SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Vascular Hemostasis Device
Device Trade Name:	Cross-Seal™ Suture-Mediated Vascular Closure Device System (Cross-Seal™ System)
Device Product Code:	MGB
Applicant's Name and Address:	Medeon Biodesign, Inc. 7F, 116, HouGang St. Taipei 11170, Taiwan
Date(s) of Panel Recommendation:	None
Premarket Approval (PMA) Number:	P210017
Date of FDA Notice of Approval:	9/26/2023

II. INDICATIONS FOR USE

The Cross-Seal Suture-Mediated Vascular Closure Device System is indicated for the percutaneous delivery of sutures for closing the common femoral artery access site while reducing time-to-hemostasis in patients who have undergone diagnostic or interventional catheterization procedures using 8F to 18F introducer sheaths. The Cross-Seal System is indicated for one access site per leg.

III. CONTRAINDICATIONS

There are no known contraindications.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Cross-Seal System labeling.

V. DEVICE DESCRIPTION

The Cross-Seal Suture-Mediated Vascular Closure Device System (Cross-Seal System) is designed to deliver two pairs of monofilament polypropylene sutures simultaneously to close the femoral artery access sites of patients who have undergone diagnostic or interventional catheterization procedures. The System employs a pre-close technique whereby sutures are delivered and pre-tied prior to an index procedure. At the conclusion of the index procedure,

the pre-tied knots in the suture are then advanced to the close the arteriotomy. The Cross-Seal System components are not made from latex rubber.

The Cross-Seal System is comprised of the Cross-Seal Device (**Figure 1**) and three accessories: (1) the Knot Tyer (**Figure 2**), (2) Knot Pusher (**Figure 3**), and (3) Suture Trimmer (**Figure 4**).

