SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Covered stent vascular connector, hemodialysis access circuit
Device Trade Name:	EndoForce™ Connector for Endovascular Venous Anastomosis
Device Procode:	SEQ
Applicant's Name and Address:	Phraxis Inc. 333 Hennepin Ave E Minneapolis, MN 55114
Date(s) of Panel Recommendation:	None
Premarket Approval Application Number (PMA) Number:	P240004
Date of FDA Notice of Approval:	May 15, 2025

II. INDICATIONS FOR USE

The EndoForce™ Connector for Endovascular Venous Anastomosis is indicated to provide an endovascular method for attachment of an arteriovenous graft to a vein in the upper arm in patients with end stage renal disease requiring hemodialysis. The EndoForce™ Connector is used together with conventional suturing of the graft to the artery during the implantation procedure. The graft is then used for vascular access during hemodialysis.

III. CONTRAINDICATIONS

The EndoForce™ Connector for Endovascular Venous Anastomosis is contraindicated in:

- Patients who have an allergy or hypersensitivity to nickel, titanium or ePTFE.
- Patients who have an allergy or sensitivity to contrast dye that cannot be adequately premedicated.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the EndoForce™ Connector for Endovascular Venous Anastomosis labeling.

V. DEVICE DESCRIPTION

The EndoForce™ Connector for Endovascular Venous Anastomosis (herein referred to as the EndoForce™ System) includes an implantable component, the EndoForce™ Connector, and a delivery system, the EndoForce™ Connector Delivery System. The EndoForce™ Connector is a venous anastomosis implant used in conjunction with a 6 mm inner diameter expanded polytetrafluoroethylene (ePTFE) arteriovenous graft (not provided). The graft is sutured to the artery using a conventional anastomosis. The graft, and not the EndoForce™ Connector, is to be used for vascular access during hemodialysis in patients with end stage renal disease. The EndoForce™ Connector is provided pre-loaded within the EndoForce™ Connector Delivery System.

EndoForce™ Connector (Implant)

The EndoForce™ Connector is a flexible, self-expanding endoprosthesis comprised of a nitinol framework encapsulated in ePTFE in the midsection and uncoated at the ends (**Figure 1**). The venous end is flared and includes 4 anchoring barbs that extend into the vein wall. The EndoForce™ Connector is deployed within a vein that is 4-7 mm in diameter at the venipuncture site. Upon deployment, the flared end allows for expansion of the EndoForce™ Connector up to 10 mm. Approximately 22 mm is implanted inside the vein and 40 mm inside the vascular access graft. A tacking suture is placed between the EndoForce™ Connector and the vascular access graft to further secure this connection.

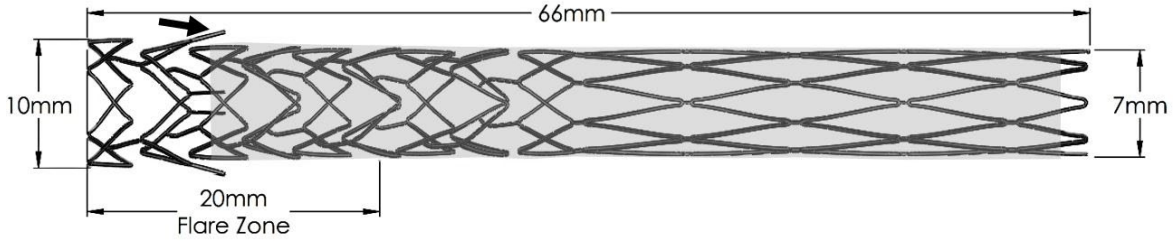


Figure 1: EndoForce™ Connector
Large arrow denotes 1 of the 4 total anchoring barbs at flared end.

EndoForce™ Connector Delivery System

The EndoForce™ Connector is provided pre-mounted and constrained within a sterile, single-use EndoForce™ Connector Delivery System for transcatheter over-the-wire delivery (**Figure 2**). The inner catheter (F) contains the guidewire lumen. The outer sheath (D) includes a radiopaque marker band (E) located 3mm from the tip that is used as a visual reference while advancing the EndoForce™ Connector

Delivery System to the target site in the vein. The outer sheath marker band is also observed during retraction of the sheath to deploy the EndoForce™ Connector and during removal of the EndoForce™ Connector Delivery System after completing deployment.

The distal catheter assembly (~12 cm, **Figure 2** inset) houses the EndoForce™ Connector (implant) that is compressed onto the inner catheter (J). A blue handle lock (B) prevents premature release of the EndoForce™ Connector. The safety lock must be removed prior to deployment. Radiopaque marker bands on the inner catheter (H and I) are used to guide positioning of the EndoForce™ Connector for deployment. To deploy the EndoForce™ Connector, the operator removes the handle lock (B), pins Y-adapter 1 (A), and slowly retracts Y-adapter 2 (C), which also retracts the outer sheath (D). The pusher rod (G) supports and maintains alignment of the EndoForce™ Connector during deployment.

The EndoForce™ Connector Delivery System has a working length of 23 cm and is compatible with an 11Fr introducer sheath and an 0.018" guide wire.

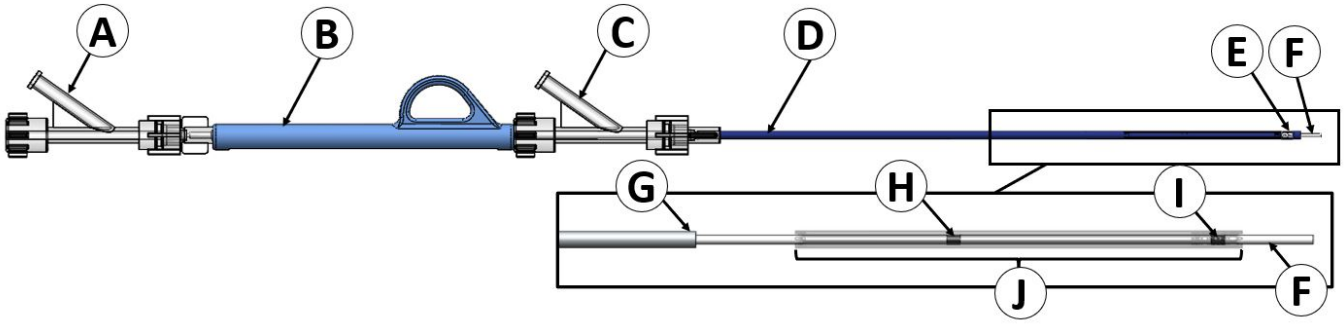


Figure 2: EndoForce™ Connector Delivery System
Top: A- Y-adapter 1 with hemostatic valve; B- handle lock; C- Y-adapter 2 with hemostatic valve; D- outer sheath; E-marker band on outer sheath; F- inner catheter. Figure 2 Inset (outer sheath has been removed to show underlying components): F- inner catheter; G- pusher rod; H- marker band 1 on inner catheter; I- marker band 2 on inner catheter; J- EndoForce™ Connector compressed within EndoForce™ Connector Delivery System.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

The alternative procedure for anastomosis of a vein to a graft is conventional suturing. Sutured vascular anastomoses have their own advantages and disadvantages. A patient should fully discuss the alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The EndoForce™ System has not been marketed in the United States or any foreign country.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

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

- Access circuit intervention
- Allergic reaction to nickel, titanium, ePTFE, contrast medium, anticoagulant and/or antithrombotic therapy
- Arm edema
- Bleeding complications and/or hemorrhage
- Death
- Embolism and/or vessel thrombosis
- Failure/malfunction of any component of the device that may lead to injury and/or need for surgical intervention including device compression, insufficient stent graft expansion, loss of permanent access, embolization, kinking, migration, misplacement, occlusion or thrombosis
- Fracture of the endoprosthesis that may or may not lead to embolism, serious injury or surgical intervention.
- Infection or fever, including device infection
- Inflammation
- Insufficient device expansion
- Ischemia
- New lesion or total occlusion of the vascular access circuit
- Numbness
- Pain
- Paresthesia
- Placement of bailout stent/stent graft
- Pruritus, stiffness or swelling of the implanted arm
- Serious injury requiring surgical intervention
- Steal Syndrome
- Venous spasm
- Vessel rupture
- Thrombosis
- Vessel or Arteriovenous Graft (AVG) injury (e.g., vessel spasm, stenosis, artery dissection, perforation, aneurysm or pseudoaneurysm), which may require surgical repair (conversion to open surgery)
- Wound site complications (e.g., bruising, edema, hematoma, erythema, seroma)

The EndoForce™ Connector is used in conjunction with a standard 6mm ePTFE vascular access graft. Potential complications that may occur with the use of any vascular graft are described in the manufacturer's Instructions for Use.

