent outer diameter to ensure that the device meets the design specifications.	(10) 12mm x 60mm (10) 12mm x 120mm (10) 16mm x 60mm (10) 16mm x 120mm	Specification 12, 14 & 16mm ±1mm Acceptance Criteria 40 of 40 stents are within spec.	**PASS:** 40 of 40 stents were within spec
	To evaluate the stent length to ensure that the device meets the design specifications.	(10) 12mm x 60mm (10) 12mm x 120mm (10) 16mm x 60mm (10) 16mm x 120mm	Specification 60, 90 & 120mm ± 3mm Acceptance Criteria 40 of 40 stents are within spec	**PASS:** 40 of 40 stents were within spec
	To evaluate the stent to ensure that the device meets the design specifications on surface defects and contamination.	(10) 12mm x 60mm (10) 12mm x 120mm (10) 16mm x 60mm (29) 16mm x 120mm	Specification Stent must conform to specs with regard to surface defects and contamination that would render the stent unsuitable for its intended use Acceptance Criteria 59 of 59 stents have no defects	**PASS:** 59 of 59 stents have no defects
Radial Strength	To characterize the force exerted by the implant as a function of implant diameter.	(10) 12mm x 60mm (10) 12mm x 120mm (10) 16mm x 60mm (10) 16mm x 120mm	Specification 12mm: RRF ≥1.6N, COF ≥0.75N 14mm: RRF ≥1.55N, COF ≥0.68N 16mm: RRF ≥1.5N, COF ≥0.6N Acceptance Criteria 12mm OD RRF: LCL≥1.6N 12mm OD COF: LCL≥0.75N 16mm OD RRF: LCL≥1.5N 16mm OD COF: LCL≥0.6N	**PASS:** 40 of 40 met the radial strength specification

Test Name	Purpose/Objective	Samples Tested	Specification/Acceptance Criteria	Results
Crush Resistance	To evaluate the ability of the stent to resist permanent deformation and demonstrate the stent's resistance to localized compressive loads.	(10) 12mm x 60mm (10) 12mm x 120mm (10) 16mm x 60mm (10) 16mm x 120mm	Specification Stent diameter must recover by at least 95% after a flat plate crush of 50% of the diameter Acceptance Criteria LCL≥95%, all sizes	**PASS:** 40 of 40 met the crush resistance specification
Flex/Kink Resistance	To evaluate the stent's flexibility and kink resistance following deployment.	(10) 12mm x 60mm (10) 12mm x 120mm (10) 16mm x 60mm (10) 16mm x 120mm	Specification At least 50% of stent diameter must be maintained when wrapped around a 2.00" disc Acceptance Criteria 40 of 40 units must maintain at least 50% of their original lumen diameter	**PASS:** 40 of 40 units maintained at least 50% of original lumen diameter
Foreshortening	To analyze the foreshortening of the stent when loaded and after deployment.	(10) 12mm x 60mm (10) 12mm x 120mm (10) 16mm x 60mm (29) 16mm x 120mm	Specification Amount of foreshortening must be less than: - 20% for 30% oversize - 30% for 10% oversize Acceptance Criteria 10% oversize: UCL<30%, all sizes 30% oversize: UCL<20%, all sizes	**PASS:** 59 of 59 units had foreshortening <30% for 10% oversize 59 of 59 units had foreshortening <20% for 30% oversize
RO Marker Pushout Force	To evaluate the RO Marker Pushout Force.	29 RO Markers (4 -16mm x 60mm stents)	Specification RO Marker Pushout Force must be ≥ 3.6N (ID to OD direction) Acceptance Criteria 29 of 29 have Pushout Force ≥ 3.6N (ID to OD direction)	**PASS:** 29 of 29 RO markers had Pushout Force ≥ 3.6N (ID to OD direction)
MRI Compatibility	To evaluate the safety and compatibility of the stent under MRI environment and ensure that stent is not affected by scanning at 1.5 and 3.0 Tesla field strengths. (Displacement Force, Rotational Force [Torque], Inductive Heating [RF] and Image Artifacts)	(1) 12mm x 60mm (7) 12mm x 90mm (2) 12mm x 120mm (7) 16mm x 120mm	The test requirements are met based on MRI Testing Laboratory assessment.	**PASS:** The stent was determined to be classified as "MRI Conditional"
Finite Element Analysis	To evaluate the design of the stent with respect to	Finite Element Analysis Model: 16mm	No 16mm stent will exhibit Type 3 fractures. If any Type 1 or Type 2 fractures	**PASS** No fractures were shown.

Test Name	Purpose/Objective	Samples Tested	Specification/Acceptance Criteria	Results
	fatigue resistance over the designated implant life.		are seen then radial strength will be measured at that location. Stent should have a min radial strength of 1.5N at the vessel diameter	
Fatigue Testing	To characterize the fatigue resistance of stents in an overlapped bend configuration over the implant life.	(12) 16mm x 60mm (6 pairs)	Specification No 16mm stent will exhibit Type III or IV fracture and having a radial strength of less than 1.5N at the fracture location. RO Markers remain intact and fully attached to the stent for the duration of the test Acceptance Criteria Stent must maintain structural integrity for 10 years of typical physiological movements	**PASS:** 12 out of 12 samples maintained structural integrity. No fractures occurred. All RO Markers stayed intact and fully attached to the stent.
Photodynamic Corrosion Resistance (ASTM F2129-17)	To evaluate the susceptibility of the implant materials to corrosion and ensure that the implant maintains corrosion resistance following implantation.	(6) 16mm x 60mm	Specification Breakdown potential $\geq$ +600mV Acceptance Criteria All samples exhibit breakdown potential $\geq$ +600mV	**PASS:** All samples had breakdown potential of $\geq$ +600mV.
Galvanic Corrosion Resistance (ASTM F3044-14)	To evaluate the susceptibility of the implant materials to corrosion and ensure that the implant maintains corrosion resistance following implantation.	(3) 16mm x 60mm	Specification Average current density $\leq 8.36 \times 10^{-6}$ A/cm^2 Acceptance Criteria The average current density of all three samples $\leq 8.36 \times 10^{-6}$ A/cm^2	**PASS:** The average current density of all three samples $\leq 8.36 \times 10^{-6}$ A/cm^2
Radiopacity	The evaluate the radiopacity of the stent and ensure that the stent is visible using angiographic or radiographic imaging to allow for proper stent placement.	(2) RO Nosecone (2) 16mm x 60mm (1) 16mm x 120mm	Specification Implant must be sufficiently visible with standard fluoroscopic imaging equipment to allow for assessment of position and integrity Acceptance Criteria All stents are radiopaque	**PASS:** The stent was visible utilizing standard fluoroscopic imaging equipment in all arms

Test Name	Purpose/Objective	Samples Tested	Specification/Acceptance Criteria	Results
VICI Stent Fatigue Testing	To characterize the crush fatigue resistance of the stent over the implant life.	(6) 16mm x 60mm	Specification Stent must not migrate more than 1cm within the vein. No 16mm stent will exhibit Type 3 fractures. If any Type 1 or Type 2 fractures are seen then radial strength will be measured at that location. stent should have a min radial strength of 1.5N at the vessel diameter. Acceptance Criteria Implant must maintain structural integrity for a minimum of 10 years of physiological movements during typical respiratory cycles and Valsalva maneuvers.	**PASS:** 6 out of 6 samples maintained structural integrity. **PASS:** No fractures occurred.
Stent Conformability	To evaluate the conformability of the stent within a simulated stenosed vein to ensure the device meets the design specifications.	(20) 12mm (20) 16mm	Average Conformability >80%	**PASS:** The average conformability was >80%.
Percent Surface Area of the VICI Stent	To calculate the percent surface area for the expanded stent post-deployment and ensure that the device meets the design specifications.	All sizes	N/A	This is characterization testing and does not have acceptance criteria.
VICI Stent Fatigue Testing	To characterize the crush fatigue resistance of the stent over the implant life.	(6) 16mm x 60mm	Specification Stent must not migrate more than 1cm within the vein. No 16mm stent will exhibit Type 3 fractures. If any Type 1 or Type 2 fractures are seen then radial strength will be measured at that location. stent should have a min radial strength of 1.5N at the vessel diameter. Acceptance Criteria Implant must maintain structural integrity for a minimum of 10 years of physiological movements during typical respiratory cycles and Valsalva maneuvers.	**PASS:** 6 out of 6 samples maintained structural integrity. **PASS:** No fractures occurred.

Test Name	Purpose/Objective	Samples Tested	Specification/Acceptance Criteria	Results
	To characterize the bend fatigue resistance of the stent over the implant life.	(12) 16mm x 120mm	Specification No stent will exhibit Type 3 fractures i.e. complete stent detachment. If any Type 1 or Type 2 fractures are seen then radial strength will be measured at that location. The stent should have a minimum radial strength (RRF) of 1.5N at the vessel diameter. Acceptance Criteria Implant must maintain structural integrity for a minimum of 10 years of physiological movements during typical respiratory cycles and Valsalva maneuvers.	**PASS:** 12 out of 12 samples maintained structural integrity. **PASS:** No Type 3 fractures occurred. A single Type 1 fracture occurred and had radial strength within the acceptance criteria.
	To characterize the fatigue resistance of stents in an overlapped configuration over the implant life.	(12) 16mm x 60mm	Specification Stent must not migrate more than 1cm within the vein. No 16mm stent will exhibit Type 3 fractures. If any Type 1 or Type 2 fractures are seen then radial strength will be measured at that location. Stent should have a min radial strength of 1.5N at the vessel diameter. Acceptance Criteria Implant must maintain structural integrity for a minimum of 10 years of physiological movements during typical respiratory cycles and Valsalva maneuvers.	**PASS:** 12 out of 12 samples maintained structural integrity. **PASS:** No fractures occurred.