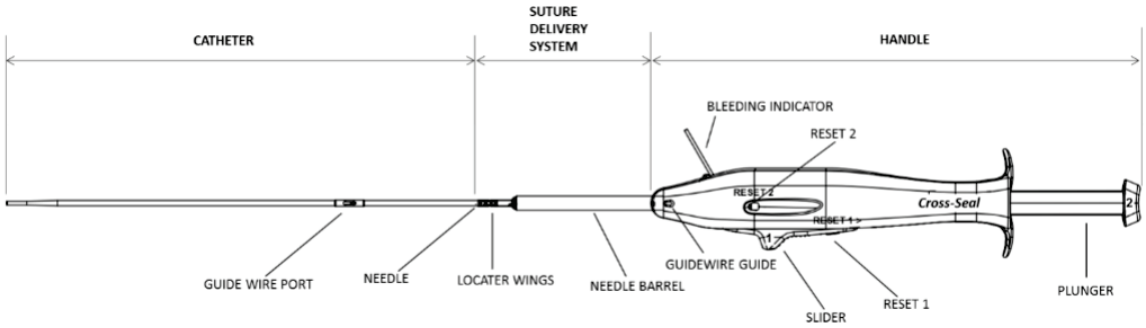

Figure 1: Cross-Seal Device

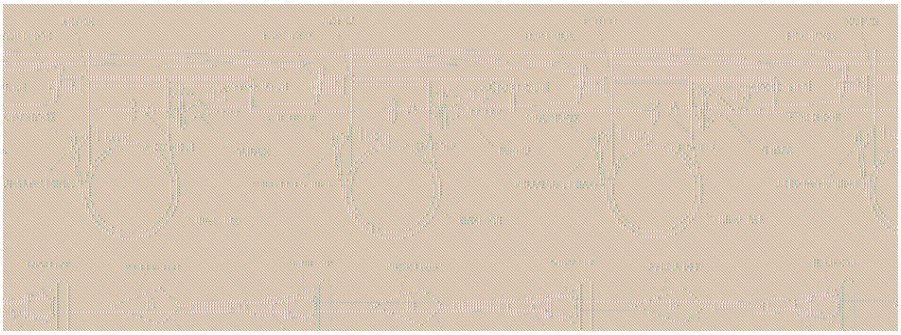

Figure 2: Knot Tyer

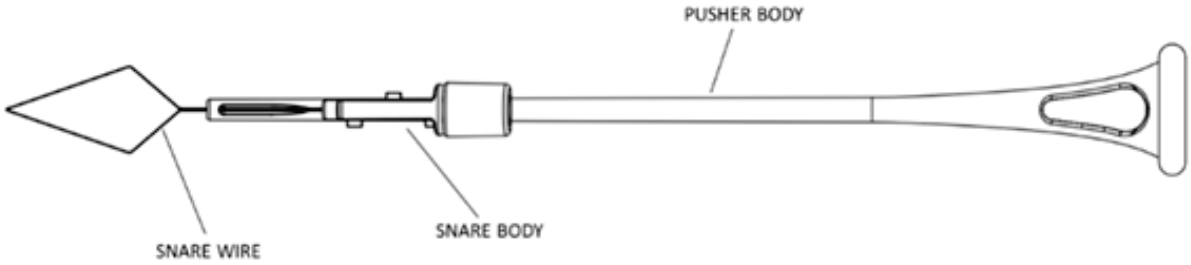

Figure 3: Knot Pusher

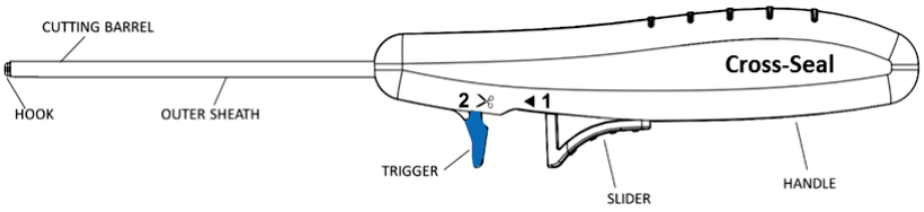

Figure 4: Suture Trimmer

The Cross-Seal System applies a pre-close technique for arteriotomy closure. After femoral puncture, a blunt dissection over an 8F dilator is performed and the Cross-Seal Device is delivered into the femoral artery over an indwelling guidewire. After the dilator and guidewire are withdrawn, the Cross-Seal Device is used to deliver two pairs of monofilament polypropylene sutures simultaneously around the femoral artery access site. The 8F dilator is reinserted and the Knot Tyer accessory is used to pre-tie Fisherman's knots for the two pairs of sutures before the diagnostic or interventional procedure. Following the diagnostic or interventional procedure, the Cross-Seal Knot Pusher and Suture Trimmer Accessories are used to advance the knots to the arteriotomy and trim the trailing ends of the sutures, respectively.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several alternatives for achieving closure or hemostasis of femoral arteriotomies following the use of access sheaths in endovascular catheterization procedures. These include manual and mechanical compression as well as other commercially available vascular closure devices which utilize collagen plugs, nitinol clips, sutures, and other methods. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

A previous generation of the Cross-Seal System received European Union CE Mark approval on September 27, 2019. Medeon Biodesign, Inc. subsequently withdrew this CE Mark on October 27, 2020 for marketing considerations unrelated to device safety or effectiveness. No other marketing authorizations were obtained for previous generations of the device in the United States or any foreign country.

The current generation of the device 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 vascular closure devices, including the Cross-Seal device:

- Allergic reaction or hypersensitivity to device components
- Anemia
- Arterial stenosis/occlusion
- Arteriovenous fistula
- Bleeding/hemorrhage
- Bruising
- Death
- Deep vein thrombosis
- Device entrapment

- Device failure/malfunction/misplacement
- Diminished pulses distal to closure site
- Embolism
- Extended Hospitalization / Delayed time to ambulation
- Hypotension / hypertension
- Hematoma
- Infection/sepsis
- Inflammation
- Intimal tear/dissection
- Ischemia distal to closure site
- Nerve injury
- Numbness
- Pain
- Perforation
- Pseudoaneurysm
- Pulmonary embolism
- Retroperitoneal hematoma/bleeding
- Superficial vein thrombosis
- Surgical exposure/closure of common femoral artery
- Thrombus formation
- Vascular injury
- Vasovagal episode
- Vasoconstriction/vasospasm
- Wound dehiscence

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

IX. SUMMARY OF NONCLINICAL STUDIES

A. Laboratory Studies

Bench testing was performed in accordance with design verification test protocols that were developed to verify that the device meets product specifications. Bench testing included the following:

Table 1: Summary of Bench (Design Verification) Testing

Test	Purpose	Acceptance Criteria	Results
Bleeding Channel Connection Test	Verify the bleeding back function of the bleeding indicator	Visual confirmation of simulated bleeding back from the bleeding indicator	Pass
Locator Wings Fatigue Test	Verify the durability of the locator wings	Visual confirmation of component integrity after cycling (> 15 cycles)	Pass
Bailout Button Function Test	Verify the retraction functionality of the bailout button	Confirmation of button functionality through cycling (5 cycles)	Pass