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

IX. SUMMARY OF NONCLINICAL STUDIES

Nonclinical studies were completed to evaluate the EndoForce™ System that included bench, biocompatibility, packaging and sterilization testing, and animal studies.

The EndoForce™ Connector was initially called the Venous InterGraft Connector. Nonclinical testing conducted on the Venous InterGraft Connector was used to support initiation of the pivotal study. After completion of the pivotal clinical study, modifications were made to the device that included changing the ePTFE material to an ultralow porosity ePTFE and an update to the manufacturing process and location. These changes were made due to a change to the contract manufacturer.

Except for the animal studies, which were completed with the Venous InterGraft Connector, all nonclinical bench, biocompatibility, packaging and sterilization testing were repeated on the EndoForce™ Connector. The rationales for leveraging any results from the previously conducted Venous InterGraft Connector evaluations are included in the relevant sections of this SSED.

A. Biocompatibility

Biocompatibility testing was performed on the final, finished EndoForce™ Connector and Delivery System following the recommendations provided in International Organization for Standardization (ISO) *10993, Biological Evaluation of Medical Devices and FDA's Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems*. The EndoForce™ Connector was classified as an implant device with permanent (>30 days) contact. The EndoForce™ Connector Delivery System (delivery system) was classified as an externally communicating device with limited (≤ 24 hours) exposure to circulating blood.

All biocompatibility tests were conducted in accordance with the Good Laboratory Practices (GLP) per 21 CFR, Part 58.

All testing performed met the pre-specified acceptance criteria. **Tables 1 and 2** provide a listing of the tests and analyses performed for the implant (**Table 1**) and delivery system (**Table 2**), and the corresponding results.

Table 1. EndoForce™ Connector (Implant) Biocompatibility Testing

Biological Evaluation Endpoint	Biological Testing or Assessment Completed	Reference	Results
Cytotoxicity	Cytotoxicity – ISO MEM Elution Using L-929 Mouse Fibroblast Cell	ISO 10993-5	Non-cytotoxic
Sensitization	Sensitization – ISO Guinea Pig Maximization Sensitization Test	ISO 10993-10	Non-sensitizing
Irritation or Intracutaneous Reactivity	Irritation – ISO Intracutaneous Irritation Test	ISO 10993-23	Non-irritating
Materials Mediated Pyrogenicity	Systemic Toxicity (Acute) – ISO / USP Materials Mediated Rabbit Pyrogenicity Test	ISO 10993-11 USP <151>	Non-pyrogenic
Implantation	4-Week Muscle Implantation Study	ISO 10993-6	Minimal to no reaction in tissue as compared to the implant control and negative control articles
	13-Week Muscle Implantation Study	ISO 10993-6	
Hemocompatibility	Hemocompatibility - ASTM Hemolysis Study – Extract and Direct Contact Method	ISO 10993-4 ASTM F756-17	Non-hemolytic
	Hemocompatibility – Partial Thromboplastin Time (PTT)	ISO 10993-4 ASTM 2382-18	The test article average clot time was not statistically significant when compared to the negative control
	Hemocompatibility – Complement Activation Assay	ISO 10993-4	Non-activator of the complement system
	Hemocompatibility – Heparinized Blood Platelet and Leukocyte Count Assay	ISO 10993-4 ASTM F2888-19	The platelet mean percentage value was within 80 to 120% of the negative control, and at least 30% above the positive control
	Thrombogenicity – 12-Week Canine implant study – performance and safety of the Connector	ISO 10993-4	No evidence of significant arterial luminal thrombus within the implant by gross and microscopic examination and no evidence of distal embolization
Acute Systemic Toxicity	Chemical Characterization and Toxicological Risk Assessment	ISO 10993-17 ISO 10993-18	Toxicological risk assessment indicates the risk of toxicity from the test article extractables is negligible
Subacute / Subchronic Toxicity			

Biological Evaluation Endpoint	Biological Testing or Assessment Completed	Reference	Results
Chronic Toxicity			
Genotoxicity			
Carcinogenicity			

Table 2. EndoForce™ Connector Delivery System Biocompatibility Testing

Biological Evaluation Endpoint	Biological Testing or Assessment Completed	Reference	Results
Cytotoxicity	Cytotoxicity – ISO MEM Elution Using L-929 Mouse Fibroblast Cell	ISO 10993-5	Non-cytotoxic
Sensitization	Sensitization – ISO Guinea Pig Maximization Sensitization Test	ISO 10993-10	Non-sensitizing
Irritation or Intracutaneous Reactivity	Irritation – ISO Intracutaneous Irritation Test	ISO 10993-23	Non-irritating
Acute Systemic Toxicity	Systemic Toxicity (Acute) – ISO Acute Systemic Injection Test	ISO 10993-11	No evidence of acute systemic toxicity
Materials Mediated Pyrogenicity	Systemic Toxicity (Acute) – ISO / USP Materials Mediated Rabbit Pyrogenicity Test	ISO 10993-11 USP <151>	Non-pyrogenic
Hemocompatibility	Hemocompatibility - ASTM Hemolysis Assay	ISO 10993-4 ASTM F756-17	Non-pyrogenic
	Hemocompatibility – Partial Thromboplastin Time (PTT)	ISO 10993-4 ASTM 2382-18	The test article average clot time was greater than the negative control, and not statistically significant when compared to the vehicle control
	Hemocompatibility – Complement Activation Assay	ISO 10993-4	Non-activator of the complement system
	Hemocompatibility – Heparinized Blood Platelet and Leukocyte Count Assay	ISO 10993-4 ASTM F2888-19	The platelet mean percentage value was within 80 to 120% of the negative control, and at least 30% above the positive control

Biological Evaluation Endpoint	Biological Testing or Assessment Completed	Reference	Results
	Hemocompatibility – Thrombogenicity (Acute canine study)	ISO 10993-4	No clinically significant adherence of thrombus or evidence of thromboembolic events

B. Bench Testing

In vitro bench testing was conducted as part of the design verification and validation to support the safety and effectiveness of the EndoForce™ System. This testing was conducted on the final, finished EndoForce™ Connector and Delivery System based on recommendations from risk assessments with consideration to FDA and industry recognized voluntary standards. The bench test results are summarized in **Table 3**. An asterisk (*) indicates that the testing was performed at baseline and after aging (accelerated to the shelf-life duration).

Table 3. Summary of *In Vitro* Bench Testing

Test	Purpose	Acceptance Criteria	Result
System Level Bench Testing			
Simulated Use*	Evaluate the Compatibility, Pushability, and Trackability of the device within a standard introducer sheath	The diameter of the Delivery System must be compatible and fit through a standard 11Fr introducer without damage.	PASS
	Evaluate the Compatibility, Pushability, and Trackability of the device over a commercial vascular guidewire	The Delivery System shall track over a standard 0.035" commercially available guidewire without damage.	PASS
	Evaluate the device Flexibility/Kink performance enabling the device to be implanted into the target location	The Delivery System must be able to be pushed and tracked to the desired implant location with no evidence of buckling or kinking.	PASS

Test	Purpose	Acceptance Criteria	Result
	Evaluate the ability of the device to provide hemostasis during the clinical implantation	The Delivery System must leak less than 2cc/minute at a pressure of 140mmHg.	PASS
	Evaluate the device torsion performance enabling the device to be implanted into the target location	The Delivery System must not be damaged and deploy the Venous Connector after a 90º rotation in each direction.	PASS
	Evaluate the ability to deploy the device within the target location	The Connector must deploy in a controlled manner with no foreshortening or watermelon seeding (spring back/undesirable and uncontrolled movement) upon deployment.	PASS
		The force to deploy the Connector must not damage the Connector.	PASS
	Evaluate the device withdrawal after deployment	The Delivery System must be able to be removed without disturbing the Connector.	PASS
		The Delivery System must be able to be removed from the anatomy without catching on or damaging the Connector or ePTFE coating.	PASS
	Following the completion of the simulated use procedure, evaluate the System Compatibility with a commercially available guidewire to ensure device does not damage the guidewire	The Delivery System shall track over a standard 0.035" commercially available guidewire without damage.	PASS
		The Delivery System shall not damage a 0.035" commercially available guidewire during treatment use such that embolization of guidewire could occur.	PASS