Table 6: Summary of Functional and Engineering Test Results for the VICI VENOUS STENT, T=3-year AA

Test Name	Purpose/Objective	Samples Tested	Specification/Acceptance Criteria	Results
Stent Visual Inspections	To evaluate the stent outer diameter to ensure that the device meets the design specifications.	(10) 12mm x 60mm (10) 12mm x 120mm (10) 16mm x 60mm (10) 16mm x 120mm	Specification 12, 14 & 16mm ±1mm Acceptance Criteria 40 of 40 stents are within spec.	**PASS:** 40 of 40 stents were within spec

Test Name	Purpose/Objective	Samples Tested	Specification/Acceptance Criteria	Results
	To evaluate the stent length to ensure that the device meets the design specifications.	(10) 12mm x 60mm (10) 12mm x 120mm (10) 16mm x 60mm (10) 16mm x 120mm	Specification 60, 90 & 120mm ± 3mm Acceptance Criteria 40 of 40 stents are within spec	**PASS:** 40 of 40 stents were within spec
	To evaluate the stent to ensure that the device meets the design specifications on surface defects and contamination.	(10) 12mm x 60mm (10) 12mm x 120mm (10) 16mm x 60mm (29) 16mm x 120mm	Specification Stent must conform to specs with regard to surface defects and contamination that would render the stent unsuitable for its intended use Acceptance Criteria 59 of 59 stents have no defects	**PASS:** 59 of 59 stents had no defects
Radial Strength	To characterize the force exerted by the implant as a function of implant diameter.	(10) 12mm x 60mm (10) 12mm x 120mm (10) 16mm x 60mm (10) 16mm x 120mm	Specification 12mm: RRF ≥1.6N, COF ≥0.75N 14mm: RRF ≥1.55N, COF ≥0.68N 16mm: RRF ≥1.5N, COF ≥0.6N Acceptance Criteria 12mm OD RRF: LCL≥1.6N 12mm OD COF: LCL≥0.75N 16mm OD RRF: LCL≥1.5N 16mm OD COF: LCL≥0.6N	**PASS:** 40 of 40 met the radial strength specification
Crush Resistance	To evaluate the ability of the stent to resist permanent deformation and demonstrate the stent's resistance to localized compressive loads.	(10) 12mm x 60mm (10) 12mm x 120mm (10) 16mm x 60mm (10) 16mm x 120mm	Specification Stent diameter must recover by at least 95% after a flat plate crush of 50% of the diameter Acceptance Criteria LCL≥95%, all sizes	**PASS:** 40of 40 met the crush resistance specification
Flex/Kink Resistance	To evaluate the stent's flexibility and kink resistance following deployment.	(12) 16mm x 120mm	Specification At least 50% of stent diameter must be maintained when wrapped around a 2.00" disc Acceptance Criteria Stent final diameter LCL >5% of their original lumen diameter.	**PASS:** 12 of 12 units maintained at least 50% of original lumen diameter
Foreshortening	To analyze the foreshortening of the stent when loaded and after deployment.	(10) 12mm x 60mm (10) 12mm x 120mm (10) 16mm x 60mm (29) 16mm x 120mm	Specification Amount of foreshortening must be less than: - 20% for 30% oversize - 30% for 10% oversize	**PASS:** 59 of 59 units had foreshortening <30% for 10% oversize

Test Name	Purpose/Objective	Samples Tested	Specification/Acceptance Criteria	Results
			Acceptance Criteria 10% oversize: UCL<30%, all sizes 30% oversize: UCL<20%, all sizes	59 of 59 units had foreshortening <20% for 30% oversize
RO Marker Pushout Force	To evaluate the RO Marker Pushout Force	(29) 16mm x 120mm (1 RO marker per stent)	Specification RO Marker Pushout Force must be ≥3.6N (ID to OD direction) Acceptance Criteria 29 of 29 have Pushout Force ≥3.6N (ID to OD direction)	**PASS:** 29 of 29 RO markers had Pushout Force ≥3.6N (ID to OD direction)

Table 7: Summary of Functional Test Results for the VICI VENOUS STENT System, T=0

Test Name	Purpose/Objective	Samples Tested	Specification/Acceptance Criteria	Results
Hemostasis	To evaluate the ability of the delivery system to maintain hemostasis during use and ensure that the delivery system performs adequately for the intended use.	(29) 16mm x 120mm	Specification Maintain hemostasis (0.7psi for 30 seconds minimum) Acceptance Criteria 29 of 29 units maintain hemostasis	**PASS:** 29 of 29 units maintained hemostasis
Flush	To ensure that the lumens and Hemostasis Valve of the delivery system can be appropriately flushed with saline using standard luer fittings.	(29) 16mm x 120mm	Specification All lumens and Hemostasis Valve can be flushed with saline using standard luer fittings Acceptance Criteria 29 of 29 units are flushable	**PASS:** 29 of 29 units were flushable
Placement Accuracy	To characterize the deployment accuracy of the stent system and verify that the delivery system performs adequately for the intended use with respect to deployment accuracy.	(29) 16mm x 120mm	Specification Delivery System must allow for accurate placement of stent ±2.5mm of target location Acceptance Criteria 29 of 29 stents are placed within ±2.5mm of target location	**PASS:** 29 of 29 stents were placed within ±2.5mm of target location
Hypotube Travel Distance	To evaluate the final delivery system Hypotube travel distance to ensure that the device meets the design specifications.	(29) 16mm x 120mm	Specification 120mm length: 170mm ± 5mm Acceptance Criteria 29 of 29 units have Hypotube travel distance of 170 ± 5mm	**PASS:** 29 of 29 units had Hypotube travel distance of 170 ± 5mm
Outer Diameter Inspection	To evaluate the final delivery system Outer Shaft outer diameter to ensure that the device meets the design specifications.	(29) 16mm x 120mm	Specification ≤0.122" (compatibility with 9F introducer) Acceptance Criteria 29 of 29 units pass through OD tool	**PASS:** 29 of 29 units passed through OD tool

Test Name	Purpose/Objective	Samples Tested	Specification/Acceptance Criteria	Results
	To evaluate the final delivery system Nosecone outer diameter to ensure that the device meets the design specifications.		Specification ≤0.122" (compatibility with 9F introducer) Acceptance Criteria 29 of 29 units pass through OD tool	
Advanceability	To evaluate the final delivery system Inner Shaft lumen inner diameter to ensure that the device meets the design specifications for compatibility with a 0.035" guidewire.	(29) 16mm x 120mm	Specification >0.035" (compatibility with 0.035" guidewire) Acceptance Criteria 29 of 29 units are advanceable	**PASS:** 29 of 29 units were advanceable
	To evaluate the final delivery system Nosecone inner diameter to ensure that the device meets the design specifications for compatibility with a 0.035" guidewire.		Specification >0.035" (compatibility with 0.035" guidewire) Acceptance Criteria 29 of 29 units are advanceable	
	To evaluate the final delivery system Inner Shaft Hub inner diameter to ensure that the device meets the design specifications for compatibility with a 0.035" guidewire.		Specification >0.035" (compatibility with 0.035" guidewire) Acceptance Criteria 29 of 29 units are advanceable	
Flex/Kink	To evaluate the pushability, trackability, and flexibility of the delivery system over a guidewire and ensure that the delivery system performs adequately for the intended use.	(29) 16mm x 120mm	Specification Delivery System will be sufficiently pushable and flexible to track over a 0.035" guidewire Acceptance Criteria 29 of 29 units don't kink at radius ≥10.6mm in catheter body, stent and transition sections	**PASS:** 29 of 29 units didn't kink at radius ≥10.6mm in catheter body, stent and transition sections
Working Length	To evaluate the final delivery system Outer Shaft length (Working Length) to ensure that the device meets the design specifications.	(29) 16mm x 120mm	Specification 1000mm ± 10mm Acceptance Criteria 29 of 29 units have working lengths within ±10mm of 1000mm	**PASS:** 29 of 29 units had Working lengths within ±10mm of 1000mm
Deployment Force	To evaluate the force required to deploy the stent from the delivery system and verify that the deployment force is adequate for the intended use.	(29) 16mm x 120mm	Specification Stent deployment requires a reasonable amount of input force from the user ≤55N Acceptance Criteria 29 of 29 units require <55N to deploy	**PASS:** 29 of 29 units required <55N to deploy
		(29) 16mm x 120mm	Specification Stent deployment requires a reasonable amount of input force from the user ≤40N	**PASS:** 29 of 29 units required <40N to deploy

Test Name	Purpose/Objective	Samples Tested	Specification/Acceptance Criteria	Results
			Acceptance Criteria 29 of 29 units require <40N to deploy	
Removability	To evaluate the removal of the delivery system from the venous anatomy and ensure that the device can be appropriately removed for the intended purpose.	(29) 16mm x 120mm	Specification Delivery System must be safely removed from typical venous anatomy Acceptance Criteria 29 of 29 units are removable	**PASS:** 29 of 29 units were removable
Torque	To evaluate the resistance of the delivery system to torqueing forces and ensure that the device can withstand an appropriate number of rotations for its intended use.	(29) 16mm x 120mm	Specification The Delivery System must withstand >3 rotations Acceptance Criteria 29 of 29 units withstand >3 rotations	**PASS:** 29 of 29 units withstood >3 rotations
Delivery System Bond Strength	To evaluate joint integrity of the Gen 1.5 Delivery System bonds.	29	Specification The tensile and compression strength of the Gen 1.5 Delivery System must meet specifications (specifications ranged from ≥10N to >55N). Acceptance Criteria 29 of 29 units meet all joint strength specifications	**PASS:** 29 of 29 units had joint strengths that met specification.

Table 8: Summary of Functional Test Results for the VICI VENOUS STENT System, T=3-year AA

Test	Purpose/Objective	Samples Tested	Specification/Acceptance Criteria	Results
Hemostasis	To evaluate the ability of the delivery system to maintain hemostasis during use and ensure that the delivery system performs adequately for the intended use.	(29) 16mm x 120mm	Specification Maintain hemostasis (0.7psi for 30 seconds minimum) Acceptance Criteria 29 of 29 units maintain hemostasis	**PASS:** 29 of 29 units maintained hemostasis
Flush	To ensure that the lumens and Hemostasis Valve of the delivery system can be appropriately flushed with saline using standard luer fittings.	(29) 16mm x 120mm	Specification All lumens and Hemostasis Valve can be flushed with saline using standard luer fittings Acceptance Criteria 29 of 29 units are flushable	**PASS:** 29 of 29 units were flushable

Test	Purpose/Objective	Samples Tested	Specification/Acceptance Criteria	Results
Placement Accuracy	To characterize the deployment accuracy of the stent system and verify that the delivery system performs adequately for the intended use with respect to deployment accuracy.	(29) 16mm x 120mm	Specification Delivery System must allow for accurate placement of stent ±2.5mm of target location Acceptance Criteria 29 of 29 stents are placed within ±2.5mm of target location	**PASS:** 29 of 29 stents were placed within ±2.5mm of target location
Hypotube Travel Distance	To evaluate the final delivery system Hypotube travel distance to ensure that the device meets the design specifications.	(29) 16mm x 120mm	Specification 120mm length: 170mm ± 5mm Acceptance Criteria 29 of 29 units have Hypotube travel distance of 170 ± 5mm	**PASS:** 29 of 29 units had Hypotube travel distance of 170 ± 5mm
Outer Diameter Inspection	To evaluate the final delivery system Outer Shaft outer diameter to ensure that the device meets the design specifications.	(29) 16mm x 120mm	Specification ≤0.122" (compatibility with 9F introducer) Acceptance Criteria 29 of 29 units pass through OD tool	**PASS:** 29 of 29 units passed through OD tool
	To evaluate the final delivery system Nosecone outer diameter to ensure that the device meets the design specifications.		Specification ≤0.122" (compatibility with 9F introducer) Acceptance Criteria 29 of 29 units pass through OD tool	
Advanceability	To evaluate the final delivery system Inner Shaft lumen inner diameter to ensure that the device meets the design specifications for compatibility with a 0.035" guidewire.	(29) 16mm x 120mm	Specification >0.035" (compatibility with 0.035" guidewire) Acceptance Criteria 29 of 29 units are advanceable	**PASS:** 29 of 29 units were advanceable
	To evaluate the final delivery system Nosecone inner diameter to ensure that the device meets the design specifications for compatibility with a 0.035" guidewire.		Specification >0.035" (compatibility with 0.035" guidewire) Acceptance Criteria 29 of 29 units are advanceable	
	To evaluate the final delivery system Inner Shaft Hub inner diameter to ensure that the device meets the design specifications for compatibility with a 0.035" guidewire.		Specification >0.035" (compatibility with 0.035" guidewire) Acceptance Criteria 29 of 29 units are advanceable	
Flex/Kink	To evaluate the pushability, trackability, and flexibility of the delivery system over a guidewire and ensure that	(29) 16mm x 120mm	Specification Delivery System will be sufficiently pushable and flexible to track over a	**PASS:** 29 of 29 units didn't kink at radius ≥10.6mm in