Test	Purpose	Acceptance Criteria	Results
Slider Adhesion Fatigue Test	Verify the fatigue performance of the slider of the Cross-Seal device	Confirmation of slider functionality through cycling (>10 cycles)	Pass
Locator Wings Loading Test	Verify the load-bearing capability of the locator wings	Confirmation of component integrity after deployment in worst case model (5.5 mm thickness)	Pass
Device Performance Test	Verify the deployment force of the plunger	Plunger force ≤ 50 N	Pass
Dish Resistant Test	Verify the dish resistance force (equivalent to the plunger deployment force) of the Cross-Seal device	Dish resistance force ≤ 50 N	Pass
Catheter Joint Force Test	Verify the connection force between the catheter module and shaft	Catheter joint force > 15N	Pass
Guidewire Port Function Test	Verify the functionality of the guidewire port of the device	Withstand 12 cycles with no damage or breaking	Pass
Guidewire Port Adhesion Force Test	Verify the connection force between the catheter and the hemostasis valve	Connection force > 5 N	Pass
MECH Base Holding Force Test	Verify the connection force between the shaft and MECH base	MECH base connection force > 50 N	Pass
Needle push element pullout force test	Verify the connection force between the central wire and bonding part on the needle push element	Pullout force > 50N	Pass
Needle base tip bending test	Verify the flexibility of the MB wire needle base tip	Visual confirmation of component integrity after 60° bend	Pass
Central wire pullout force test	Verify the connection force between the central wire and rack module	Pullout force > 50 N	Pass
Catcher head holding force test	Verify the connection force between the catcher head and catcher link tube	Catheter head connection force > 50 N	Pass
Catcher link coupler holding force test	Verify the connection force between the catcher link coupler and the catcher link tube	Catheter link coupler connection force > 50 N	Pass
Slider holding force test	Verify the connection force between the slider and the needle barrel of the device	Connection force between the Slider and Needle Barrel > 5 N	Pass
Suture Attached Force Test	Verify that the connection force between the Suture and the needle of the device	Needle-Suture connection force > 5 N	Pass
Catcher Link Head Module Adhesion Force Test	verify the connection force between the Catcher Link Head and the Bleeding Indicator of the device	Connection force of the Bleeding Indicator > 5 N without dislodgement	Pass
Needle detention force test	Verify the detention force between the MB wire and the needle	Needle tip retention force within 3-12 N	Pass
Catheter joint torque test	Verify the connection torque between the shaft and the catheter module	Catheter joint torque force > 300 gf-cm	Pass

Test	Purpose	Acceptance Criteria	Results
Catheter kink test	Verify that the kink resistance of the catheter	Visual confirmation of component integrity after 60-degree bend	Pass
Needle base pullout force test	Verify the connection force between the MB wire and needle push element	Pullout force > 18 N	Pass
Dish Catching Ability Test	Verify the Dish performance and Needle catching force of the device	Catching force of the Needle tip > 14 N /needle	Pass
Dish Deconstruction Test	Verify the durability of the Dish of the device	Dish load bearing capability > 40 N without deconstruction	Pass
Pusher knot trapping test	Verify that the suture knot will not become trapped in the Knot Pusher	Force to release knots from the knot pusher < 3 N	Pass
Pusher Yielding Test	Verify the yielding force of the Knot Pusher	1) No crack/breakage on Pusher body at 30N preload force along the pushing direction 2) Bending ratio < 1% under 5N preload	Pass
Pusher Snare Function Test	to verify the Snare function of the Knot Pusher	1) Disengagement force between the snare and pusher body within 1-8 N 2) Suture loading force < 8 N	Pass
Trimmer functionality test	Verify the suture cutting functionality of the Trimmer	Visual confirmation of cutting functionality and residual suture limb length (> 5.0mm)	Pass
Trimmer durability test	Verify the cutting durability of the Suture Trimmer	cut at least 4 times with two sutures loaded	Pass
Tyer functionality test	Verify the functionality of the Tyer	Confirmation of successful knot creation	Pass
Tyer trigger force test	Verify the disengagement force between the pull ring and Tyer body of the Knot Tyer	Disengagement force between the pull ring and the Tyer body 8N+/-5N.	Pass
Tyer suture holding test	Verify the suture holding force of the Knot Tyer	Top Hook suture holding force > 3 N	Pass

B. Sterilization

The Cross-Seal System is sterilized using ethylene oxide (EO) through a process validated per ISO 11135:2014. Results obtained from the sterilization validation demonstrate that the product satisfies a minimum Sterility Assurance Level (SAL) of 10^{-6}. In addition, the amount of EO residuals and bacterial endotoxins was verified to be within appropriate specification limits.

C. Biocompatibility

The biocompatibility of the Cross-Seal System was assessed in accordance with ISO 10993-1 and relevant FDA guidance. Within the Cross-Seal System, the Cross-Seal Device Delivery System, the Knot Tyer, the Knot Pusher and the Suture Trimmer are classified as external communicating devices in contact with tissue and/or circulating blood for limited duration (less than 24 hours); the sutures within the device are classified as an implant device with circulating blood contact for a permanent duration (greater than 30 days). The following tests were carried out on the Cross-Seal Delivery System, Knot Tyer, Knot Pusher, and Suture Trimmer. The sutures used in the Cross-Seal System were

previously cleared for cardiovascular use under K153076 and the biocompatibility of the sutures was previously assessed through testing in compliance with ISO 10993-1.