Test	Purpose	Acceptance Criteria	Result
	Following the completion of the simulated use procedure, evaluate the System Compatibility as the ability to deploy the device without incurring device damage	The force to deploy the Connector must not damage the Delivery System.	PASS
	Following the completion of the simulated use procedure, evaluate the System Compatibility as the ability to perform in a simulated clinical environment without exhibiting device defects	The Delivery System must not exhibit any mechanical defect after simulated use.	PASS
	Following the completion of the simulated use procedure, evaluate the System Compatibility as the ability to reach its target implant location without experiencing buckling or kinking	The Delivery System must be able to be pushed and tracked to the desired implant location with no evidence of buckling or kinking.	PASS
	Following the completion of the simulated use procedure, evaluate the System Compatibility as the ability to deploy the implant after expected user manipulation without incurring damage	The Delivery System must not be damaged and deploy the Connector after a 90º rotation in each direction.	PASS
	Evaluate the deployment accuracy in relation to the target implant location	The Connector must have sufficient depth in the vein, a minimum of 2cm.	PASS
	Evaluate the deployment accuracy in relation to the target implant location	The Connector must be deployed at the desired location, ±5mm.	PASS
	Evaluate the revision capability of the system (ballooning) in yielding a Connector free of damage	The revision procedure indicated in the IFU must not damage the frame of the Connector or the ePTFE covering.	PASS

Test	Purpose	Acceptance Criteria	Result
Particulate Capture	Evaluate the System for particulate generation under simulated use conditions	The EndoForce Connector for Endovascular Venous Anastomosis is not to exceed 6,000 particles ≥ 10µm per device and is not to exceed 600 particles ≥ 25µm per device. Additionally, particulate in the ranges of 50um and 100um will be quantified and reported for characterization.	PASS
Delivery System Bench Testing			
Bond Tensile Strength*	Evaluate the tensile strength of the Venous Extrusion to Pusher bond	The tensile strength of all joints and bonds must be ≥ 15N.	PASS
	Evaluate the tensile strength of the Pusher to Hub bond		PASS
	Evaluate the tensile strength of the Sheath to Hub bond		PASS
Force to Deploy*	Evaluate the Insertion Force of the Delivery System into a mock vessel.	The insertion force of the Delivery System must be less than 15N.	PASS
	Evaluate the Deployment Force of the Delivery System into a mock vessel.	The Delivery System must deploy the Connector with a force ≤10lbs.	PASS
	Evaluate the Withdrawal Force of the Delivery System into a mock vessel.	The withdrawal force of the Delivery System must be less than 15N.	PASS
Delivery System Visual and Dimensional*	Evaluate the Delivery System Visual appearance to ensure it is free of particulate	The external surface of the working length of the Delivery System shall appear free from particulate with a volume greater than $0.905mm^3$ at normal, or corrected to normal vision, with a minimum of 2.5 magnification.	PASS

Test	Purpose	Acceptance Criteria	Result
	Evaluate the Delivery System Visual appearance to ensure it is free of defects	The external surface of the working length of the Delivery System, including the distal end, should be free from process and surface defects that could cause trauma to vessels during use.	PASS
	Evaluate the Delivery System Dimensions to ensure the effective length meets requirements	Effective length of the Delivery System shall be 225mm ± 5mm.	PASS
	Evaluate the Delivery System visual appearance to ensure the tightness of the proximal tuohy-borst component.	The proximal tuohy-borst component must be present and attached to Y-Connector.	PASS
Implant Level Bench Testing			
Corrosion Resistance	Evaluate the Nickel Ion Release rate of the Connector.	The Maximum nickel release rate must be less than 35µg/day for all specimens throughout a 64-day testing duration.	PASS
Compression*	Evaluate the Compression Force of the implant to ensure resistance to external compression	The Connector requires a force > 2N to collapse under a compressive force (6mm displacement).	PASS
Radial Force*	Characterize the radial resistive (RR) Force at Min and Max Treatment Diameter – Proximal End	The Connector radial force data will be collected for reference only.	Characterized Avg = 0.118 ± 0.32 N/mm
	Characterize the chronic outward (CO) Force at Min and Max Treatment Diameter – Proximal End		Characterized Avg = 0.042 ± 0.007 N/mm
	Characterize the RR Force at Min Treatment Diameter – Distal End		Characterized Avg = 1.152 ± 0.121 N/mm
	Characterize the RR Force at Max Treatment Diameter – Distal End		Characterized Avg = 0.335 ± 0.036 N/mm
	Characterize the CO Force at Min Treatment Diameter – Distal End		Characterized Avg = 0.408 ± 0.025 N/mm
	Characterize the CO Force at Max Treatment Diameter – Distal End		Characterized Avg = 0.085 ± 0.012 N/mm

Test	Purpose	Acceptance Criteria	Result
Kink Radius*	Evaluate the Kink Radius of the implant to maintain a patent blood lumen	Radius at which kink occurs is less than 20mm.	PASS
Pulsatile Fatigue	Diameter-controlled Connector pulsation equivalent to 10 years of cardiac cycling.	The Connector must withstand an equivalent of 10 years of accelerated durability testing. Upon completion of testing, the Connector must maintain structural integrity with no clinically significant mechanical faults.	PASS
Finite Element Analysis	Finite Element Analysis (FEA) was used to analyze the Connector under simulated in-vivo loading conditions that included radial pulsatile and cyclic axial loads.	All resulting safety factors must be greater than 1.	PASS
Axial Fatigue	Evaluate the Connector barb Active Fixation Fatigue over 190 million cycles.	The Connector must withstand an equivalent of 5 years of accelerated active fixation fatigue and durability testing. Upon completion of testing, the Connector must maintain structural integrity with no clinically relevant mechanical faults.	PASS
Conformability*	Evaluate the Conformability of the implant within a mock vessel for embedment of tines	The Connector tines must deploy into the wall of the vein.	PASS
Connector Fixation*	Evaluate the Connector Fixation force for preventing disengagement in a mock vessel	The Connector shall not be dislodged from a vein at a force less than 200 grams.	PASS
Graft Retention*	Evaluate the Graft Retention force of the suture connection between the implant and graft	The force required to dislodge the Connector from the Graft shall exceed 200 grams.	PASS
Migration Resistance*	Evaluate the Migration Resistance of the implant under physiologic fluid pressures	The Connector shall migrate less than 2mm from the initial implant position.	PASS

Test	Purpose	Acceptance Criteria	Result
Porosity-Internodal Distance*	Evaluate the Porosity of the implant encapsulation layer	The Connector ePTFE encapsulation must have a maximum internodal distance of 40µm	PASS
Integral Water Permeability*	Evaluate the Integral Water Permeability of fluid across the implant encapsulation layer under physiologic pressures	The Connector ePTFE encapsulation must have a maximum leakage rate of 2cc/min.	PASS
Water Entry Pressure*	Evaluate the Water Entry Pressure of the implant encapsulation layer	The Connector ePTFE encapsulation water entry pressure must be ≥ 90 mmHg.	PASS
Burst Strength*	Evaluate the Burst Strength of the implant encapsulation layer	The burst pressure of the Connector must exceed 300mmHg	PASS
MRI	The purpose of this study was to evaluate the Connector compatibility for use with MRI.	The Connector must demonstrate acceptable MR-Conditional safety per ASTM F2503-20. Testing conducted in accordance with ASTM F2052, ASTM F2213, ASTM F2119 and ASTM F2182.	PASS
Connector Visual and Dimensional*	Evaluate the Implant Visual appearance to ensure it is free of particulates	The Connector must have no surface irregularities, foreign material, or particulates that exceed 0.10mm^2 when examined at normal, or corrected to normal, vision.	PASS
	Evaluate the Frame Integrity to ensure it is free of sharp or rough features	The Connector must not have sharp corners or rough surfaces.	PASS
	Evaluate the Frame Integrity to ensure it is free of defects (bent, broken or deformed struts)	The Connector must not have bent, broken or deformed struts	PASS
	Evaluate the Encapsulation Integrity to ensure it is free of defects (displacement)	The ePTFE encapsulation on the Connector must not exhibit displacement of the proximal ePTFE edge past the adjacent strut intersection.	PASS

Test	Purpose	Acceptance Criteria	Result
	Evaluate the Encapsulation Integrity to ensure it is free of defects (delamination)	The ePTFE encapsulation on the Connector must not exhibit delamination (separation of inner/outer ePTFE layers) beyond the length of 1 strut.	PASS
	Evaluate the Encapsulation Integrity to ensure it is free of defects (fraying)	The ePTFE encapsulation on the Connector must not exhibit fraying	PASS
	Evaluate the Encapsulation Integrity to ensure it is free of defects (holes or tears)	The ePTFE encapsulation on the Connector must not exhibit Type 1 holes or tears (through one layer, inner/outer) in the distal section of ePTFE. Type 1 holes are acceptable in the region 17.5mm from the proximal end	PASS
	Evaluate the Encapsulation Integrity to ensure it is free of defects (holes or tears)	The ePTFE encapsulation on the Connector must not exhibit Type 2 holes or tears (through both layers) in the ePTFE	PASS
	Evaluate the Implant Dimensions to ensure the total length meets requirements	Connector and coating dimensions meet the following critical dimensions: Total Length: 2.6" ± 0.3"	PASS
	Evaluate the Implant Dimensions to ensure the Outer Diameter - Distal meets requirements	Flare OD - Distal: 0.39+0.04"/-0.06"	PASS
	Evaluate the Implant Dimensions to ensure the Outer Diameter - Proximal meets requirements	Straight OD - Proximal: 0.28" ± 0.02"	PASS
	Evaluate the Implant Dimensions to ensure the Exposed Stent Length - Distal meets requirements	Distal Non-Coated Length: 0.3" +0.09"/-0.02"	PASS