Test	Purpose/Objective	Samples Tested	Specification/Acceptance Criteria	Results
	the delivery system performs adequately for the intended use.		0.035" guidewire Acceptance Criteria 29 of 29 units don't kink at radius ≥10.6mm in catheter body, stent and transition sections	catheter body, stent and transition sections
Working Length	To evaluate the final delivery system Outer Shaft length (Working Length) to ensure that the device meets the design specifications.	(29) 16mm x 120mm	Specification 1000mm ± 10mm Acceptance Criteria 29 of 29 units have working lengths within ±10mm of 1000mm	**PASS:** 29 of 29 units had Working lengths within ±10mm of 1000mm
Deployment Force	To evaluate the force required to deploy the stent from the delivery system and verify that the deployment force is adequate for the intended use.	(29) 16mm x 120mm (29) 16mm x 120mm	Specification Stent deployment requires a reasonable amount of input force from the user ≤55N Acceptance Criteria 29 of 29 units require <55N to deploy	**PASS:** 29 of 29 units required <55N to deploy
			Specification Stent deployment requires a reasonable amount of input force from the user ≤40N Acceptance Criteria 29 of 29 units require <40N to deploy	**PASS:** 29 of 29 units required <40N to deploy
Removability	To evaluate the removal of the delivery system from the venous anatomy and ensure that the device can be appropriately removed for the intended purpose.	(29) 16mm x 120mm	Specification Delivery System must be safely removed from typical venous anatomy. Acceptance Criteria 29 of 29 units are removable	**PASS:** 29 of 29 units were removable
Torque	To evaluate the resistance of the delivery system to torqueing forces and ensure that the device can withstand an appropriate number of rotations for its intended use.	(29) 16mm x 120mm	Specification The Delivery System must withstand >3 rotations Acceptance Criteria 29 of 29 units withstand >3 rotations	**PASS:** 29 of 29 units withstood >3 rotations
Delivery System Bond Strength	To evaluate joint integrity of the Gen 1.5 Delivery System bonds.	(29) 16mm x 120mm	Specification The tensile and compression strength of the Gen 1.5 Delivery System must meet specifications	**PASS:** 29 of 29 units had joint strengths that met specification.

Test	Purpose/Objective	Samples Tested	Specification/Acceptance Criteria	Results
			(specifications ranged from ≥10N to >55N). Acceptance Criteria 29 of 29 units meet all joint strength specifications	

D. Packaging Testing

Packaging verification testing was performed to demonstrate that the design of the VICI VENOUS STENT System packaging can withstand the hazards of the distribution environment and that the sterility of the device is maintained throughout the labeled shelf life. Packaging verification testing included a visual assessment, bubble leak testing, and seal strength testing at both the baseline condition and for packages aged to the product's shelf life.

E. Shelf Life Testing

Functional device and packaging performance testing were conducted to demonstrate that the device and packaging performs within product specifications for a labeled shelf life of 3 years. Tables 5-8 above show which tests were performed at baseline and shelf-life aged conditions.

The combination of the Packaging and Shelf Life testing supports the VICI VENOUS STENT System shelf life of 3 years.

F. Sterilization

The VICI VENOUS STENT System is terminally sterilized using 100% ethylene oxide (EO) gas. The sterilization validation for the VICI VENOUS STENT System was originally based on the guidelines for an Overkill approach sterilization cycle in accordance with ANSI/AAMI/ISO 11135-1:2007 "Sterilization of health care products – Ethylene oxide – Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices", AAMI TIR16:2009 "Microbiological aspects of ethylene oxide sterilization", ANSI/AAMI/ISO 11135-2:2008 "Sterilization of health care products — Ethylene oxide — Part 2: Guidance on the application of ANSI/AAMI/ISO 11135-1" and ISO 10993-7:2008 "Biological evaluation of medical devices – Part 7: Ethylene oxide sterilization residuals".

A gap assessment has also been performed against the new requirements of ISO 11135:2014 "Sterilization of health-care products – Ethylene oxide – Requirements for the development, validation and routine control of a sterilization process for medical devices". This gap assessment established that VICI VENOUS STENT System's original sterilization validation also meets the requirements of EN ISO 11135:2014.

The test results obtained from the sterilization testing demonstrated that the product can be adequately sterilized to the desired level of sterility assurance of 10^{-6}.

G. Animal Studies

Good Laboratory Practice (GLP) *in vivo* animal testing was performed on the VICI VENOUS STENT and Delivery System.

Table 9 provides a summary of the animal studies performed. The results support the safety and performance of the VICI VENOUS STENT and Delivery System.

Table 9: Summary of Animal Studies

Study Description	Test Article/ Control	Study Summary and Results
Acute GLP Thrombogenicity Study in Ovine	VICI VENOUS STENT/Wallstent	This acute thrombogenicity study was conducted in ovine to evaluate the thrombogenic potential of the VENITI VICI VENOUS STENT in comparison to a commercially available device (Boston Scientific Wallstent). Three animals were enrolled with a total of six external jugular and six external femoral/iliac veins successfully implanted with either the test or control devices (stents were placed in the external jugular veins and the delivery systems were placed in external femoral/iliac veins). Thrombus coating on one test article was observed and may be an anomalous finding. The other test articles had an equivalent thrombogenic response as the control stents. Histopathological evaluations were performed, and all were within normal limits. There was no physiologic or mechanical causative event or finding attributable to the abnormal thrombus coating on one of the test stents
GLP Animal Study for VICI VENOUS STENT System	VICI VENOUS STENT System/Wallstent	The VICI VENOUS STENT System performance characteristics and mechanical integrity requirements were evaluated using visual inspection, fluoroscopy and intravascular ultrasound (IVUS) techniques. The animal study included three study arms (Acute, 56-Day and 180-Day) with four animals in each arm. Tissue interaction was evaluated using visual examination at gross necropsy. Chronic thromboresistance was evaluated in the 56-Day and 180-Day chronic arms. Prior to sacrifice, a venogram was performed to generally evaluate the vein and stents for presence of thrombus. Additionally, a visual inspection was performed during gross necropsy to generally evaluate the iliac vein and stent site for the presence of thrombus. The results showed VICI VENOUS STENT remained intact and in place in all chronic animals. Vessel trauma during implantation or at follow-up was not noted and the impact on the endothelium was considered minimal and expected. The VICI VENOUS STENT performed similarly to the Wallstent and no difference was seen between the two stent types.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of the implantation of a venous stent into the iliofemoral vein with the VICI VENOUS STENT System to treat patients with post-thrombotic or non-thrombotic disease in the US, France, Germany, Ireland, Spain, and the United Kingdom under IDE G140016. The study included a feasibility cohort (the first 30 subjects enrolled) and a pivotal cohort (170 subjects). Data from the pivotal cohort of this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below. Data from the

feasibility cohort were analyzed separately and are not included in this summary.

A. Study Design

Subjects were enrolled in the pivotal cohort between March 20, 2015 and November 2, 2016. The database for this PMA reflected pivotal cohort data collected through November 1, 2018. There were 22 sites in the pivotal study.

The VIRTUS study was conducted as a prospective, global, multi-center single-arm trial with outcomes compared to performance goals developed from medical literature. Enrollment in the VIRTUS study was stratified according to each subject's disease etiology, i.e., post-thrombotic or non-thrombotic. A Statistical Analysis Plan (SAP) for the VIRTUS study was generated for this study protocol.

The VIRTUS pivotal cohort consisted of 170 subjects. A total of 127 subjects, approximately 74% of the pivotal cohort enrollees, were to be enrolled with an iliofemoral venous segment obstruction associated with thromboembolic disease. These subjects are referred to as the post-thrombotic (PT) group in this summary. A total of 43 subjects, approximately 26% of the pivotal cohort enrollees, were to be enrolled with iliofemoral venous segment obstruction without previous thromboembolic disease and without intraluminal disease. These subjects are referred to as the non-thrombotic (NT) group in this summary.

Subjects in the VIRTUS study were evaluated preoperatively and were followed through their index procedure (when they were officially enrolled) and hospital discharge. The study subjects had follow-up evaluations at Month 1, Month 6 and Month 12 post-procedure. The VIRTUS subjects will continue to be followed for a total of 5 years, as described further below.

All imaging modalities (venography, duplex ultrasound (DUS), intravascular ultrasound (IVUS), X-ray) were assessed by independent core labs. Safety events were adjudicated by an independent Clinical Events Committee and an independent Data Safety Monitoring Board assessed the ongoing risk/benefit profile of the study device based on aggregate and individual study subject data.

1. Clinical Inclusion and Exclusion Criteria

   Enrollment in the VIRTUS study was limited to patients who met the following inclusion criteria:

   A. *Pre-Procedural Inclusion Criteria*

      1. Age ≥18 years
      2. Willing and capable of complying with all follow-up evaluations at the specified times
      3. Able and willing to provide written informed consent prior to study specific procedures
      4. Presence of unilateral, clinically significant, chronic non-malignant obstruction of the common femoral vein, external iliac vein, common iliac vein, or any combination thereof, defined as a ≥50% reduction in target

vessel lumen diameter (to be measured by venogram during procedure, per Exclusion 25).

5. Clinically significant venous obstruction defined as meeting at least one of the following clinical indicators:
    - Clinical severity class of CEAP classification ≥3 (See Appendix 4 of VIRTUS protocol.)
    - VCSS Pain Score ≥2 (See Appendix 7 of VIRTUS protocol.)
6. Negative pregnancy test in females of child-bearing potential
7. Intention to stent the target lesion only with the VICI VENOUS STENT

Patients were <u>not</u> permitted to enroll in the VIRTUS study if they met any of the following exclusion criteria:

B. *Pre-Procedural Exclusion Criteria*

1. Presence or history of clinically significant pulmonary emboli within 6 months prior to enrollment
2. Venous obstruction that extends into the inferior vena cava
3. Contralateral disease of the common femoral vein, external iliac vein, common iliac vein, or any combination thereof with planned treatment within 30 days after subject enrollment
4. Life expectancy <12 months
5. Female of childbearing potential who is pregnant or plans to become pregnant during the duration of the clinical study
6. A. Uncontrolled or active coagulopathy OR

   B. Known, uncorrectable bleeding diathesis with the following definitions:
    - Uncorrected INR ≥2.0 or aPTT ≥1.5 X normal local lab value
    - Platelet count <80,000
7. Uncorrected hemoglobin of ≤9 g/dL
8. Patients with an estimated glomerular filtration rate (eGFR) <30 mL/min. In patients with diabetes mellitus, eGFR <45 mL/min.
9. Known hypersensitivity to nickel or titanium
10. Contrast agent allergy that cannot be managed adequately with pre-medication
11. Intended concurrent thrombolysis or thrombectomy procedure OR intended or planned (within 30 days) adjuvant procedure such as creation of temporary AV fistula, placement of IVC filter, endovenectomy or saphenous vein ablation
12. Current or recent (within 30 days) active participation in another drug or device clinical trial (Participation in observational studies is acceptable)

13. Patient judged to be a poor candidate by the primary investigator

14. Patients who have had any prior surgical or endovascular intervention of the target vessel

    Note: Patients who have had catheter-directed or mechanical thrombolysis in the target vessel for DVT at least 3 months (90 days) prior to the VIRTUS index procedure may be included in the trial

C. *Intra-procedural Exclusion Criteria:* If patients met any of the following exclusion criteria, they were not counted in the study sample size.