Table 2: Summary of Biocompatibility Testing

Biocompatibility Endpoint	Standard Followed	Specific Test	Result
Cross-Seal Device Delivery System, Knot Tyer, Knot Pusher, and Suture Trimmer			
Cytotoxicity	ISO 10993-5	ISO MEM Elution / MTT Assay Using L929 Mouse Fibroblast Cells	Pass
Sensitization	ISO 10993-10	ISO Guinea Pig Maximization Sensitization Test	Pass
Intracutaneous reactivity/irritation	ISO 10993-10	ISO Intracutaneous Irritation Test	Pass
Acute systemic toxicity	ISO 10993-11	ISO Acute Systemic Injection Test	Pass
Hemolysis	ISO 10993-4	ASTM Hemolysis – Direct Contact and Extract Method	Pass
Complement activation	ISO 10993-4	Complement Activation SC5b-9 Assay	Pass
In vivo thrombogenicity	ISO 10993-4	Thrombogenicity Study in Ovine Model	Pass
Material mediated pyrogenicity	ISO 10993-11	ISO Materials Mediated Rabbit Pyrogen Test	Pass

The Cross-Seal System passed all assessments to which it was subjected, demonstrating the biocompatibility of the device as per ISO 10993-1.

D. Packaging Testing

The packaging of the Cross-Seal System was evaluated in accordance with the requirements of ISO 11607-1. The packaging integrity test samples were subjected to sterilization, environmental conditioning, simulated shipping, and 12-month real time aging that were in accordance with the applicable ASTM standards. The device passed the packaging simulations and confirmed the sterile barrier integrity and minimum seal strength for the Cross-Seal System device packaging could be maintained per the standard test methods. Following the shipping simulations, it was confirmed that the Cross-Seal System meets the performance specifications.

E. Shelf-Life Testing

The Cross-Seal System was evaluated for performance and durability to support a shelf life of 12 months. Samples utilized in this testing were subjected to environmental conditioning, transit simulation, and real time aging for a period of 12 months. Testing was then conducted to assess the integrity, functionality, and performance of the aged samples against set specifications. The test samples met all the pre-defined acceptance criteria. Based upon the testing, the Cross-Seal System is labeled with a 12-month shelf life.

F. Animal Studies

Several *in vivo* acute and chronic animal studies using the previous generation and the current generation of the Cross-Seal device were conducted to demonstrate the safety and feasibility of the Cross-Seal System. A total of 27 closures were performed in 22 animals (ovine) using previous generations of the device. To confirm system performance and evaluate thrombogenicity, an acute study in 2 animals (ovine) was performed on the current generation device. The following table provides a summary of the design validation animal studies.

Table 3: Summary of Animal Studies

Device	Studies Conducted	Key Findings
Previous Generations	Acute + Chronic (30D)	• In the acute studies, procedural evaluations were performed to assess the ability of the device to achieve hemostasis absent safety complications, as well as technical evaluations which assessed the ability to track the device to the arteriotomy percutaneously • The acute assessments demonstrated a high degree of success for the use of the Cross-Seal device and accessories • In the chronic studies, necropsy and histopathology assessments were used to assess vessel damage and healing after 30 days • The chronic studies revealed healing of the arteriotomies with neointima formation and endothelialization on the luminal surface of the closure site
Current Generation	Acute	

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of vascular closure with the Cross-Seal System under IDE G180143. Data from this clinical study was the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

The study was a prospective, multi-center, single arm clinical study designed to investigate the safety and effectiveness of the Cross-Seal System for closure of the femoral artery access site in patients who had undergone interventional catheterization procedures using 8-18 French (Fr) internal diameter procedural sheaths. The study was conducted at 19 investigational sites in the United States. The clinical study protocol stipulated that the study patients were scheduled to undergo elective (not emergent or

urgent) percutaneous procedures for transcatheter aortic valve replacement/implantation (TAVR/TAVI); endovascular aortic aneurysm repair (EVAR), which is usually endovascular abdominal aortic aneurysm repair; thoracic endovascular aortic repair (TEVAR); or balloon aortic valvuloplasty (BAV). However, in the study there were no patients who underwent BAV. All of the study patients underwent TAVR/TAVI, EVAR, or TEVAR.

The study data for the primary safety and primary effectiveness endpoints were compared to performance goals (PGs) The primary safety endpoint was freedom from major complications of the target limb access site within 30 days post-procedure, and was compared to a PG of 85.2% for major complications, expressed as an event-free rate and based on clinical data in the Summary of Safety and Effectiveness Data (SSED) for the Abbott Vascular Perclose ProGlide VCD. The primary effectiveness endpoint was time-to-hemostasis (TTH), and was compared to a PG of 15 minutes for TTH, based on the results observed for TTH in the ProGlide VCD PEVAR trial, published by Nelson *et al.* in 2014.