Test	Purpose	Acceptance Criteria	Result
Coating Adherence*	Evaluate the implant Coating Adherence to ensure it is free of defects (holes or tears) after being used in a simulated clinical environment	The Connector ePTFE encapsulation must not exhibit any damage during a simulated implant that could impact device function: • Type 2 holes or tears (through both layers) in the ePTFE • No Type 1 holes or tears (through one layer, inner/outer) in the distal section of ePTFE. Type 1 holes are acceptable in the region 17.5mm from the proximal end • No delamination (separation of inner/outer ePTFE layers) beyond the length of 1 strut • No displacement of the proximal ePTFE edge past the adjacent strut intersection	PASS
Af Profile	Determine the Af temperature per ASTM F2004 "Standard Test Method for Transformation Temperature of Nickel-Titanium Alloys by Thermal Analysis."	The Connector Af temperature data will be collected for reference only.	Characterization Only

C. Sterility, Packaging and Shelf-Life Testing

Sterility

The EndoForce™ System is a single-use device that is distributed sterile to the end user. Sterilization is performed using a validated Ethylene Oxide (EO) process resulting in a Sterility Assurance Level (SAL) of 10^{-6}. The validated cycle, performed at Sterilization Services of Georgia, was developed for a process challenge device that served as a comparison for product adoption of the EndoForce™ System into the same cycle. The product adoption assessments and testing followed the requirements for adding a new or modified product into a previously validated EO sterilization process per AAMI/ANSI/ISO *11135-1:2014 Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for the Development, Validation, and Routine Control of Ethylene Oxide Sterilization Process for Medical Devices*.

Packaging

The EndoForce™ System is a single use, disposable, sterile device. Product packaging was designed and validated to ensure the sterility and integrity of individually packaged and sealed devices. The environmental and distribution conditions selected comply with the specifications in *ISTA 3A, Packaged Products for Parcel Delivery System Shipment 70 kg (150lb) or Less*, and ASTM D4169, *Standard Practice for Performance Testing of Shipping Containers and Systems*. Each device is individually packaged in a tray with a sealed peelable Tyvek covering. The sealed tray is then packaged in a shelf carton and is secured with a tamperproof seal on the shelf carton.

Packaging performance testing (T=0) and packaging stability testing (T=2yr) were performed results of which are presented below:

Table 4. Summary of Packaging Studies

Test	Test Method	Acceptance Criteria	Result
Packaging Performance Testing (after conditioning per ISTA 3A and ASTM-D4169 distribution cycle 13, assurance level II)			
Visual Inspection & Label Integrity	ASTM F1886-10	All Labels must maintain integrity (remain adhered and legible)	Pass
Bubble Leak Test	ASTM F2096-11	No damage to the sterile barrier or product after conditioning	Pass
Seal peel Strength	ASTM F88/F88M-21	≥1.00 lbf/in	Pass
Packaging Stability Testing (after conditioning per ISTA 3A and ASTM-D4169 distribution cycle 13, assurance level II, followed by 2-yr accelerated aging)			
Visual Inspection	ASTM F1886-16	All Labels must maintain integrity (remain adhered and legible)	Pass
Bubble Leak Test	ASTM F2096-11	No damage to the sterile barrier or product after conditioning and 2-yr accelerated aging	Pass
Seal peel Strength	ASTM F88/F88M-21	≥1.00 lbf/in	Pass

Shelf-Life

A shelf life of 2 years has been established for the EndoForce™ System based on product and package shelf-life testing.

D. Animal Studies

The EndoForce™ Connector was initially called the Venous InterGraft Connector (referred to as the Connector in this summary). The animal studies described in this section were conducted using the Connector and evaluated both the venous anastomotic connector and an arterial anastomotic connector. A total of three animal studies were conducted using a canine model. Further development of the arterial connector was subsequently discontinued. The arterial and venous connectors do not interact with each other in anatomic space or function.

Subsequent to the completion of the animal studies, design and manufacturing modifications were made to the device as described in section IX above. Comparative bench testing assessments between the original and modified device as well as the battery of biocompatibility testing conducted on the final, finished device confirmed that the changes are not associated with any negative impacts on device performance. Based on the supporting information, previously conducted animal studies were deemed acceptable to support in vivo safety of the EndoForce™ Connector.

The animal study endpoints used in the studies of overall health, device deployment and procedure success, major adverse events, and arteriovenous graft (AVG) patency are relevant for the EndoForce™ Connector used for venous anastomosis of an AVG.

Three *in vivo* animal studies (acute and chronic) were conducted using a canine model.

See **Table 5** below for results of the animal studies.

Table 5. Summary Results of Animal Studies

Animal Study Description	Methods	Purpose/Objectives	Results
Study ID: MUV011 **GLP Canine Study** N=7 with primary endpoint at 12 weeks and planned follow-up to 20 weeks	Implant using anastomotic connectors at one femoral site and a standard surgical (sutured) AVG at the contralateral femoral site	Endpoint Outcomes: (1) Overall Health (2) Deployment Success (3) Acute Procedure Success (4) Major Adverse Events (5) AV Graft Patency (6) Simulated Needle Access (7) Percutaneous Intervention (8) Healing of Surgical Site	5 animals survived AVG implantation and had 12-week assessment. 3 animals survived to 20 weeks (1 could not be resuscitated after 12-week angio and 1 suffered a graft infection after a fight, unrelated to the study device or procedure). Study outcomes evaluated at 12 (primary) and 20 (secondary) weeks (or termination) showed that the connector was successfully delivered, deployed, remained patent, and remained in position in all cases. No fractures/deformities were noted. No deleterious tissue response was observed as compared with conventional sutured venous anastomoses.
Study ID: MUV010 **Non-GLP Canine Study** N=4 with follow-up to 28 days	Implant using anastomotic connectors at both femoral sites	The purpose was to evaluate performance and safety of the device in a unilateral femoral model. Histopathologic examination at 4 weeks (or after re-occlusion following one allowed intervention, whichever occurs first) was to assess inflammation score, endothelialization score, and thrombus score.	The following summarize the results: • All 4 AVG patent at 28 days • No significant luminal defects observed within the AVG or connectors. • Acceptable flow rates in all AVGs at 14 days following implant. • AVGs could be punctured with hemodialysis needles using standard techniques and hemostasis was achieved after needle removal. • No evidence of infection, hemorrhage, or other clinical sequelae throughout the entire follow-up period • At termination, all connectors securely implanted and encapsulated in the subcutaneous connective tissue. • Histopathologic exam confirmed that the connectors and AVGs were widely patent and only minimal to mild thrombus was seen in select sections. • No device-related findings present in any of the peripheral organs and tissues examined. • Gross and microscopic appearances of the connector implant sites were fairly uniform and similar between dogs. • Failure of the delivery system occurred in two animals and was associated with significant bleeding that was subsequently resolved. In both animals, the graft implant

Animal Study Description	Methods	Purpose/Objectives	Results
			procedure was successfully completed using another connector, without further sequelae. There were no other major adverse events observed throughout the 28-day follow-up period.
MUV009 **Non-GLP Canine Feasibility Study** N=11; follow-up time varied from acute termination to 14 months	Implants using AVGs with anastomotic connectors and standard sutured anastomoses implanted in femoral locations.	Further development of the device implantation technique, animal model, and optimization of the anticoagulation regimen	Developed and confirmed the technical Connector implantation procedure. Determined proper coagulation regimen for the animal model. Findings allowed for transition to the definitive animal studies to support clinical use of the Connector system.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of the EndoForce^{TM} System in the US under G140221. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below. The investigational device is referred to as the Connector in this summary.

Subsequent to the completion of the pivotal clinical study, design and manufacturing modifications were made to the device as described in Section IX. These modifications did not warrant additional clinical evaluation because comparative bench testing assessments between the original and modified device as well as the battery of biocompatibility testing confirmed that the changes are not associated with any negative impacts on device performance.