1. Patients in whom the lesions cannot be traversed with a guide wire.
2. Patients where the obstruction extends into the inferior vena cava or below the level of the lesser trochanter.
3. Patients whose vein diameters are not within limits stated in current Instructions for Use as determined by venogram.
4. Patients who do not meet the venogram binary stenosis definition above, as determined by the treating physician.

2. Follow-up Schedule

The VIRTUS pivotal subjects were followed in accordance with the protocol-specified visit schedule of: 1 Month Evaluation (30 days -7/+14 days), 6 Month Evaluation (180 days ± 30 days), and 12 Month Evaluation (365 days ± 60 days). Enrolled VIRTUS subjects will continue to be followed at 24 Months, 36 Months, 48 Months and 60 Months. All adverse events and complications were recorded at all visits through the 12 Month Evaluation. Serious adverse events and complications will continue to be collected through the 60 Month Evaluation. **Table 10** provides the follow-up schedule and tests conducted through the 60 Month visit.

Table 10: Summary of Procedures

Visit (window)	Description	Screening	Baseline Evaluation (30 days from implant)	Implant Procedure (Day 0)	Post-stent placement assessment	Discharge or 3 days post-procedure[a]	1 Month Evaluation (30 days -7/+14 days)	6 Month Evaluation (180 ±30 days)	12 Month Evaluation (365 ±60 days)	24 and 36 Month Evaluation (±90 days)	48 and 60 Month Evaluation (±90 days)	Interval Evaluation[b]
Assessment of Inclusion and Exclusion Criteria	Medical records	X	X	X[c]								
Informed Consent	IC		X[d]									
Assessment of baseline characteristics	H&P, labs, CEAP		X				Physical Exam Only	Physical Exam Only	Physical Exam Only			Physical Exam
Duplex Ultrasound	DUS					X		X[e]	X	X[i]		X
Venogram	VG			X	X				X[h]			X
IVUS	IVUS			X	X				X			X
AE Assessment				X	X	X	X	X	X			X
SAE Assessment										X[j]	X[j]	
Anticoagulation Regimen				X		X	X	X	X			X
Pregnancy Test (women of child bearing years)			X[f]									
CIVIQ-2			X					X	X			
VAS			X					X	X			
VCSS			X					X	X			
Biplane X-ray[g]									X			

a: Discharge or 3 days post-procedure, whichever comes first
b: Performed if patients present with symptoms of clinically significant obstruction of the target vessel.
c: Evaluate intra-procedural exclusion criteria prior to implant
d: Informed consent may be collected before or at the Baseline Evaluation visit.
e: Required only for the feasibility patients to assess patency
f. Pregnancy test in females of child-bearing age must be collected within 48 hours of implant procedure
g: To assess stent integrity.
h: To assess primary patency
i: To assess patency
j: SAE Assessment may be performed via telephone.

3. Clinical Endpoints

Primary Effectiveness Endpoint

The primary effectiveness endpoint was the primary patency rate at 12 months post-intervention, defined as freedom from occlusion by thrombosis (assessed via venogram) and freedom from surgical or endovascular intervention on target vessel which are found to have re-stenosis or stent occlusion to maintain patency and freedom from in-stent stenosis more than 50% by venogram. Target vessel revascularization (TVR) was adjudicated by an independent Clinical Events Committee (CEC).

Using literature, a single primary effectiveness performance goal was derived. The performance goal was based on both PT and NT etiologies and assumed a fixed proportion population (75% of the patients were expected to be PT and 25% were expected to be NT). The estimated patency rate from literature was 77.6% for PT subjects and 95.5% for NT subjects, respectively. The combined patency rate was 82.1% using a weighted average of the patency rates for each etiology. A 10% margin was applied to arrive at a combined, weighted primary effectiveness performance goal of 72.1%. Sample size was calculated using a one-sided significance level of α=0.025 and power of 84%.

The null and alternative hypotheses can be expressed as:

HO: $P_{Eff} \leq 72.1\%$ HA: $P_{Eff} > 72.1\%$

where P_{Eff} is the proportion of subjects with a successful outcome.

Secondary Effectiveness Endpoint

The secondary effectiveness endpoint for this study was a binary response variable based on an improvement in Venous Clinical Severity Score (VCSS) by at least 50% at 12 months post-intervention.

Additional Effectiveness Endpoint

The following additional effectiveness endpoints were evaluated:

Estimate Primary-Assisted Patency
Primary-assisted patency is defined as freedom from occlusion regardless of whether an intervention (subsequent to the index procedure) was performed.

Estimate Secondary Patency
Secondary patency is defined as freedom from "permanent" loss of patency determined through last follow-up (irrespective of the number of interventions).

Procedural Technical Success
Procedural technical success is achievement of a final residual target vessel diameter stenosis of 50% as measured on the post-procedural venogram, without skipped lesion regions, with placement of the study device alone with or without post-stenting balloon dilation as needed.

Lesion Success

Lesion success is defined as achievement of ≤50% residual diameter stenosis of the target lesion using any percutaneous method (including the use of non-study devices).

Procedural Success

Procedural success is defined as procedural technical success without the occurrence of a Major Adverse Event (MAE) between the index procedure and discharge.

Late Technical Success

Late technical success (through 12 months) is the absence of device movement >10mm related to anatomical landmarks or any migration leading to symptoms or requiring therapy; absence of stent occlusion by thrombosis or restenosis, defined as reduction in treated segment lumen more than 50% from the post-procedure vessel lumen diameter as measured by post-procedural venogram or DUS and maintenance of structural integrity, defined as the absence of pinching (focal compression), kinking (stent doubling or bending upon itself) that results in >50% diameter reduction of the stent, recoil (poor radial resistive force) or absence of fractures.

Change in the Quality of Life (CIVIQ-2)

The area under the curve will be calculated for the CIVIQ-2. The mean and 95% confidence intervals for the study patients will be presented.

Primary Safety Endpoint

The primary safety endpoint for this study was a composite endpoint of any major adverse event within 30 days, as adjudicated by a Clinical Events Committee. The VIRTUS protocol-defined Major Adverse Events (MAEs) are listed below:

- Device or procedure-related death;
- 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 outside of the target vein segment;
- Clinically significant pulmonary embolism defined as being symptomatic with chest pain, hemoptysis, dyspnea, hypoxia etc. AND be documented on CT; or
- Embolization of stent.

The primary safety endpoint was the proportion of subjects free of a MAE through Day 30 post-index procedure. The performance goal was 94% and was derived using literature. In the absence of controlled studies to indicate a true adverse event rate, a conservative approach was taken and 1% was used as the pre-specified safety rate. Sample size was calculated using a one-sided significance level of α=0.025 and power of 90%.

The null and alternative hypotheses can be expressed as:

HO: $P_{Safe} \leq 94\%$ HA: $P_{Safe} > 94\%$

where P_{Safe} is the proportion of subjects free from a MAE.

Secondary Safety Endpoints

The secondary safety endpoints for this study included adverse events, all serious adverse events and all device-related adverse events.

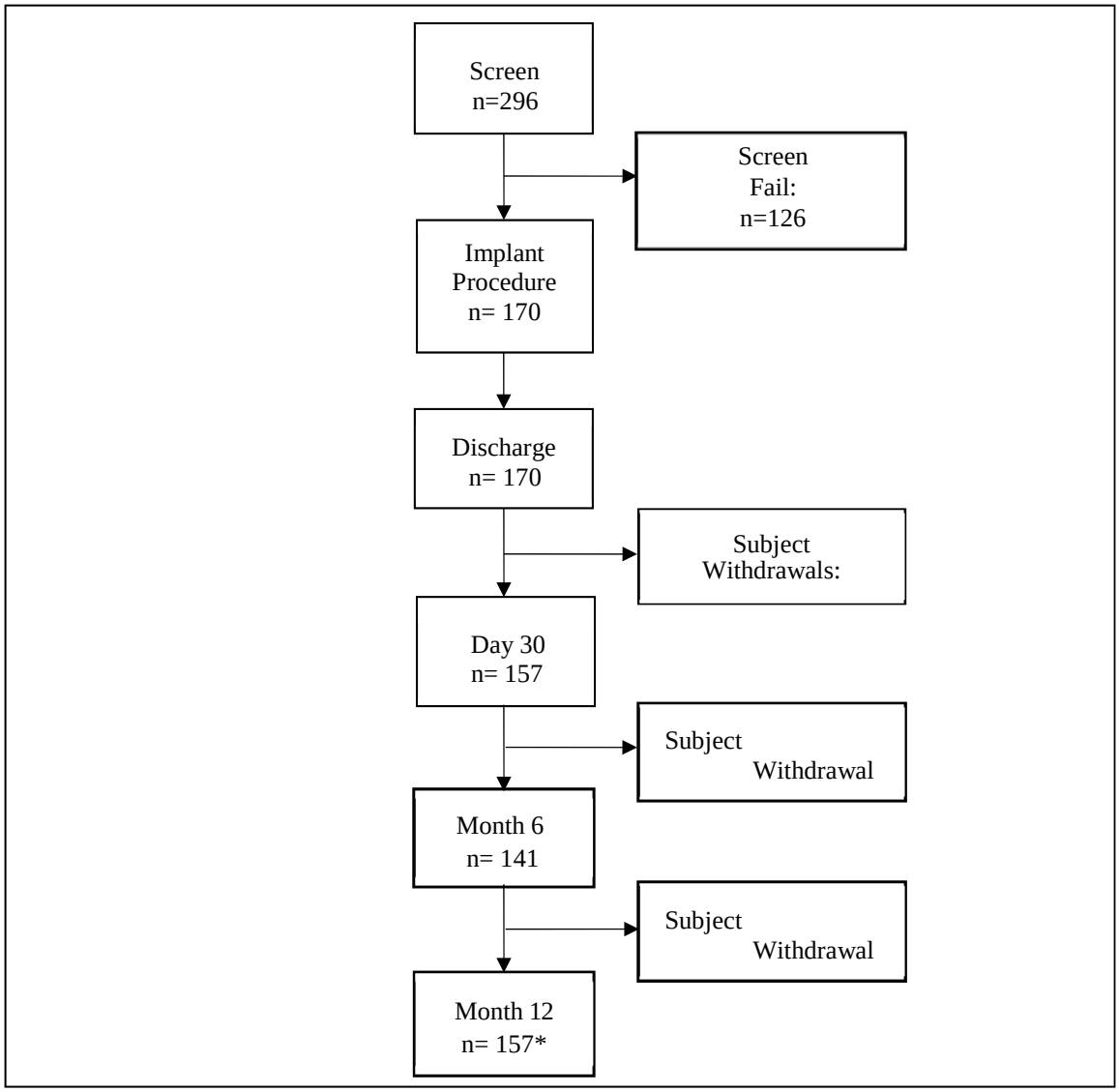
B. Accountability of PMA Cohort

All 170 pivotal cohort subjects had one or more VICI stents successfully implanted and were discharged from the hospital.