A total of 147 subjects were enrolled in the study, with 51 subjects in the roll-in cohort and 96 subjects in the pivotal cohort. Up to 2 roll-in patients per investigator were allowed to give investigators an opportunity to learn how to use the Cross-Seal device. Patient enrollment in the study was suspended by Terumo Medical and the study was then terminated by Terumo Medical earlier than planned due to the COVID-19 pandemic, since travel limitations as a result of the COVID-19 pandemic had adversely impacted study enrollment, patient follow-up, and ongoing data monitoring. This early termination was approved by the FDA, with there being a sufficient number of enrolled patients to evaluate the Cross-Seal device.

When enrollment of the study patients was suspended, the clinical protocol was accordingly revised to accommodate the challenges of patient follow-up during the COVID-19 pandemic. In order to address the potential for underpowered analyses of the primary safety and effectiveness endpoints due to the decrease in the number of enrolled study patients from the number originally planned, the statistical analysis plan was revised such that if the number of evaluable patients for the primary safety and effectiveness endpoints dropped below the estimated sample size for each, then the sample size would be augmented by adding the last 18 consecutively enrolled patients from the roll-in arm. The evaluable sample size for the primary safety endpoint was 88 which exceeded the 78 patients required from the sample size justification, so there was no need to add roll-in patients for this safety analysis. The term “pivotal safety cohort” was used to refer to the 96 pivotal-only patients for the safety analysis cohort and to refer in general to the 96 pivotal-only patients. For the primary effectiveness endpoint, the evaluable sample size was 85 which was just below the 86 patients required from the sample size justification. Therefore, the last 18 roll-in patients were added for this effectiveness analysis and the term “pivotal effectiveness cohort” was used to refer to the effectiveness analysis cohort of 114 patients consisting of 96 pivotal plus 18 roll-in patients.

For the roll-in patients, the first date of enrollment was 8/9/19, the last date of enrollment was 2/24/20, and the last follow-up completion date was 5/13/20. For the pivotal patients, the first date of enrollment was 9/5/19, the last date of enrollment was 3/12/20, and the last follow-up completion date was 10/8/20.

As noted below, follow-up visits were done at 30-days post-procedure. Duplex ultrasound (DUS) imaging was done at the 30-day follow-up visit, and DUS exam was to be repeated at 60 days post-procedure if there was an abnormal DUS finding at the 30-day visit.

An independent Core Laboratory was used to evaluate all ultrasound images. An independent Data and Safety Monitoring Board (DSMB) reviewed aggregated data from the study at 3 time-points during study enrollment. An independent Clinical Events Committee (CEC) was responsible for systematic review and adjudication of major complications, minor complications and unanticipated adverse device effects (UADEs).

1. Clinical Inclusion and Exclusion Criteria

   Enrollment in the Cross-Seal VCD IDE clinical study was limited to patients who met the following inclusion criteria:

   1) Subject was ≥ 18 years old
   2) Subject was scheduled for elective or planned (i.e., not emergent, or urgent) percutaneous transcatheter interventional procedures involving access through the femoral artery using 8-18 French (Fr) ID procedural sheaths (i.e., BAV, TAVR/TAVI, EVAR, TEVAR)
   3) Subject was able to undergo emergent vascular surgery if a complication related to the vascular closure necessitates such surgery
   4) Subject was willing and able to complete follow-up requirements
   5) Subject had the mental capacity to consent for themselves (i.e., does not require the use of a Legally Authorized Representative), and signs a written Informed Consent Form (ICF) prior participating in the study

   Patients were not permitted to enroll in the Cross-Seal IDE clinical study if they met any of the following exclusion criteria:

   1) Prior intra-aortic balloon pump at access site
   2) Subjects with severe inflow disease (iliac artery diameter stenosis > 50%) and/or severe peripheral arterial disease (Rutherford Classification 5 or 6), as confirmed with prior standard of care CT Imaging, duplex ultrasound, and/or intra-procedural fluoroscopy
   3) Common femoral artery lumen diameter was< 5 mm
   4) In opinion of the investigator, significant scarring of the target access site which would preclude use of the device in accordance with the IFU
   5) Prior target artery closure with any closure device < 90 days, or closure with manual compression ≤ 30 days prior to index procedure
   6) Prior vascular surgery, vascular graft, or stent in region of access site
   7) Subjects receiving glycoprotein IIb/IIIa inhibitors before, during, or after the catheterization procedure