A. Study Design

Patients were treated between February 21, 2018 and July 21, 2021. The database for this PMA reflected data collected through January 25, 2022 and included 158 enrolled patients and 13 roll-in patients. There were 10 investigational sites. One additional site enrolled roll-in patients but did not contribute to pivotal study enrollment.

The study was a prospective, multicenter, single-arm clinical study. All enrolled patients underwent arteriovenous graft (AVG) implantation using the Connector for the venous anastomosis and standard suturing of the arterial anastomosis. Prior to starting enrollment in the pivotal study, investigators were required to enroll at least one roll-in patient as part of the training requirements. Roll-in patients were treated and followed according to the same protocol that was applied to pivotal study patients. Results for the roll-in subjects are reported separate from the results for the pivotal study subjects below.

The primary endpoint was cumulative patency at 6 months, defined as the percentage of subjects free from loss of access of the study graft for hemodialysis. The primary endpoint was pre-specified to be compared to a performance goal (PG) of 75% based on published literature and was evaluated in the following hypotheses:

H_0: $(\text{Cumulative Patency Rate})_{6\ \text{Months}} \leq PG$

H_1: $(\text{Cumulative Patency Rate})_{6\ \text{Months}} > PG$

Where, PG = Performance Goal, here equal to 75%.

Kaplan-Meier estimate of cumulative patency rate at 6 months was used, with assumptions of expected cumulative patency rate of 84.6% using a one-sided binomial exact test, a type I error rate of 2.5%, and 80% statistical power. Based on these assumptions, a total of 146 evaluable patients were required. With an expected loss-to-follow-up rate of 8% over 6 months (12 patients), a total of 158 patients were required.

A Clinical Events Committee (CEC) reviewed and adjudicated all adverse events. An independent Data and Safety Monitoring Board (DSMB) had responsibility for safeguarding the interests of study patients, assessing the safety and efficacy of study procedures, and for monitoring the overall conduct of the study.

1. Clinical Inclusion and Exclusion Criteria

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

1) Subject is ≥ 18 years of age.
2) Subject requires the creation of a vascular access graft for hemodialysis, secondary to a diagnosis of end stage renal disease.
3) Subject is able to have the vascular access graft placed in an upper extremity.
4) Baseline imaging shows suitable vascular anatomy/ vessel size for the Connector and an artery at least 3.5 mm in diameter that is suitable for creating the arterial anastomosis.
5) Subject has a reasonable expectation of remaining on hemodialysis for at least 6 months.
6) Subject or his/her legal guardian understands the study and is willing and able to comply with the dialysis schedule and follow-up requirements.
7) Subject or his/her legal guardian provides written informed consent.
8) Physician's examination at time of surgery shows no significant vessel lesions, calcification(s), anatomic structures, or abnormalities that may limit ability to safely deploy the Connector or create a sutured arterial anastomosis.

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

1) Subject has a documented and unsuccessfully treated ipsilateral central venous stenosis as determined by imaging.
2) Subject currently has a known or suspected bacterial, fungal, or HIV infection. NOTE: Subjects with hepatitis B or C may be included in the study.
3) Subject has a known hypercoagulable or bleeding disorder or requires treatment with warfarin or heparin.
4) Subject has had a previous instance of Heparin Induced Thrombocytopenia type 2 (HIT-2) or has known sensitivity to heparin.
5) Subject has co-morbid conditions that may limit their ability to comply with study and follow-up requirements.
6) The patient has had >2 previous arteriovenous accesses in treatment arm.
7) Subject is currently taking Aggrenox®.
8) Subject is in need of or is scheduled for any major surgery within 30 days of the study procedure.

9) Subject is currently taking maintenance immunosuppressant medication such as rapamycin, mycophenolate or mycophenolic acid, prednisone (>10 mg), cyclosporine, tacrolimus, or cyclophosphamide.
10) Life expectancy is less than 12 months.
11) Subject is pregnant.
12) Subject is a poor compliance risk (i.e.. history of IV or oral drug abuse).
13) The subject is enrolled in another dialysis or vascular investigational study.

2. Follow Up Schedule

All patients were scheduled for follow-up evaluation at 2 weeks and at 30-, 60-, 90-, 120-, 150-, and 180- days post-procedure. **Table 6** summarizes the evaluations and assessments performed pre- and post-operatively.

Table 6. Schedule of Events and Evaluations

Assessment	**Pre-procedure**	**Procedure**	**Discharge**	**2 weeks** (14 +4/-7 days) **30, 60, 90, 120, 150, and 180 days** (± 14 days)
Informed consent	X			
Medical history/dialysis history	X			
Laboratory assessments[1]	X	X		
Baseline imaging/mapping of vessels at planned graft implant site (standard-of-care assessment)[2]	X	X		
Confirmation of graft flow		X	X	
Medication use	X	X		X
Adverse event assessment		X	X	X
Clinical follow up with graft assessment. Graft ultrasound examination at 90- and 180 days.				X
Assessment of graft interventions				X

[1] Laboratory assessments included pre-procedure hemoglobin, hematocrit, white blood cell count, and platelet count within 30 days, and urine pregnancy test within 24 hours (if applicable); and post-procedure hemoglobin and hematocrit within 48 hours.
[2] Baseline imaging was required at time of procedure. Pre-procedure imaging data were collected as available.

3. Clinical Endpoints

The primary endpoint was cumulative patency at 6 months, defined as the percentage of subjects free from loss of access of the study graft for hemodialysis.

Secondary endpoints for the study included:

- Acute device success, defined as AVG flow at the end of the procedure (determined by palpable graft thrill and/or audible bruit), without significant bleeding or emergent surgery.

- Primary Unassisted Patency at 6 Months, defined as the percentage of subjects free from the first occurrence of either access thrombosis or an access procedure performed to maintain access patency.

- Time to First Cannulation, defined as the time from initial access placement to the first graft cannulation for hemodialysis.

- Number and type of interventions required to maintain secondary patency.

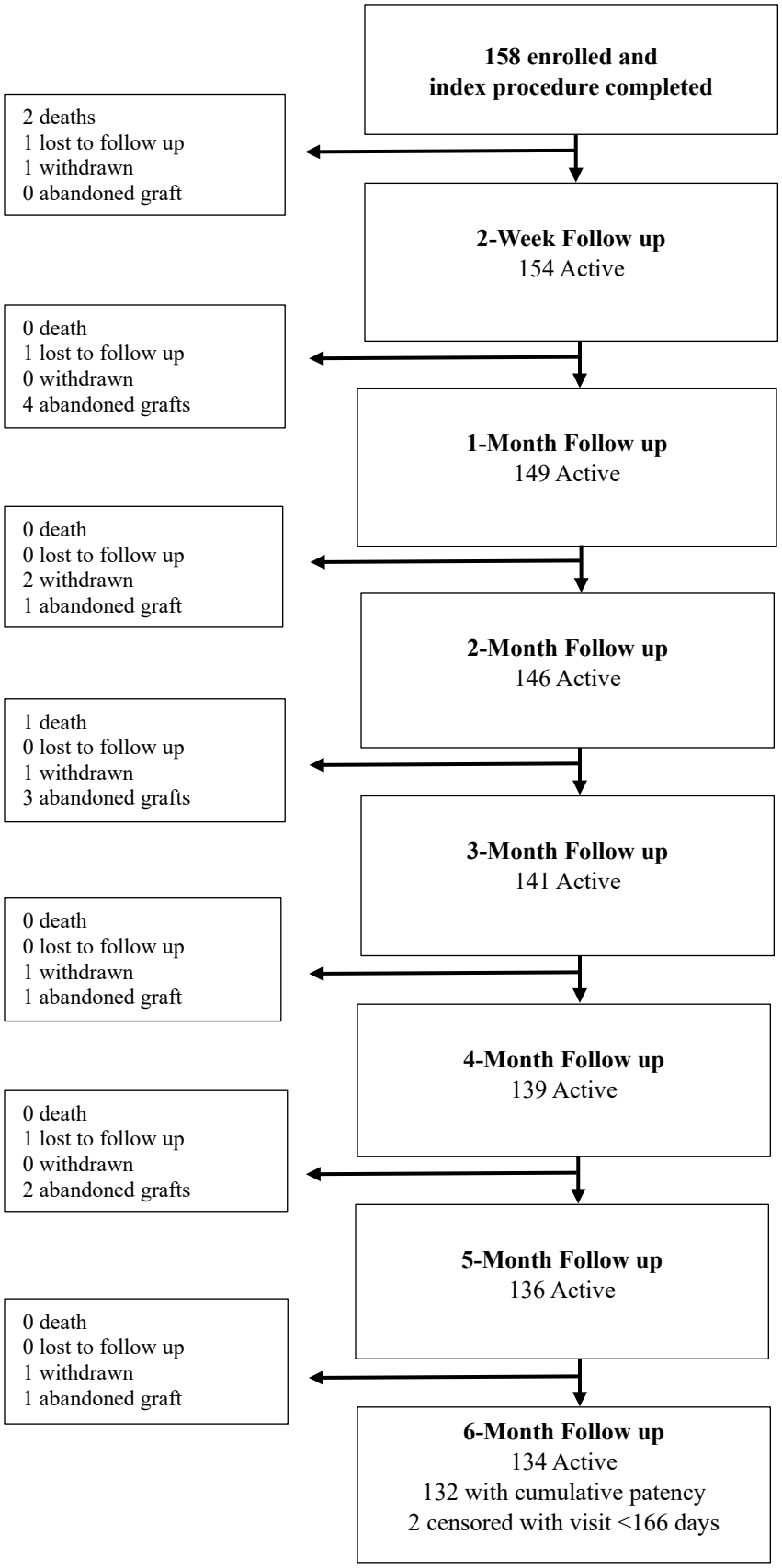
- Number and type of serious adverse events (SAEs) through 6 months. SAEs include the following: death, emergent surgery, vascular access infection, significant bleeding, and pseudoaneurysm.