In total, seven subjects withdrew prior to the Month 12 visit. One subject did not return for follow-up after discharge. Two subjects withdrew prior to the Month 6 visit and an additional four subjects discontinued the study prior to the Month 12 visit. None of the subjects were discontinued for safety reasons. Six additional subjects missed the Month 12 visit.

A detailed breakdown of the VIRTUS pivotal subjects available at each visit and the subjects who missed each visit is presented in **Figure 2**. A detailed breakdown of the evaluable imaging for the VIRTUS pivotal subjects is presented in **Table 11**.

There were data integrity issues at one US center, affecting 24 subjects. Primary patency and safety results for these subjects are included in the primary analyses; however, survey data (VCSS, CIVIQ, VAS) are not included. Primary patency was assessed via venogram by an independent core lab and as such, patency results for this center were determined to be unlikely to be affected by the data integrity issues and are included in the primary effectiveness endpoint analysis. To ensure safety events were verified and comprehensively captured, a full review of the institution's electronic medical records was completed. A detailed review of electronic medical records from surrounding institutions was also completed by sponsor and CRO personnel. Adverse event data was verified for all 24 subjects either via electronic medical record review or documented contact with the subject. Survey data was not able to be verified and is not included in the analyses. FDA performed an inspection to audit the study data and to verify the results of the medical record review.



*Six subjects missed the 12 Month follow-up visit.

Figure 2: Subject Accountability – Pivotal Cohort

Table 11: Core Lab Imaging – Evaluability for Month 12 Primary Patency Analyses – Pivotal Cohort

Month 12 Imaging[1]	**Subject Count (N = 157)**
Venogram[2]	118
Duplex Ultrasound (DUS)	126
Intravascular Ultrasound (IVUS)	113
Any Imaging (Venogram, DUS and/or IVUS)	147

[1]TVR status is not taken into consideration when determining evaluability of imaging
[2]Pre-specified imaging modality for the Primary Effectiveness Endpoint

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for the type of study performed in the US and EU for this condition. The mean ± SD subject age was 54.4 ± 16.2 years with a range of 20 to 88 years old for the VIRTUS pivotal cohort. The majority of subjects were white, 127/170 (74.7%), and female, 96/170 (56.5%). A large majority of subjects, 145/170 (85.3%), had venous disease in their left leg and, of the remaining subjects, 24/170 (14.1%) had venous disease in their right leg and 1/170 (0.6%) had bilateral venous disease. Four subjects (4/170, 2.4%) were assessed as either CEAP Class 0, 1 or 2. The majority of subjects were assessed as either CEAP Class 3 (45/170, 26.5%) or Class 4 (78/170, 45.9%). Twenty-two subjects (22/170, 12.9%) were classified as CEAP Class 5 and 21 subjects (21/170, 12.4%) were classified as CEAP Class 6. Fifteen subjects (15/146, 10.3%) had VCSS leg pain reported as "Absent", 35/146 subjects (24.0%) had VCSS leg pain reported as "Mild", 54/146 subjects (37.0%) had VCSS leg pain reported as "Moderate" and 42/146 subjects (28.8%) had VCSS leg pain reported as "Severe".

Table 12 provides a summary of the demographics and baseline characteristics for the pivotal cohort of the VIRTUS study. **Table 13** provides a summary of the VIRTUS pivotal cohort's medical history.

Table 12: Demographics and Baseline Characteristics – Pivotal Cohort

Subject Demographic and Baseline Characteristics	Statistic	Results
Age, years	N	170
	median [Q1, Q3]	56 [41, 66]
	mean ± SD	54.4 ± 16.2
	(min, max)	(20, 88)
Sex:		
Male	n/N (%)	74/170 (43.5%)
Female	n/N (%)	96/170 (56.5%)
Race:		
American Indian or Alaska Native	n/N (%)	1/170 (0.6%)
Asian	n/N (%)	5/170 (2.9%)
Black or African American	n/N (%)	20/170 (11.8%)
Native Hawaiian or Pacific Islander	n/N (%)	1/170 (0.6%)
White	n/N (%)	127/170 (74.7%)
White African	n/N (%)	1/170 (0.6%)
Latin American	n/N (%)	1/170 (0.6%)
Not Answered	n/N (%)	14/170 (8.2%)
Ethnicity:*		
Hispanic or Latino	n/N (%)	13/154 (8.4%)
Not Hispanic or Latino	n/N (%)	141/154 (91.6%)
Chronic non-malignant obstruction present in:		
Left Leg	n/N (%)	145/170 (85.3%)
Right Leg	n/N (%)	24/170 (14.1%)

Subject Demographic and Baseline Characteristics	Statistic	Results
Both Legs	n/N (%)	1/170 (0.6%)
CEAP Assessment:		
0 (No visible or palpable signs of venous disease, only symptoms)	n/N (%)	2/170 (1.2%)
1 (Telangiectasia or reticular veins)	n/N (%)	0/170 (-)
2 (Varicose Veins)	n/N (%)	2/170 (1.2%)
3 (Edema)	n/N (%)	45/170 (26.5%)
4 (Skin changes ascribed to venous disease (e.g. pigmentation, venous eczema, lipodermatosclerosis))	n/N (%)	78/170 (45.9%)
5 (Skin changes as defined above with healed ulceration)	n/N (%)	22/170 (12.9%)
6 (Skin changes as defined above with active ulceration)	n/N (%)	21/170 (12.4%)
VCSS Leg Pain (Target Limb):†		
Absent	n/N (%)	15/146 (10.3%)
Mild	n/N (%)	35/146 (24.0%)
Moderate	n/N (%)	54/146 (37.0%)
Severe	n/N (%)	42/146 (28.8%)

* Sixteen subjects from Sites 40 and 41 did not provide their ethnicity per the policy at each site.
† Results for 24 subjects from a single US center are not included. Please refer to section B for more details.

Table 13: Medical History – Pivotal Cohort

Medical History	Subject Count n/N (%)
Diabetic	29/170 (17.1%)
Smoking History:	
Current Smoker	21/170 (12.4%)
Former Smoker	41/170 (24.1%)
Non-Smoker	108/170 (63.5%)
History of:	
Thromboembolic Disease	130/170 (76.5%)
Pulmonary Embolism	28/130 (21.5%)
Deep Vein Thrombosis	119/130 (91.5%)
CAD	14/170 (8.2%)
MI within past 5 years	1/170 (0.60%)
CABG	4/170 (2.4%)
PTCA/Stent	4/170 (2.4%)
CHF	4/170 (2.4%)
HTN	68/170 (40.0%)
Hepatic Disease	5/170 (2.9%)
Renal Disease	8/170 (4.7%)
PVD	29/170 (17.1%)
Coagulation Disorder	23/170 (13.5%)
CVA	10/170 (5.9%)
Cancer	18/170 (10.6%)
Recent Trauma	3/170 (1.78%)
Allergies	60/170 (35.3%)

D. Procedural Parameters

The VICI stent was successfully implanted in all 170 VIRTUS pivotal cohort subjects. **Table** 14 summarizes the VICI stent implant procedure parameters. The VICI stent implant procedure was performed using intravenous sedation for the majority of subjects, 109/170 (64.1%), and general anesthesia for the remaining subjects. Nearly all procedures, 166/170 (97.6%), were performed using an ipsilateral anterograde approach with access obtained using the femoral vein in 148/170 (87.1%). Pre-dilatation was performed in 109/170 (64.1%) of the cases and post-dilatation was performed in 154/170 (90.6%) of the cases. One VICI stent was placed in 85/170 (50%) of the cases, two VICI stents were placed in 62/170 (36.5%) of the cases, three VICI stents were placed in 20/170 (11.8%) of the cases and four VICI stents were placed in 3/170 (1.8%) of the cases.

Table 14: Implant Procedure Parameters – Pivotal Cohort

Parameter	Category	n/N (%)
Sedation Type	IV Sedation	109/170 (64.1%)
	General	61/170 (35.9%)
Puncture Type	Ipsilateral Anterograde	166/170 (97.6%)
	Contralateral Retrograde/Crossover	4/170 (2.4%)
Access Approach	Femoral	148/170 (87.1%)
	Popliteal	15/170 (8.8%)
	Jugular	4/170 (2.4%)
	Both	3/170 (1.8%)
Dilatation	Pre-Implant	109/170 (64.1%)
	Post-Implant	154/170 (90.6%)
Number of VICI Stents Placed Per Subject	1 stent	85/170 (50%)
	2 stents	62/170 (36.5%)
	3 stents	20/170 (11.8%)
	4 stents	3/170 (1.8%)

Table 15 provides a summary of the VICI stent sizes that were implanted per subject and the sizes of the VICI stents implanted for the pivotal cohort of the VIRTUS study. A total of 281 VICI stents were implanted in 170 subjects in the VIRTUS pivotal cohort.

Table 15: VICI Stent Sizes Utilized – Pivotal Cohort

Diameter	Length		
	60mm	90mm	120mm
12mm	3	2	4
14mm	10	26	44
16mm	29	43	120

E. Safety and Effectiveness Results

1. Safety Results

The analysis of the primary safety endpoint for this study was based on a composite endpoint of any Major Adverse Event within 30 days, as adjudicated by a Clinical Events Committee (CEC), including the following:

- Device or procedure-related death;

- 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 outside of the target vein segment;
- Clinically significant pulmonary embolism defined as being symptomatic with chest pain, hemoptysis, dyspnea, hypoxia etc. AND be documented on CT; or
- Embolization of stent.

Safety data through 30 days post-procedure were available for 169/170 of the VIRTUS pivotal subjects. One subject never returned for follow-up after discharge.

The status of the safety events was determined by adjudication of the VIRTUS CEC. There were 2 adjudicated MAEs for the pivotal cohort within 30 days. **Table 16** provides the MAE criteria and provides the proportion of pivotal cohort subjects that failed each defined criterion. Both of the MAEs observed (arteriovenous fistulas at the access site) failed the criterion of an arterial or venous injury requiring surgical or endovascular intervention. There were no failures for any other MAE criterion.

The estimated rate free from MAE in this study was 167/169 (98.8%) with a 95% two-sided exact confidence limit of 95.8% to 99.9%. Since the lower confidence limit lies above the safety performance goal of 94%, the primary safety endpoint has been successfully demonstrated for the primary safety objective of the study.