8) Subjects with significant anemia (Hgb < 10 g/dL, Hct < 30%)
9) Subject with known bleeding disorder including thrombocytopenia (platelet count < 100,000), thrombasthenia, hemophilia or Von Willebrand's disease
10) Subject with renal insufficiency (serum creatinine level > 221µmol/L or 2.5 mg/dL), on dialysis therapy, or with renal transplant
11) Known severe allergy to contrast reagent that cannot be managed with premedication
12) Inability to tolerate aspirin and/or other anticoagulation/antiplatelet treatment
13) Planned anticoagulation therapy post-procedure such that ACT was expected to be elevated above 350 seconds for more than 24 hours after the procedure
14) Connective tissue disease (e.g., Marfan's Syndrome)
15) Thrombolytics (e.g., t-PA, streptokinase, urokinase), Angiomax (bivalirudin) or other thrombin-specific anticoagulants ≤ 24 hours prior to the procedure
16) Recent (within 8 weeks) cerebrovascular accident or Q-wave myocardial infarction
17) Subjects who are morbidly obese (BMI > 40 kg/m2)
18) Planned major intervention or surgery, including planned endovascular procedure in the target leg, within 30 days following the interventional procedure
19) Subject unable to ambulate at baseline (i.e., confined to wheelchair or bed)
20) Currently participating in a clinical study of an investigational device or drug that has not completed its primary study endpoint
21) Known allergy to any device component
22) Subject was known or suspected to be pregnant or lactating
23) Evidence of active systemic or local groin infection
24) Subject has other medical, social, or psychological problem that in the opinion of the investigator precludes them from participating
25) Subject was mentally incompetent or a prisoner
26) New York Heart Association (NYHA) Class IV heart failure that was uncontrolled and requires treatment in the Intensive Care Unit within 24 hours prior to the index procedure
27) Left Ventricular Ejection Fraction (LVEF) < 20%
28) Unilateral or bilateral lower extremity amputation
29) Known existing nerve damage in the target leg
30) Subjects who have already participated in this IDE study

During the procedure, patients were <u>not</u> permitted to enroll in the study if they met any of the following intra-procedure exclusion criteria:

1) Access site above the most inferior border of the inferior epigastric artery (IEA) and/or above the inguinal ligament based upon bony landmarks
2) Access site in the profunda femoris or superficial femoral arteries, or the bifurcation of these vessels
3) Ipsilateral femoral venous sheath during the catheterization procedure
4) Common femoral artery calcium, which was visible with prior CT Imaging and/or duplex ultrasound

5) Subject in which there was difficulty inserting the procedural sheath or need for greater than 2 ipsilateral arterial punctures at the start of the catheterization procedure
6) Difficulty in obtaining vascular access resulting in multiple arterial punctures and/or posterior arterial puncture
7) Evidence of a pre-existing hematoma (> 1.5 cm in diameter), arteriovenous fistula, pseudoaneurysm, or intraluminal thrombosis at the access site
8) Marked tortuosity (at the investigator's discretion) of the femoral or external iliac artery in the target leg based on prior CT imaging, fluoroscopy, and/or duplex ultrasound
9) Angiographic evidence of arterial laceration, dissection, or stenosis in the femoral artery that would preclude use of the investigational device 40. Target arteriotomy > 18Fr sheath
10) Target arteriotomy > 18Fr sheath

2. Follow-up Schedule

Patients were scheduled to return for follow-up examinations at 30 ± 7 days and 60 ± 14 days post-procedure (if an abnormal finding was encountered at the 30-day visit) and, if affected by the COVID-19 pandemic, an unscheduled visit was permitted through 1-year post-procedure. All patients underwent a physical exam and femoral Duplex ultrasound (DUS) imaging at the 30-day visit. Physical exam and DUS exam was to be repeated at 60 days post-procedure if there was an abnormal DUS finding at the 30-day visit. DUS was used to evaluate the access site for complications including vessel stenosis, vessel occlusion, thrombus, hematoma, pseudoaneurysm, arteriovenous fistula, or foreign body post-deployment of the Cross-Seal device.

Preoperatively, a medical history was obtained including a record of the subject's demographic (i.e., age, race, ethnicity, and gender) and baseline information (i.e., height, weight, and labs). A baseline (within 180 days prior to consent) Computed Tomography Angiography (CTA) scan of the aorta, iliac, and common femoral vessels was optional to measure vessel size and assess potential access sites for disease and calcium deposits. These criteria could be assessed by a combination of angiography and ultrasound on the day of procedure if a CT scan was not available. Various laboratory tests were performed within 2 weeks of the index procedure. Subjects were evaluated against the inclusion and exclusion criteria. At the beginning of the endovascular procedure, the access site was assessed to verify the intra-procedure eligibility criteria. The Cross-Seal device was then deployed, sutures were pre-tied using accessories included with the device, the procedural sheath was inserted, and the procedure was completed. At the end of the endovascular procedure, the procedural sheath was removed, and the pre-tied knots were advanced to the arteriotomy and tightened while time-to-hemostasis was recorded.