B. Accountability of PMA Cohort

Study results are available for 158 subjects, with 144 evaluable at six months. A total of 14 subjects were censored with partial follow-up observation through six months. Reasons for censoring included death (3 subjects), lost to follow up (3 subjects), subject withdrew from the study (6 subjects), and 6-month follow up < 166 days (2 subjects). An additional 12 of the 144 evaluable subjects also did not complete their six-month follow-up because of graft abandonment, and their outcomes were included in the endpoint assessments. At six months, there were 134 active subjects in the study.

Subject accountability is shown in **Figure 3**.

Figure 3. Subject Accountability for Pivotal Study



C. Study Population Demographics and Baseline Parameters

The demographics and co-morbidities of the study population are typical for an AVG study performed in the US with the exception of a higher proportion of females and African Americans. However, there were no clinically meaningful differences within these subgroups (male vs. female, African American vs. non-African American). Therefore, the results can be considered generalizable to the broader patient population. Subject demographics, baseline clinical characteristics and dialysis history information is shown in **Table 7.**

Table 7. Demographics, Baseline Characteristics, and Vascular Access History[1]

Characteristic	Roll-in patients (N=13)	Pivotal Study (N=158) .
Age, years, mean ± SD (range)	63.7 ± 12.3 (41.0 -84.0)	62.6 ± 14.8 (24.0 - 92.0)
Sex at Birth:		
Male	7 (54)	61 (39)
Female	6 (46)	97 (61)
Ethnicity:		
Hispanic or Latino	0	3 (2)
Not Hispanic or Latino	13 (100)	154 (97)
UNK/not reported	0	1 (1)
Race:		
Asian	0	1(1)
Black or African American	10 (77)	123 (78)
White	3 (23)	34 (22)
Diabetes mellitus	12 (92)	98 (62)
Obesity	8 (62)	51 (32)
Hypertension	5 (38)	89 (56)
Cardiovascular disease	8 (62)	78 (49)
Previous permanent vascular accesses for hemodialysis, any location:		
0	7 (54)	64 (41)
1	4 (31)	66 (42)
≥ 2	2 (15)	28 (18)
Previous permanent vascular access for hemodialysis in target limb:		
0	8 (62)	90 (57)
≥ 1	5 (38)	68 (43)
Current vascular access using catheter	12 (92)	134 (85)
Duration of hemodialysis:		
< 6 months	5 (38)	69 (44)
≥ 6 and <12 months	0	15 (9)
≥ 12 months	7 (54)	59 (37)
NA (no current hemodialysis)	1 (8)	15 (9)

[1] Table values shown are number (%) unless otherwise indicated.

The study procedure details are provided in **Table 8**.

Table 8. Summary of the Implant Procedure*

Parameter	Roll-in Patients (N=13)	Pivotal Study (N=158)
Implanted graft location: Left upper arm Right upper arm	 7 (54) 6 (46)	 96 (61) 62 (39)
Vein used for anastomosis using the Connector: Axillary Basilic Brachial Cephalic	 7 (54) 5 (38) 1 (8) 0	 63 (40) 24 (15) 69 (44) 2 (1)
Graft type implanted: Early cannulation Standard ePTFE	 12 (92) 1 (8)	 118 (75) 40 (25)
Heparin during procedure Amount used, IU, mean ± SD	11 (85) 4018.2 ± 2309.5	81 (51) 4067.9 ± 1887.0
Contrast dye during procedure, ml, mean ± SD	75.1 ±112.8	64.1 ± 94.7
Procedure time, minutes, mean ± SD *[Time from 'first incision to tunnel AVG' to 'AVG connected, flow confirmed']*	59.8 ± 21.2	45.4 ± 15.9

*Values are n (%) unless otherwise specified.

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on the pivotal analysis cohort of 158 pivotal patients.

Safety was evaluated as the number and type of serious adverse events (SAEs) through 180 days, including: death, emergent surgery, vascular access infection, significant bleeding, and pseudoaneurysm.

Table 9. Summary of Safety Endpoint Results

Endpoint	Roll-in patients (N=13)	Pivotal Study (N=158)
Patients with protocol-specified SAEs: Death AVG infection Emergent surgery Significant bleeding Pseudoaneurysm	 23% (3/13) 0% (0/13) 8% (1/13) 0% (0/13) 0% (0/13)	 2% (3/158) 4% (6/158) 0% (0/158) 0% (0/158) 0% (0/158)

The overall protocol-defined SAE rate in the pivotal study was 5.70%. Graft infections occurred in 6 patients (3.80%) in the pivotal study. None of the infections were related to the Connector. One (1) roll-in patient developed an

upper-extremity hematoma the day after graft implantation requiring emergent surgery. During surgery it was noted that the tacking suture had not engaged the Connector and the Connector dislodged from the graft. The Connector was re-inserted into the graft and the tacking suture properly placed without further sequelae. All deaths (3 in roll-in patients and 3 in pivotal patients) were unrelated to the study device or the AVG implant procedure. No patients had significant bleeding or pseudoaneurysm.

Protocol-specified SAEs and additional SAEs that were reported as related to the Connector (study device) or AVG implant procedure are listed in **Table 10**. Non-serious adverse events (AEs) that were reported as related to the study device or AVG implant procedure are listed in **Table 11**.

Table 10. Relatedness of Serious Adverse Events[1]

SAE Type *(*denotes protocol-specified SAE)*	**Number of Patients**	**Relationship to Study Device**			**Relationship to AVG Implant Procedure[7]**		
		Related	**Possibly related**	**Not related**	**Related**	**Possibly related**	**Not related**
Pivotal Study (N=158)							
Bacteremia	1	0	0	1	1	0	0
*Bleeding, significant	0	-	-	-	-	-	-
Cellulitis	1	0	0	1	1	0	0
*Death[2]	3	0	0	3	0	0	3
*Emergent Surgery	0	-	-	-	-	-	-
Hospitalization, prolonged[3]	3	0	1	2	2	1	0
*Infection, implanted AVG[4]	6	0	0	6	1	0	5
Ischemia/Vascular steal, implanted arm	5	0	0	5	5	0	0
*Pseudoaneurysm	0	-	-	-	-	-	-
Roll-in Patients (N=13)							
*Bleeding, significant	0	-	-	-	-	-	-
*Death[2]	3	0	0	3	0	0	3
*Emergent Surgery[5]	1	1	0	0	1	0	0
*Infection, implanted AVG	0	-	-	-	-	-	-
Ischemia/Vascular steal	1	0	0	1	1	0	0
Seroma, infected[6]	1	0	1	0	0	1	0

[1] All events were reviewed and adjudicated by the CEC.

[2] All deaths were adjudicated as unrelated to the Connector or AVG implant procedure. The deaths in the 3 pivotal patients were due to 1) atrial fibrillation 4 days post-procedure, 2) patient with coronary artery disease was found deceased at home 3 months post-procedure, and 3) patient went to ER with volume overload and died in the hospital 15 days post-procedure. The deaths in the 3 roll-in patients were due to 1) septic shock 2.5 months post-procedure, 2) cardiac arrest/anoxic brain injury 3 months post-procedure, and 3) cardiac arrest 2 days post-procedure.

[3] Three pivotal patients had extended hospitalization following the implant procedure for further monitoring. All were subsequently discharged without sequelae.