Table 16: Summary of Major Adverse Events – Pivotal Cohort

MAE Criteria	Failures n/N (%) [95% CI]
Major adverse events (MAE) within 30 days*	2/169 (1.2%) [95.8%, 99.9%]
Device or procedure-relate death	0/169 (0%)
Device or procedure-related bleeding requiring surgical or endovascular intervention or blood transfusion ≥ 2 units	0/169 (0%)
Device or procedure-related arterial or venous injury requiring surgical or endovascular intervention	2/169 (1.2%)
Device or procedure-related acute DVT outside the target vein segment	0/169 (0%)
Clinically significant pulmonary embolism	0/169 (0%)
Embolization within stent	0/169 (0%)

*Safety data through 30 days post-procedure were available for 169/170 of the VIRTUS pivotal subjects as one subject never returned for follow-up after discharge.

There were no deaths or CEC-adjudicated UADEs reported in the VIRTUS study through the Month 12 follow-up.

Access Site Related Adverse Events: In the VIRTUS study, there were 13 adverse events in 12 subjects that were related to the access site, either during the index procedure or for a follow-up procedure. The overall access site-related adverse event rate was 7% (12/170). The type of reported access site events was within expectation, with hematoma with and without pseudoaneurysm being the most common access site event.

The site reported Serious Adverse Events (SAEs) from the VIRTUS pivotal cohort are summarized in **Table 17** by MedDRA System Organ Class (SOC) and Preferred Term. The site reported Adverse Events (AEs) that are device or procedure related are summarized in
Table 18**.**

Table 17: Rates of Site-Reported Serious Adverse Events to 425 Days Intent-to-Treat, All Subjects (N=170)

MedDRA System Organ Classification	Rate of Subjects with Event n (%) [95% CI]
SOC: Blood and lymphatic system disorders (Events=5)	4 (2.4%) [0.6%;5.9%]
Anaemia (Events=1)	1 (0.6%) [0.0%;3.2%]
Sickle cell anaemia with crisis (Events=1)	1 (0.6%) [0.0%;3.2%]
Thrombocytopenia (Events=1)	1 (0.6%) [0.0%;3.2%]
Haemorrhagic anaemia (Events=1)	1 (0.6%) [0.0%;3.2%]
White blood cell disorder (Events=1)	1 (0.6%) [0.0%;3.2%]
SOC: Cardiac disorders (Events=9)	7 (4.1%) [1.7%;8.3%]
Acute myocardial infarction (Events=2)	2 (1.2%) [0.1%;4.2%]
Bradycardia (Events=1)	1 (0.6%) [0.0%;3.2%]
Cardiac failure congestive (Events=1)	1 (0.6%) [0.0%;3.2%]
Pericardial effusion (Events=1)	1 (0.6%) [0.0%;3.2%]
Ventricular tachycardia (Events=1)	1 (0.6%) [0.0%;3.2%]
Atrial fibrillation (Events=3)	1 (0.6%) [0.0%;3.2%]
SOC: Gastrointestinal disorders (Events=4)	3 (1.8%) [0.4%;5.1%]
Gastric perforation (Events=1)	1 (0.6%) [0.0%;3.2%]
Ileus (Events=1)	1 (0.6%) [0.0%;3.2%]
Melaena (Events=1)	1 (0.6%) [0.0%;3.2%]
Rectal haemorrhage (Events=1)	1 (0.6%) [0.0%;3.2%]
SOC: General disorders and administration site conditions (Events=24)	18 (10.6%) [6.4%;16.2%]
Vascular stent thrombosis (Events=13)	9 (5.3%) [2.4%;9.8%]
Vascular stent restenosis (Events=3)	3 (1.8%) [0.4%;5.1%]
Vascular stent occlusion (Events=2)	2 (1.2%) [0.1%;4.2%]
Vascular stent stenosis (Events=2)	2 (1.2%) [0.1%;4.2%]
Oedema peripheral (Events=1)	1 (0.6%) [0.0%;3.2%]
Peripheral swelling (Events=1)	1 (0.6%) [0.0%;3.2%]
Puncture site haemorrhage (Events=1)	1 (0.6%) [0.0%;3.2%]
Stenosis (Events=1)	1 (0.6%) [0.0%;3.2%]
SOC: Infections and infestations (Events=6)	5 (2.9%) [1.0%;6.7%]
Sepsis (Events=3)	3 (1.8%) [0.4%;5.1%]

MedDRA System Organ Classification	Rate of Subjects with Event n (%) [95% CI]
Cellulitis (Events=1)	1 (0.6%) [0.0%;3.2%]
Parotitis (Events=1)	1 (0.6%) [0.0%;3.2%]
Urinary tract infection (Events=1)	1 (0.6%) [0.0%;3.2%]
SOC: Injury, poisoning and procedural complications (Events=4)	4 (2.4%) [0.6%;5.9%]
Hip fracture (Events=1)	1 (0.6%) [0.0%;3.2%]
Wound (Events=1)	1 (0.6%) [0.0%;3.2%]
Post procedural haematoma (Events=1)	1 (0.6%) [0.0%;3.2%]
Delayed haemolytic transfusion reaction (Events=1)	1 (0.6%) [0.0%;3.2%]
SOC: Investigations (Events=3)	2 (1.2%) [0.1%;4.2%]
Blood culture positive (Events=1)	1 (0.6%) [0.0%;3.2%]
Haemoglobin decreased (Events=1)	1 (0.6%) [0.0%;3.2%]
Specific gravity urine abnormal (Events=1)	1 (0.6%) [0.0%;3.2%]
SOC: Metabolism and nutrition disorders (Events=1)	1 (0.6%) [0.0%;3.2%]
Diabetic ketoacidosis (Events=1)	1 (0.6%) [0.0%;3.2%]
SOC: Musculoskeletal and connective tissue disorders (Events=7)	7 (4.1%) [1.7%;8.3%]
Back pain (Events=3)	3 (1.8%) [0.4%;5.1%]
Pain in extremity (Events=2)	2 (1.2%) [0.1%;4.2%]
Arthralgia (Events=1)	1 (0.6%) [0.0%;3.2%]
Rhabdomyolysis (Events=1)	1 (0.6%) [0.0%;3.2%]
SOC: Nervous system disorders (Events=7)	4 (2.4%) [0.6%;5.9%]
Seizure (Events=2)	2 (1.2%) [0.1%;4.2%]
Cerebral haemorrhage (Events=1)	1 (0.6%) [0.0%;3.2%]
Cerebrovascular accident (Events=1)	1 (0.6%) [0.0%;3.2%]
Encephalopathy (Events=1)	1 (0.6%) [0.0%;3.2%]
Sciatica (Events=1)	1 (0.6%) [0.0%;3.2%]
Encephalomalacia (Events=1)	1 (0.6%) [0.0%;3.2%]
SOC: Psychiatric disorders (Events=1)	1 (0.6%) [0.0%;3.2%]
Mental status changes (Events=1)	1 (0.6%) [0.0%;3.2%]
SOC: Renal and urinary disorders (Events=3)	2 (1.2%) [0.1%;4.2%]
Acute kidney injury (Events=2)	2 (1.2%) [0.1%;4.2%]
Chronic kidney disease (Events=1)	1 (0.6%) [0.0%;3.2%]
SOC: Respiratory, thoracic and mediastinal disorders (Events=4)	4 (2.4%) [0.6%;5.9%]
Pulmonary embolism (Events=2)	2 (1.2%) [0.1%;4.2%]
Respiratory depression (Events=1)	1 (0.6%) [0.0%;3.2%]
Respiratory failure (Events=1)	1 (0.6%) [0.0%;3.2%]
SOC: Skin and subcutaneous tissue disorders (Events=2)	2 (1.2%) [0.1%;4.2%]
Skin ulcer (Events=2)	2 (1.2%) [0.1%;4.2%]
SOC: Surgical and medical procedures (Events=27)	19 (11.2%) [6.9%;16.9%]
Venous angioplasty (Events=8)	7 (4.1%) [1.7%;8.3%]
Thrombolysis (Events=4)	4 (2.4%) [0.6%;5.9%]
Varicose vein operation (Events=4)	4 (2.4%) [0.6%;5.9%]
Vascular stent insertion (Events=2)	2 (1.2%) [0.1%;4.2%]
Angioplasty (Events=1)	1 (0.6%) [0.0%;3.2%]
Cholecystectomy (Events=1)	1 (0.6%) [0.0%;3.2%]

MedDRA System Organ Classification	Rate of Subjects with Event n (%) [95% CI]
Hip arthroplasty (Events=1)	1 (0.6%) [0.0%;3.2%]
Myomectomy (Events=1)	1 (0.6%) [0.0%;3.2%]
Thrombectomy (Events=1)	1 (0.6%) [0.0%;3.2%]
Hernia repair (Events=1)	1 (0.6%) [0.0%;3.2%]
Venous stent insertion (Events=1)	1 (0.6%) [0.0%;3.2%]
Transfusion (Events=1)	1 (0.6%) [0.0%;3.2%]
Interventional procedure (Events=1)	1 (0.6%) [0.0%;3.2%]
SOC: Vascular disorders (Events=26)	19 (11.2%) [6.9%;16.9%]
Deep vein thrombosis (Events=12)	8 (4.7%) [2.1%;9.1%]
Arteriovenous fistula (Events=2)	2 (1.2%) [0.1%;4.2%]
Aortic aneurysm (Events=1)	1 (0.6%) [0.0%;3.2%]
Varicose ulceration (Events=1)	1 (0.6%) [0.0%;3.2%]
Varicose vein (Events=1)	1 (0.6%) [0.0%;3.2%]
Vena cava thrombosis (Events=1)	1 (0.6%) [0.0%;3.2%]
Venous thrombosis (Events=1)	1 (0.6%) [0.0%;3.2%]
Venous stenosis (Events=1)	1 (0.6%) [0.0%;3.2%]
Paget-Schroetter syndrome (Events=1)	1 (0.6%) [0.0%;3.2%]
Venous occlusion (Events=1)	1 (0.6%) [0.0%;3.2%]
Vascular compression (Events=1)	1 (0.6%) [0.0%;3.2%]
Peripheral venous disease (Events=1)	1 (0.6%) [0.0%;3.2%]
Phlebitis (Events=2)	1 (0.6%) [0.0%;3.2%]
SOC: Product issues (Events=6)	6 (3.5%) [1.3%;7.5%]
Device dislocation (Events=3)	3 (1.8%) [0.4%;5.1%]
Stent malfunction (Events=2)	2 (1.2%) [0.1%;4.2%]
Device occlusion (Events=1)	1 (0.6%) [0.0%;3.2%]

Table 18: Rates of Site-Reported Device or Procedure Related Adverse Events to 425 Days Intent-to-Treat, All Subjects (N=170)

MedDRA System Organ Classification	Rate of Subjects with Event n (%) [95% CI]
SOC: General disorders and administration site conditions (Events = 16)	15 (8.8%) [5.0%; 14.1%]
Vascular stent thrombosis (Events = 4)	4 (2.4%) [0.6%; 5.9%]
Peripheral swelling (Events = 4)	4 (2.4%) [0.6%; 5.9%]
Vascular stent occlusion (Events = 3)	3 (1.8%) [0.4%;5.1%]
Puncture site hemorrhage (Events = 1)	1 (0.6%) [0.0%; 3.2%]
Vascular stent stenosis (Events = 2)	2 (1.2%) [0.1%; 4.2%]
Localized oedema (Events = 1)	1 (0.6%) [0.0%; 3.2%]
Vascular stent restenosis (Events = 1)	1 (0.6%) [0.0%; 3.2%]
SOC: Injury, poisoning and procedural complications (Events = 4)	4 (2.4%) [0.6%; 5.9%]
Fall (Events = 1)	1 (0.6%) [0.0%; 3.2%]
Post procedural constipation (Events = 1)	1 (0.6%) [0.0%; 3.2%]
Vascular access site hemorrhage (Events = 1)	1 (0.6%) [0.0%; 3.2%]
Vascular access site pain (Events = 1)	1 (0.6%) [0.0%; 3.2%]
SOC: Investigations (Events = 2)	1 (0.6%) [0.0%; 3.2%]

MedDRA System Organ Classification	Rate of Subjects with Event n (%) [95% CI]
Blood creatinine increased (Events = 1)	1 (0.6%) [0.0%; 3.2%]
Oxygen saturation decreased (Events = 1)	1 (0.6%) [0.0%; 3.2%]
SOC: Metabolism and nutrition disorders (Events = 2)	2 (1.2%) [0.1%; 4.2%]
Dehydration (Events = 1)	1 (0.6%) [0.0%; 3.2%]
Hyperglycemia (Events = 1)	1 (0.6%) [0.0%; 3.2%]
SOC: Musculoskeletal and connective tissue disorders (Events = 17)	14 (8.2%) [4.6%;13.4%]
Back pain (Events = 11)	10 (5.9%) [2.9%;10.6%]
Pain in extremity (Events = 3)	3 (1.8%) [0.4%;5.1%]
Arthralgia (Events = 1)	1 (0.6%) [0.0%;3.2%]
Groin pain (Events = 1)	1 (0.6%) [0.0%;3.2%]
Musculoskeletal chest pain (Events = 1)	1 (0.6%) [0.0%;3.2%]
SOC: Psychiatric disorders (Events = 1)	1 (0.6%) [0.0%; 3.2%]
Drug use disorder (Events = 1)	1 (0.6%) [0.0%; 3.2%]
SOC: Renal and urinary disorders (Events = 1)	1 (0.6%) [0.0%; 3.2%]
Acute kidney injury (Events = 1)	1 (0.6%) [0.0%; 3.2%]
SOC: Reproductive system and breast disorders (Events = 1)	1 (0.6%) [0.0%; 3.2%]
Scrotal pain (Events = 1)	1 (0.6%) [0.0%; 3.2%]
SOC: Surgical and medical procedures (Events = 4)	4 (2.4%) [0.6%; 5.9%]
Thrombolysis (Events = 1)	1 (0.6%) [0.0%; 3.2%]
Varicose vein operation (Events = 1)	1 (0.6%) [0.0%; 3.2%]
Vascular stent insertion (Events = 1)	1 (0.6%) [0.0%; 3.2%]
Venous stent insertion (Events = 1)	1 (0.6%) [0.0%; 3.2%]
SOC: Vascular disorders (Events = 8)	8 (4.7%) [2.1%; 9.1%]
Hematoma (Events = 2)	2 (1.2%) [0.1%;4.2%]
Deep vein thrombosis (Events = 2)	2 (1.2%) [0.1%; 4.2%]
Hypotension (Events = 1)	1 (0.6%) [0.0%; 3.2%]
Peripheral coldness (Events = 1)	1 (0.6%) [0.0%; 3.2%]
Hemorrhage (Events = 1)	1 (0.6%) [0.0%; 3.2%]
Peripheral venous disease (Events = 1)	1 (0.6%) [0.0%; 3.2%]
SOC: Product issues (Events = 2)	2 (1.2%) [0.1%; 4.2%]
Device dislocation (Events = 1)	1 (0.6%) [0.0%; 3.2%]
Stent malfunction (Events = 1)	1 (0.6%) [0.0%; 3.2%]

Stent Fractures

A total of 10 subjects (10/170 = 5.9%) had stent fractures as confirmed by the independent X-Ray Core Laboratory. The overall stent fracture rate was 10/281 (3.6%) for the total number of implanted stents. There was one Type I fracture, eight Type II fractures, and one Type IV fracture. The fractures did not appear to have an impact on patency, as the fractured stents for all ten subjects were patent at the Month 12 visit. None of the subjects experienced symptoms that were related to their stent fractures and no interventions were required as a result of the stent fractures. Nine of the ten fractures occurred in the common femoral vein of PT subjects and one fracture occurred in the common iliac vein of an NT subject. None of the fractures occurred within overlapped areas of the stents.

2. Effectiveness Results

The primary effectiveness endpoint was the primary patency rate at 12 months post-intervention, defined as freedom from occlusion by thrombosis (assessed via venogram) and freedom from surgical or endovascular intervention on target vessel which are found to have re-stenosis or stent occlusion to maintain patency and freedom from in-stent stenosis more than 50% by venogram.

Among the 170 pivotal subjects, 125 had a known patency outcome, 99 in the PT sub-population and 26 in the NT sub-population. Sixteen (16) subjects had a qualifying Target Vessel Revascularization (TVR), as adjudicated by the VIRTUS Clinical Events Committee (CEC). Seventy-nine (79) subjects had a venogram result within the Month 12 window assessed by the Venography Core Laboratory. Thirty (30) subjects were missing the result for their Month 12 venogram but had a venogram demonstrating patency as assessed by the Venography Core Laboratory that was beyond the upper limit of the Month 12 visit window.

There were 45 subjects (28 PT,17 NT) that did not have a known patency outcome at Month 12. Among the 45 subjects, seven withdrew prior to Month 12, four missed the Month 12 Visit, and 34 did not have venography at Month 12 Visit but remained in the study These 45 subjects had their patency status imputed as described in the Statistical Analysis Report. The imputation was performed 15 times and the results were compared to the primary effectiveness Performance Goal of 72.1% that had been previously established, as described below.

Primary Effectiveness Endpoint – Intent-to-Treat (ITT) Population

The results of the primary effectiveness analysis in the ITT population, defined as all subjects who had the VICI VENOUS STENT Delivery System enter the venous system, regardless of whether the stent was delivered to the target lesion or deployed, is provided in **Table 19**. The analysis was based on 125 subjects with observed and 45 subjects with imputed venogram outcomes at 12 months post intervention. The combined p-value of the comparisons to the primary effectiveness performance goal is <0.0001, which is less than the study specified α level for success of 0.025. Therefore, the primary effectiveness endpoint for the study was successfully achieved.

Table 19: Primary Effectiveness Analysis – Pivotal ITT Cohort (N=170)

Proportion of Subjects at Month 12	Combined SE	t-statistic	p-value
84.0%	2.8%	4.0	<0.0001

Primary Effectiveness Endpoint – Completed Cases (CC) Population

The primary endpoint was also analyzed for the 125 of the 170 subjects with a known patency outcome at Month 12, i.e., the Completed Cases (CC) population, with no imputation performed. Among the CC population, 104/125 (83.2%) of the subjects were patent at Month 12. Twenty (20) of the 99 PT subjects (20.2%) failed to demonstrate patency at Month 12. Of those 20 subjects, 16 (16.1%) had a qualifying

TVR within the first 12 months and 4 (4.0%) had greater than 50% stenosis on their Month 12 venogram. Only 1/26 NT subjects (3.8%) failed to demonstrate patency at Month 12 with greater than 50% stenosis on their Month 12 venogram. The CC effectiveness results at Month 12 are presented in **Table 20**.

Table 20: Completed Cases Effectiveness Analysis – Pivotal Cohort

Overall Success n/N (%)	NT Subject Success n/N (%)	PT Subject Success n/N (%)	Combined Success Proportion*	Combined SE	t-statistic	p-value
104/125 (83.2%)	25/26 (96.2%)	79/99 (79.8%)	83.9%	3.2%	3.72	0.0002

*Derived from a weighted average of the NT and PT populations.

Primary Patency Failures

There was a total of 21 pivotal cohort subjects who were primary effectiveness failures due to patency issues or qualifying TVRs. There were 16 subjects that had one or more qualifying TVRs within the first 12-months, as adjudicated by the CEC. An additional five subjects had greater than 50% stenosis, based on their Month 12 venogram assessment by the Venography Core Laboratory.

Additional Imaging Results (DUS and IVUS)

Per the VIRTUS protocol and the SAP, venography was the imaging modality used to determine patency at Month 12 for the primary effectiveness endpoint. Two additional imaging modalities were utilized as part of the VIRTUS study, duplex ultrasound (DUS) and intravascular ultrasound (IVUS). Both imaging modalities were performed at Month 12 and the images were assessed by independent Core Laboratories.

Although analyses of these additional imaging modalities were not pre-specified in the protocol or in the SAP, the primary patency endpoint was analyzed in a post-hoc fashion using additional data from the DUS and IVUS images following Core Laboratory adjudication. In addition, the IVUS images were also analyzed for the percentage area stenosis by the IVUS Core Laboratory. Since the definition of patency used for the primary effectiveness endpoint would not necessarily apply to the area of stenosis, these results at Month 12 are presented descriptively. These additional imaging analyses are being provided for informational and comparative purposes.

For subjects with an unknown patency outcome, the result beyond Day 425 was used to define the subject as a success if there was <50% stenosis and the subject had not had a prior qualifying TVR.

There were 133 subjects for whom their Month 12 patency outcome could be determined by DUS. The results for these subjects are provided in **Table 21**. The estimated patency rate based on DUS was 83.5% (combined success proportion), which is similar to the result for the Completed Cases as determined by venogram

(83.9%). The lower 95% confidence limit for the combined success proportion was 76.0%.

There were 120 subjects that had a patency outcome that could be determined by IVUS segment diameter. The results for these subjects are provided in **Table 21**. The estimated patency rate based on IVUS diameter was 80.1% (combined success proportion), which is similar to the result reported for the Completed Cases as determined by venogram (83.9%). The lower 95% confidence limit for the combined success proportion was 70.8%.

Table 21: Month 12 Patency Result Based on DUS and IVUS

Imaging Modality	Overall Success n/N (%)*	NT Subject Success n/N (%)	PT Subject Success n/N (%)
DUS[1]	111/133 (83.5%)	33/35 (94.3%)	78/98 (79.6%)
IVUS	95/120 (79.2%)	24/25 (96.0%)	71/95 (74.7%)

[1]Based on subjects with core lab evaluable DUS at or beyond the Month 12 interval or prior qualifying TVR as of November 1, 2018.
*Derived from a weighted average of the NT and PT populations.

IVUS Stenosis Result Based on Segment Areas

There were no pre-defined patency criteria based on the IVUS percent area stenosis computed by the IVUS Core Laboratory. Since patency by IVUS had not been defined, a descriptive summary of the IVUS percent area stenosis at Month 12 was computed. Subjects that had a qualifying TVR, as determined by the CEC, prior to Day 425 were excluded from this descriptive summary. For subjects without a qualifying TVR, the maximum percent area stenosis within the Month 12 window (Days 305 to 425) among the three segments, EIV, CIV and CFV, based on the IVUS Core Laboratory assessment was analyzed. If there was no result available within the Month 12 window, a percentage area stenosis beyond Day 425 was used for the analysis if available.