[4] The AVG infections were adjudicated as unrelated to the Connector by the CEC.

[5] One roll-in patient developed an upper-extremity hematoma the day after graft implantation requiring emergent surgery. During surgery it was noted that the tacking suture had not engaged the Connector and the Connector dislodged from the graft.
[6] One roll-in patient underwent evacuation of an infected seroma noted at the post-implant follow up visit.
[7] AVG Implant Procedure includes the implantation of the AVG using the study device (Connector)

Table 11. Relatedness of Non-Serious Adverse Events

Non-Serious AE Type	Number of Patients	Relationship to Study Device			Relationship to AVG Implant Procedure[1]		
		Related	Possibly related	Not related	Related	Possibly related	Not related
Pivotal Study (N=158)							
Bleeding	2	1[2]	0	1	2	0	0
Desquamation	1	0	0	1	1	0	0
Erythema	1	1	0	1	1	0	0
Ischemia *(mild vascular steal, numbness in implanted limb)*	8	0	0	8	5	3	0
Pain	3	1	0	2	3	0	0
Paresthesia	1	0	0	1	0	1	0
Pruritus	2	0	0	2	2	0	0
Seroma	1	0	1	0	0	0	1
Stiffness, arm	1	0	0	1	1	0	0
Swelling, arm	7	0	2	5	4	3	0
Roll-in Patients (N=13) There were no non-serious AEs related to study device or AVG implant procedure							

[1] AVG Implant Procedure includes the implantation of the AVG using the study device (Connector)
[2] During the procedure, gutter bleeding with ~600 cc of blood noted and was subsequently controlled by placing a purse string suture at the venotomy site. The patient was hemodynamically stable and did not require pressors for hypotension.

2. Effectiveness Results

The 6-month primary endpoint analysis was based on 144 evaluable patients (132 reached the 6-month visit, and 12 patients had an abandoned graft prior to the 6-month visit). Key effectiveness outcomes are presented in **Figures 4** and **5**, and **Table 12** through **13**.

The primary endpoint of cumulative graft patency at 6 months with comparison to a target Performance Goal of 75% was met (P-value < .001). Kaplan Meier survival analysis is shown in **Figure 4**. The cumulative patency was 92.08% [estimated at 180 days] with a lower 95% Confidence Bound of 86.98% [Survival – 1.96 SE).

A total of 14 subjects were censored with partial follow-up observation through six months with 12 subjects having graft abandonment.

FIGURE 4. Kaplan-Meier Survival for Cumulative Patency (Primary Endpoint)

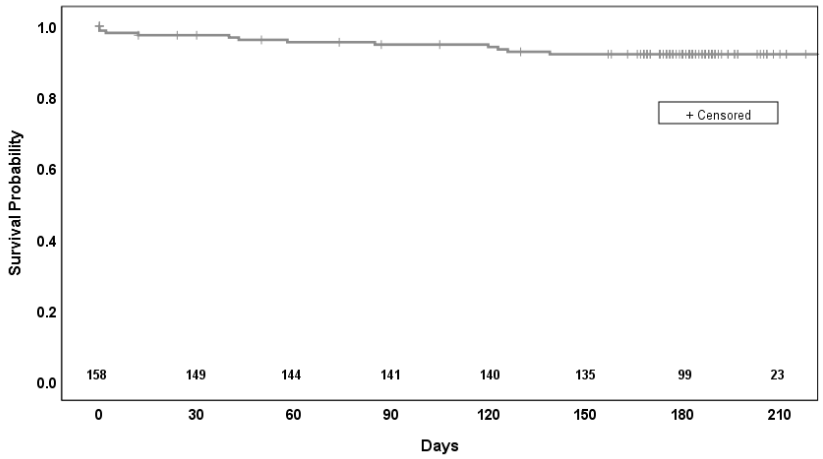
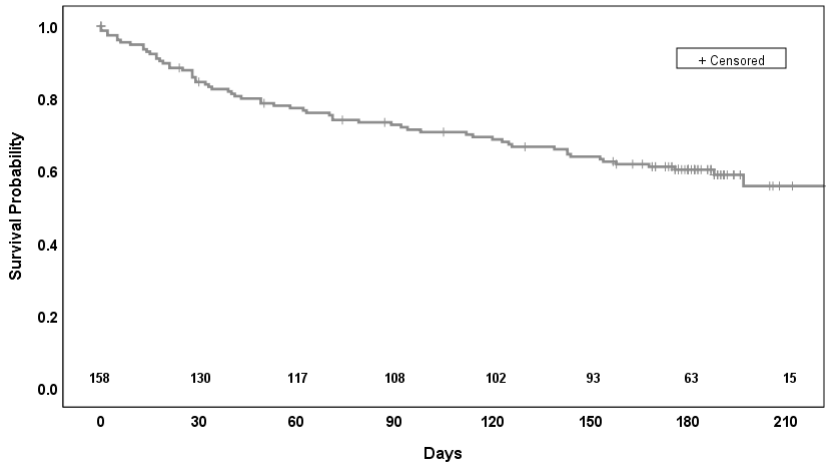


Table 12. Primary Endpoint Results – Cumulative Patency

Endpoint	Roll-in Patients (N=13)	Pivotal Study (N=158)
Cumulative patency at 6 months (primary endpoint)	77% (10/13)	92.08%[1]

3. Secondary Endpoints
   - Primary unassisted patency was 60.21% [estimated at 180 days] with a lower 95% Confidence Bound at 180 days of 50.84% [Survival – 1.96 SE][1]. Kaplan-Meier survival analysis is shown in **Figure 5**.

FIGURE 5. Kaplan-Meier Survival for Primary Unassisted Patency



[1] Hypothesis tests were not pre-specified for this endpoint and no multiplicity adjustment was applied.

Table 13. Primary Unassisted Patency

Endpoint	Roll-in patients	Pivotal Study
Primary unassisted patency at 6 months	46% (6/13)	60.21%[1]

- Acute device success was achieved in 100% of the 158 patients, with time to first cannulation at approximately 20 days (**Table 14**).

Table 14. Acute Device Success and Time to First Cannulation

Endpoint	Roll-in Patients	Pivotal Study
Acute device success: % of patients (n/N)	100% (13/13)	100% (158/158)
Time to first cannulation of AVG, days All subjects/grafts: Mean ± SD (range)	27.6 ± 24.8 (1.0 - 81.0)	20.1 ± 23.5 (1.0 - 134.0)

- **Table 15** summarizes the additional interventions required to maintain AVG patency**.** In the pivotal study, a total of 97 interventions to maintain secondary AVG patency were performed in 55 patients. Reasons for intervention were clinically driven in all cases. No AEs occurred during the intervention procedures. Stenoses were treated in 83 of the 97 interventions. In 14 interventions, there was no stenosis identified, and the intervention was performed for graft banding (5 patients), thrombectomy only (7 patients), and surgical revision (2 patients). During all interventions, the Connector was observed to be intact and properly positioned.

Table 15. Summary of Additional Interventions

Endpoint	Roll-in Patients (N=13)	Pivotal Study (N=158) .
Patients with at least 1 intervention to maintain AVG patency by 6 months	31% (4/13)	35% (55/158)
1 intervention	0% (0/13)	21% (33/158)
2 interventions	8% (1/13)	9% (14/158)
≥ 3 interventions	23% (3/13)	5% (8/158)[1]
Types of procedures during intervention, number of procedures[2]: *(NOTE: multiple types of procedures may have been performed during a single intervention.)*		
Angioplasty	76% (13/17)	79% (77/97)
Thrombectomy	76% (13/17)	71% (69/97)
Thrombolytic infusion	47% (8/17)	10% (10/97)
Stent placement	6% (1/17)	24% (23/97)
Embolectomy	0% (0/17)	1% (1/97)
Other surgery *(AVG banding, revision)*	18% (3/17)	13% (13/97)

[1] The majority of interventions were angioplasties; in 6 subjects the intervention was in the location of the device; a hematoma was noted in 2 cases; all others were completed without complication.
[2] Interventions were based on clinically driven best practices and standard of care in vascular access surveillance and monitoring at the discretion of the treating physician.

4. Sub-group Analyses

Two sub-group analyses were conducted to assess potential differences in key baseline criteria. The gender analysis was prespecified in the protocol. The analysis evaluating potential differences between African Americans and non-African Americans was conducted post-hoc due to the proportion of African Americans in the study being higher than what would be expected in the general population.

Cumulative Patency by Gender:

Cumulative patency for females estimated at 180 days was 90.4% (Peto SE 3.4%), with a 95% confidence interval of (83.7%, 97.1%). For males, 94.9% (Peto SE 3.8%), with a 95% confidence interval of (87.5%, 100.0%). Although the cumulative patency for males was observed to be higher than that for females, the difference was not found to be statistically significant (logrank p-value = 0.343). The lower 95% confidence bounds for both genders exceeded the Performance Goal of 75%.

Cumulative Patency by Race Category:

A higher percentage of Black or African American patients participated in the study (77.8%) than is present in the general US population. The cumulative patency at 6 months in Black or African American patients was 93.5%, compared to 88.6% in the non-Black or African American subjects No baseline factors were found to contribute to the nonsignificant but observed difference between cumulative patency results in the racial subgroups.

5. Pediatric Extrapolation

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

XI. 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 study included 14 investigators and sub-investigators of which none 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: none
- Significant payment of other sorts: 2 investigators

- Proprietary interest in the product tested held by the investigator: none
- Significant equity interest held by investigator in sponsor of covered study: none

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. Statistical analyses were conducted by FDA to determine whether the financial interests/arrangements had any impact on the clinical study outcome. The information provided does not raise any questions about the reliability of the data.

XII. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

A. Extended Follow Up Study

An Extended Follow-up Study was conducted under G140221 to collect an additional six months of follow-up information to establish the rate of post-intervention patency for pivotal subjects with a Connector in their access circuit. Among 37 total subjects with extended follow-up data collected, continued vascular access at the end of the extended follow-up period was reported in 29 subjects. Five subjects had abandoned grafts and three subjects died during the extended follow-up period. The deaths were not related to the device as reported by the sites. One or more additional graft interventions were performed in 13 subjects. All of these interventions were successful and there were no major procedural adverse events reported. There were no reports of migration, kink, compression, or other damage/defect to the implanted Connector. A rate of 1.32 interventions per patient-year was estimated.

B. Continued Access Study

A Continued Access Study was conducted under G140221 with similar study methods and data collection to those used in the pivotal study. A total of 12 patients were enrolled. Six-month follow-up was completed in accordance with the protocol.

Acute device success was achieved in all patients. There were no procedural complications. Five subjects completed the study with cumulative patency at six months. Death occurred in two subjects (unrelated to the Connector or AVG implant as reported by the sites) and one other subject was removed early from the study after receiving a kidney transplant. Reasons for AVG abandonment in four subjects included: graft infection (n=1), recurrent thrombosis (n=2), and puncture site hematoma with graft damage (n=1); all reasons were unrelated to the Connector, as determined by the site investigators. Twelve AVG intervention procedures were performed among 5 subjects and all interventions were successful (graft flow restored), with no adverse events. There were no reports of migration, damage, or defect to the implanted Connector.

XIII. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory System Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIV. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The Performance Goal of the primary endpoint (cumulative graft patency at 6 months) was met (p-value < .001). By Kaplan Meier survival analysis, cumulative patency was 92.08% with a lower 95% Confidence Bound of 86.98%. Primary unassisted patency (secondary endpoint) was 60.21% with a lower 95% Confidence Bound of 50.84%. The patency rates are comparable to those reported in literature for AVGs with sutured anastomosis[1-4].

Acute Technical Success was 100% and the average time to first cannulation was 20 days. The number and type of interventions were consistent with clinical expectations through 6 months.

These data suggest that the EndoForce™ System is effective at providing a secure venous anastomosis while maintaining adequate patency of the access circuit. It is important to note that use of this device warrants adjunct use of traditional suturing for the arterial anastomosis of an arteriovenous graft.

There were no meaningful outcome differences by sex or race impacting the effectiveness of the device.

B. Safety Conclusions

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

Protocol defined serious adverse events included: death, emergent surgery, infection requiring treatment, significant bleeding, and pseudoaneurysm. The site-reported relatedness was reviewed and adjudicated by a Clinical Events Committee (CEC). There were three deaths during the pivotal study, none of which were considered related to the Connector by the CEC. Six subjects had AVG infections that required surgical excision of the graft. None of the AVG infections were considered to be related to the Connector by the CEC. There were no reports of emergent surgery, significant bleeding or pseudoaneurysm.

There were no meaningful outcome differences by sex/gender or race impacting the safety of the device.

C. Benefit-Risk Determination

The probable benefits of the device are also based on data collected in the clinical study conducted to support PMA approval as described above. The probable benefit of using the EndoForce™ System is allowing creation of a secure venous anastomosis while maintaining the patency of the access circuit. The likelihood of a patient experiencing a benefit is high, based on a 6-month cumulative patency rate of 92%. The probable risks of the device are also based on data collected in the clinical study conducted to support PMA approval as described above. The overall rate of serious adverse events observed in the study was 5.7%. Overall, the type and rate of serious adverse events observed in the clinical study were similar or lower than those reported in literature for this patient population.

Additional factors to be considered in determining probable risks and benefits for the EndoForce™ System included:

- Absence of longer term clinical follow-up data;
- Absence of clinical data on devices built post implementation of design and manufacturing changes

1. Patient Perspectives

This submission either did not include specific information on patient perspectives or the information did not serve as part of the basis of the decision to approve or deny the PMA for this device

In conclusion, given the available information above, the data support that for the venous anastomosis of an arteriovenous graft for hemodialysis, the probable benefits of the EndoForce™ Connector for Endovascular Venous Anastomosis outweigh the probable risks.

D. Overall Conclusions

The data in the PMA 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 clinical study demonstrate safety and effectiveness of the EndoForce™ System in creating an anastomosis by endovascular attachment of an arteriovenous graft to the vein. The benefits of the use of the EndoForce™ System include a satisfactory cumulative patency rate at 6 months and were achieved with minimal added risk.

XV. CDRH DECISION

CDRH issued an approval order on May 15, 2025. The final clinical conditions of approval cited in the approval order are described below.

1. EndoForce Post-Approval Study: This is a prospective, multi-center study to evaluate the safety and effectiveness of the EndoForce Connector for Endovascular Venous Anastomosis in the long term and under real world conditions. The study will enroll 150 subjects with end stage renal disease (ESRD) and who are candidates for vascular grafts placed in the upper extremity in up to 20 centers in the US. The study will have a minimum of 75 evaluable subjects at 24-months post implantation. Clinical outcomes at 1, 3, 6, 12, 18 and 24 months will include cumulative patency, primary patency, time to first cannulation and number, reason, and type of reinterventions until access abandonment or through study completion. Acute device success will be evaluated at end of index procedure. Safety will be assessed by reporting all device and/or procedure-related events and all major adverse events that reasonably suggest the involvement of the device and that require or result in any of the following: death, emergent surgery, events requiring hospitalization, events requiring percutaneous interventions, vascular access infection requiring treatment, significant bleeding, pseudoaneurysm and serious adverse events through all follow-up visits. Device migration, inadequate seal and leakage will also be reported at all follow-up visits. All endpoints will be analyzed descriptively.

From the date of study protocol approval, the following timelines will be met for the EndoForce Post-Approval Study:

- First subject enrolled within 6 months
- 20% of subjects enrolled within 12 months
- 50% of subjects enrolled within 18 months
- 100% of subjects enrolled within 24 months

In addition, separate periodic reports will be submitted on the progress of EndoForce Post-Approval Study as follows:

- PAS Progress Reports every six (6) months until subject enrollment has been completed, and annually thereafter, from the date of the PMA approval letter, unless otherwise specified by FDA.
- If any enrollment milestones are not met, you must begin submitting quarterly enrollment status reports every 3 months in addition to your periodic (6-month) PAS Progress Reports, until FDA notifies you otherwise.
- Submit the Final PAS Report three (3) months from study completion (i.e., last subject's last follow-up date).

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

XVI. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

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

Post-approval Requirements and Restrictions:
See approval order.

XVII. REFERENCES

1. Glickman MH, Burgess JB, Cull D et al. Prospective multicenter study with a 1-year analysis of a new vascular graft used for early cannulation in patients undergoing hemodialysis. *J Vasc Surg* 2015; 62:434-41

2. Ottaviani N, Deglise S, Brizzi V et al. Early Cannulation of the Flixene™ Arteriovenous Graft. *J Vasc Access* 2016; 17: S75-78

3. Halbert RJ, Nicholson G, Nordyke RJ et al. Patency of ePTFE Arteriovenous Graft Placements in Hemodialysis Patients: Systematic Literature Review and Meta-analysis *Kidney360* 2020;1(12):1437-1446

4. Hurlbert SN, Mattos MA, Henretta JP et al. Long-term patency rates, complications and costeffectiveness of polytetrafluoroethylene (PTFE) grafts for hemodialysis access: a prospective study that compares Impra versus Gore-tex grafts. Cardiovas Surg 1998; 6:652-656