There were 106 subjects that had a Month 12 percentage stenosis area computed by the IVUS Core Laboratory. The results for these subjects are provided in **Table 22**. The mean (SD) maximum percentage stenosis at Month 12 based on the IVUS images is 35.6% (19.4%).

Table 22: Month 12 Maximum Percentage Stenosed Based on IVUS Areas

Parameter	Month 12 Stenosis
N	106
Mean (SD)	35.6% (19.4%)
Median (Min, Max)	32.5% (3.2%, 78.8%)
95% Confidence Interval	[31.9%; 39.3%]

3. Secondary Endpoints

Secondary Effectiveness Endpoint Analysis

The secondary effectiveness analysis is based on the change in the Venous Clinical Severity Score (VCSS) at Month 12 as compared to Baseline.

There were 132 subjects who had VCSS results at both Month 12 and Baseline. (Note that data from one US center, affecting 24 subjects, were specifically excluded because the information could not be verified as accurate.) A total of 65/132 (49.2%) subjects reported a reduction in VCSS at Month 12 of 50% or more, with 95% exact confidence interval of 40.4% to 58.1%. The lower limit of the 95% exact confidence interval falls below the stated performance goal of 50%; therefore, this endpoint was not met. Upon retrospective evaluation of the VIRTUS protocol, it appears that there was no statistical justification for this performance goal, and a sample size computation was not performed. Therefore, the performance goal was not appropriately defined in the original VIRTUS protocol.

Additional Effectiveness Analyses

This section provides the additional effectiveness analyses performed for the VIRTUS study. These analyses were not hypothesis driven and are presented descriptively.

Estimate Primary-Assisted Patency

Primary-assisted patency was defined as freedom from occlusion regardless of whether an intervention (subsequent to the index procedure) was performed. This endpoint also required a 12-month or later Venography Core Laboratory assessment, but a complete occlusion any time during the study was considered a failure. There were 126 subjects with either a Month 12 core lab assessed venogram within the Month 12 visit window, or 100% occlusion via core lab assessed venogram at any point during the first 12 months, or a Month 12 core lab assessed venogram that was after the Month 12 visit window but was < 100% stenosed. The rate of primary-assisted patency was 117/126 (92.9%).

Estimate Secondary Patency

Secondary patency was defined as freedom from “permanent” loss of patency determined through last follow-up (irrespective of the number of interventions). This endpoint also required a 12-month or later Venography Core Laboratory assessment. There were 121 subjects with either a Month 12 core lab assessed venogram in-window or Month 12 core lab assessed venogram that was after the Month 12 visit window but was < 100% stenosed. The rate of secondary patency was 119/121 (98.4%).

Procedure Technical Success

Procedural technical success is defined as any subject without a post procedural residual stenosis greater than 50% that had adequate stent overlap and with placement of the study device alone. This endpoint is based on the presence of a Venography Core Laboratory assessment of the post-procedural venogram. Four subjects did not have a post-procedural venographic image; therefore, procedure technical success was evaluated in 166 subjects. There were two subjects who failed procedure technical success due to the use of non-study stents. The number of subjects with procedural technical success was 164/166 (98.8%)

Lesion Success

Lesion success is defined as any subject without a post procedural residual stenosis greater than 50%. This endpoint is based on the presence of a Venography Core Laboratory assessment of the post-procedural venogram. Four subjects did not have a post-procedural venographic image; therefore, lesion success was evaluated in 166 subjects. The rate of lesion success was 166/166 (100%). The difference between procedural technical success and lesion success was the use of non-study stents, which was not considered a failure for lesion success.

Procedural Success

Procedural success is defined as any subject with procedural technical success without a MAE. As with the two analyses above, procedural success depends on the Venography Core Laboratory assessment of the post-procedure venogram. Four subjects did not have a post-procedural venographic image; therefore, procedural success was evaluated in 166 subjects. There were two subjects who failed procedural success due to the use of non-study stents (see procedural technical success) and two subjects who failed due to a MAE. Thus, the rate of procedural success was 162/166 (97.6%)

Late Technical Success

Late technical success is defined as subjects without a qualifying TVR as adjudicated by the VIRTUS CEC, a Month 12 restenosis greater than 50%, a stent compression or a stent fracture. Late technical success was evaluated at 12 months and the results were based on a 12-month (or later if demonstrating patency) venogram, a reintervention for complete occlusion prior to 12-months or an X-Ray Core Laboratory confirmed stent fracture. There were 127 subjects with a 12-month venogram and/or stent fracture assessment. There were 30 subjects who were considered to be a failure for late technical success. Sixteen (16) of these subjects had a qualifying TVR, 5 subjects were not considered patent at Month 12 and 9 subjects had a stent fracture. One subject who had a TVR also had a stent fracture; this subject is accounted for in the qualifying TVRs. The rate of late technical success was 97/127 (76.4%)

Change in the Quality of Life (CIVIQ-20)

The CIVIQ-20 results were analyzed as the change from Baseline at 12 months for the VIRTUS pivotal cohort. This instrument is scored from 20 to 100 points with lower scores indicating a lesser impact on health. **Table 23** provides the available CIVIQ-20 results from Baseline, 12-month and the 12-month change from Baseline.

Table 23: CIVIQ-20 Results – Pivotal Cohort

Visit	Parameter	CIVIQ-20 Global Score
Screen/Baseline	N	146*
	Mean ± SD	55.4 ± 19.40
	95% CI	[52.2; 58.5]
	Median (Min, Max)	53 (20, 98)
Month 12	N	133†
	Mean ± SD	41.7 ± 20.05
	95% CI	[38.3; 45.2]
	Median (Min, Max)	35 (20, 98)
Month 12 Change from Screen/Baseline	N	133†
	Mean ± SD	-13.1 ± 18.56
	95% CI	[-16.3; -10.0]
	Median (Min, Max)	-12 (-72, 32)

* Results for 24 subjects from a single US center are not included. Please refer to section B for more details.
† In addition to the above data that is not included, 11 subjects did not have a Month 12 visit and 2 subjects did not complete the CIVIQ forms.

In addition to the summary of the results, a summary of the responders, where a decrease of nine (9) or more is considered a responder, was also performed. Seventy-seven (77) of the 133 subjects with Month 12 results had a decrease in score of 9 or more, indicating that over 57% (57.9%) of the subjects treated in the VIRTUS pivotal cohort had a clinically significant improvement in their quality of life.

4. Subgroup Analyses

The primary effectiveness endpoint was evaluated for differences by gender. There was no significant difference in patency rates between genders.

Table 24: Primary Patency by Gender

Gender	Patent	Not Patent	p-value[a]
Female	57/66 (86.36%)	9/66 (13.64%)	0.3467
Male	47/59 (79.66%)	12/59 (20.34%	
Total	104	21	

[a] Two-sided Fisher's exact test

5. Pediatric Extrapolation

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

F. 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 pivotal clinical trial included 27 Principal Investigators (48 sub-investigators) none of which were full-time or part-time employees of the sponsor and 2 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: 2
- 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. An initial analysis was conducted which did 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 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.

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 3 years.

The VIRTUS study was conducted as a prospective, global, multi-center single-arm trial designed to evaluate the VICI VENOUS STENT for the treatment of symptomatic iliofemoral venous outflow obstruction. The primary effectiveness endpoint was primary patency at 12 months, as defined as defined as freedom from occlusion (assessed via venogram) by thrombosis and freedom from surgical or endovascular intervention on target vessel which are found to have re-stenosis or stent occlusion to maintain patency and freedom from in-stent stenosis more than 50% by venogram. At Month 12, the VICI VENOUS STENT had an estimated patency rate of 84% based on venography in evaluable patients. This result met the effectiveness performance goal of 72.1%, $p<0.0001$, which was derived from the literature for previous studies of iliofemoral stenting for chronic venous obstruction. Further, the Completed Cases cohort (N=125) demonstrated a combined, weighted 12-month patency of 83.9%, consistent with the ITT primary patency analysis. In the Completed Cases cohort, the 12-month patency rate for the PT etiology (N=99) was 78.9% and the 12-month patency for the NT etiology (N=26) was 96.2%. Analyses were also performed to assess the Month 12 patency of the VICI stent using additional imaging modalities. At Month 12, the overall patency rate was 83.5% as assessed by DUS in 133 evaluable subjects, and 79.2% as assessed by IVUS in 120 evaluable subjects. In total, 147 subjects had some form of core lab-adjudicated imaging available to assess the Month 12 primary patency of the VICI stent and the supplementary imaging analyses supported the patency of the stent at Month 12. The secondary endpoint of at least a 50% reduction in VCSS was not successfully met (N=132).

B. Safety Conclusions

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

In the VIRTUS clinical study, the primary safety endpoint was based on a composite endpoint of any Major Adverse Event within 30 days, as adjudicated by the CEC. The proportion of subjects with freedom from a Major Adverse Event was 167/169 (98.8%) with a lower limit of the exact 95% confidence interval of 95.8%. The safety performance goal was 94%; therefore, the primary safety endpoint was met. There were no deaths or CEC-adjudicated UADEs reported in the VIRTUS study through the Month 12 follow-up. There were ten stent fractures in the VIRTUS study through the Month 12 follow-up with no associated clinical sequelae or safety events.

C. Benefit-Risk Conclusion

The probable benefits of the device are based on data collected in the clinical study conducted to support PMA approval, as described above. The probable benefits of the VICI VENOUS STENT System include improving or restoring blood flow in patients with iliofemoral venous disease to improve the patient symptoms and quality of life.

The probable risks of the device are also based on data collected in the clinical study conducted to support PMA approval, as described above, and the frequency and types of the adverse events reported throughout the pivotal clinical study 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.

1. Patient Perspectives

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

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 of the VIRTUS trial show that the VICI VENOUS STENT System provides clinical benefits that are better than what has been reported for comparable patients 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 5/02/2019. The final conditions of approval cited in the approval order are described below.

Post-Approval Study – VIRTUS Continued Follow-Up Study. This study should be conducted per protocol STE-HUM-007P, Rev C (dated November 6, 2015). This study is a prospective, multi-center follow-up of the VIRTUS pivotal study (G140016) that treated 170 subjects from 22 investigational sites. It will evaluate the long-term safety and effectiveness of the VICI VENOUS STENT System. All 163 remaining subjects (7 subjects have discontinued the study), active at the end of the 12-month evaluation, will continue to be followed annually through at least 36 months. The primary endpoint to be assessed is primary patency by duplex ultrasound (DUS) at 36 months, as defined by the protocol. The secondary endpoints to be assessed include the following:

1. Overall rate and incidence of type of major adverse events from Day 0 through completion of Study follow-up at Month 36.
2. Overall rate and incidence of type of serious adverse events from Day 0 through completion of Study follow-up at Month 36.
3. Freedom from target vessel revascularization (TVR) at Month 24 and Month 36, defined as freedom from any re-intervention in the target vessel segment and freedom from thrombosis/stenosis > 50% as measured by DUS.
4. Primary assisted stent patency rate: determined at Month 24 and Month 36, defined patency as regardless of whether an intervention (subsequent to the index procedure) was performed to maintain patency.
5. Secondary stent patency rate: determined at Month 24 and Month 36, defined as freedom from permanent loss of patency determined through last follow-up (regardless of the number of interventions).

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.