Postoperatively, the objective parameters measured during the study included any access site-related events, events occurring in the ipsilateral leg, or systemic events that could be Cross-Seal device related. Adverse events and complications were

recorded at all visits. **Table 4** below summarizes the schedule of assessments following Cross-Seal deployment:

Table 4: Cross-Seal Pivotal Trial Schedule of Assessments

Assessment	Screening / Baseline	Index Procedure	Post Procedure to Hospital Discharge	30-Day and 60-Day Follow-up	Unscheduled Visit
Informed Consent	X				
Eligibility Criteria	X	X			
Medical History/Demographics	X				
Pregnancy Test	X				
Blood Testsμ	X				
Femoral Artery Imaging (CT scan)– within 6 months prior to index procedure§	X				
Femoral Artery Angiography±		X			
Activated Clotting Time (ACT)		X			
Time-to-Hemostasis (TTH)		X			
Time-to-Ambulation			X		
Time-to-Discharge (TTD)			X		
Targeted Physical Exam, including groin exam				X	X[a]
Femoral Duplex Ultrasound (DUS)*				X	X[a]
Concomitant Medications (Anticoagulation / Antiplatelets Only)	X	X	X	X	X
Adverse Events ⌘		X	X	X	X
Phone Call assessment of AEs and patient condition					X

μ Blood Tests include Complete Blood Count (CBC), Platelet Count, Serum Creatinine, Hemoglobin (HGB), Blood Urea Nitrogen (BUN), and Hematocrit (HCT) to assess eligibility criteria (collected within 2 weeks prior to index procedure) Pregnancy test if female of child-bearing potential (collected within 7 days prior to index procedure according to site standard of care)

* Femoral Duplex Ultrasound is required for assessment of groin/access site related complications. If subject has an abnormal 30-day DUS, subject will be required to return for an additional DUS at 60 days post-index procedure.

§ Standard of care CT Imaging modality performed to assess femoral artery quality per trial criteria (collected within 6 months prior to index procedure). *Note: If subject does not have a previous CT imaging modality, a micro puncture and angiogram intra-procedure may be utilized to confirm eligibility criteria.*

± Femoral Angiography for assessment of quality of femoral artery and puncture site prior to utilizing investigational device.

⌘ Adverse events were recorded at any time during the course of the study from time of enrollment through 30 days post-index procedure. Should a subject require a repeat DUS, AEs will be collected through 60 days post-index procedure.

[a] If clinically indicated.

3. Clinical Endpoints

As noted above, the primary safety endpoint was freedom from major complications of the target limb access site within 30 days post-procedure. The secondary safety endpoints were freedom from minor complications of the target limb access site within 30 days post-procedure, device-related-complications (DRCs), procedural complications within 30 days post-procedure, and an evaluation of all adverse events (AEs) from the time of investigational device use to 30 days post-procedure or to 60 days post-procedure for patients requiring a repeat DUS/physical exam, including major and minor complications.

Major Complications were defined as:

- Vascular injury attributable to the investigational device that requires surgical repair, stent-graft, or balloon angioplasty
- Access site-related bleeding attributable to the investigational device that requires transfusion
- Any new access site-related ipsilateral lower extremity ischemia attributable to the investigational device and documented by patient symptoms, physical exam, and/or decreased or absent blood flow on lower extremity angiogram
- Surgery for access site-related nerve injury attributable to the investigational device
- Permanent (lasting > 30 days) access site-related nerve injury attributable to the investigational device
- Access site infection requiring intravenous antibiotics and/or extended hospitalization

Minor Complications were defined as:

- Non-treated pseudoaneurysm attributable to the investigational device and documented by DUS
- Pseudoaneurysm attributable to the investigational device and treated with ultrasound-guided compression, ultrasound-guided thrombin injection. or ultrasound-guided fibrin adhesive injection
- Non-treated or treated arteriovenous (AV) fistula attributable to the investigational device and documented by DUS
- Access site hematoma greater than or equal to 10 cm in diameter, attributable to the investigational device, and confirmed by DUS
- Late (following hospital discharge) access site-related bleeding in target limb
- Lower extremity arterial emboli attributable to the investigational device
- Vein thrombosis attributable to the investigational device
- Transient access site-related nerve injury attributable to the investigational device
- Access site wound dehiscence
- Access site infection treated with intramuscular or oral antibiotics

As noted above, the primary effectiveness endpoint was time to hemostasis (TTH). The secondary effectiveness endpoints were time-to-ambulation, time-to-discharge,

technical success, access site closure success, treatment success, occurrence of device failure, subjects requiring adjunctive surgical or endovascular intervention, and subjects receiving adjunctive manual compression. The definitions for the effectiveness endpoints were as follows:

- Time-to-hemostasis: defined as the elapsed time from procedural sheath removal to the first observed cessation of common femoral artery bleeding (excluding cutaneous or subcutaneous oozing at access site).
- Time-to-ambulation: defined as the elapsed time from final procedural sheath removal to time when the subject stands and walks at least 20 feet without re-bleeding.
- Time-to-discharge (time of actual discharge): defined as the elapsed time between final procedural sheath removal and when the subject is discharged from the hospital.
- Technical success: defined as achievement of hemostasis with the investigational device without the need for any access-site-related adjunctive surgical or endovascular intervention (target limb only).
- Access site closure success: defined as technical success and freedom from major complications within 48 hours of the index procedure or hospital discharge, whichever occurs first (target limb only).
- Treatment success: defined as technical success and freedom from major complications through 30 days follow-up.
- Occurrence of device failure: defined as when the device is used in accordance with the IFU, but does not perform as described in the IFU, and negatively impacts treatment of the study subject.
- Subjects requiring adjunctive surgical or endovascular intervention to achieve hemostasis of the access site (target limb only), including type of adjunctive intervention. Adjunctive intervention was defined as any use of surgical or endovascular intervention or firm/occlusive manual pressure needed to achieve hemostasis of the access site (target limb only). Light/non-occlusive pressure to control cutaneous or subcutaneous oozing at the access site was excluded.
- Subjects receiving adjunctive manual compression following use of the investigational device to achieve hemostasis of the access site (target limb only). Regarding the type of manual compression applied (light or firm), light compression was defined as non-occlusive (i.e., "patent hemostasis") allowing distal blood flow, and firm compression was defined as occlusive prohibiting distal blood flow.

B. Accountability of PMA Cohort

At the time of the database lock, of the 96 patients in the pivotal safety cohort and 114 patients in the pivotal effectiveness cohort, 88 (91.7%) of the pivotal safety patients and 101 (88.6%) of the pivotal effectiveness patients completed the 30-day follow-up. The accountability of the primary analysis cohorts is presented in **Table 5** below.

Table 5: Accountability of Primary Analysis Cohorts

Disposition	Totals	Percentage
Enrolled subjects: total	147/147	100%
Pivotal Safety Cohort		
Enrolled subjects allocated to pivotal safety cohort	96/96	100%
Received allocated intervention	96/96	100%
Completed 30-day follow-up (evaluable for primary safety endpoint)	88/96	91.7%
Did not complete 30-day follow-up	8/96	8.3%
Visit out of window (<23 days)*	7	7.3%
Death**	1	1.0%
Pivotal Effectiveness Cohort		
Enrolled subjects allocated to pivotal effectiveness cohort	114/114	100%
Received allocated intervention	114/114	100%
Did not receive adjunctive intervention (evaluable for primary effectiveness endpoint)	101/114	88.6%
Not evaluable for primary effectiveness endpoint. Secondary to receiving adjunctive intervention.	9/114	7.9%
Not evaluable for primary effectiveness endpoint. Secondary to not receiving the investigational device for hemostasis.	4/114	3.5%

* No complications reported in any of the 7 subjects with early out-of-window visits
** Death occurred on post-procedure day 1 and was adjudicated by the CEC as not device-related

C. Study Population Demographics and Baseline Parameters

1. Demographics and Baseline Parameters

   The demographics of the study population are typical for a large bore vascular closure device study performed in the US. For the pivotal safety cohort, the mean age was 76.3 ± 10.59 years, the percentage of male subjects was 67.7% (65/96), and the mean BMI was 28.0 ± 5.17. For the pivotal effectiveness cohort, the mean age was 76.4 ± 10.26 years, the percentage of male subjects was 66.7% (76/114), and the mean BMI was 28.2 ± 5.08. Demographic statistics for the pivotal cohorts are presented in **Table 6** below.

Table 6: Subject Demographics

Characteristic	Pivotal Safety Cohort	Pivotal Effectiveness Cohort
Age (years)		
N	96	114
Mean ± SD	76.3 ± 10.59	76.4 ± 10.26
Median (Interquartile Range, IQR)	77.5 (72 - 82.5)	78 (72 - 83)

Characteristic	Pivotal Safety Cohort	Pivotal Effectiveness Cohort
Min, Max	22, 96	22, 96
Gender		
Female	32.3% (31/96)	33.3% (38/114)
Male	67.7% (65/96)	66.7% (76/114)
BMI (kg/m²)		
N	96	114
Mean ± SD	28.0 ± 5.17	28.2 ± 5.08
Median (IQR)	27.67 (23.75 - 31.77)	28.09 (24.32 - 31.64)
Min, Max	16.38, 39.87	16.38, 39.87
Ethnicity		
Hispanic or Latino	6.3% (6/96)	6.1% (7/114)
Not Hispanic or Latino	82.3% (79/96)	82.5% (94/114)
Not Provided	11.5% (11/96)	11.4% (13/114)
Race		
White	86.5% (83/96)	88.6% (101/114)
Black/African American	4.2% (4/96)	3.5% (4/114)
Asian	0.0% (0/96)	0.0% (0/114)
Native Haw/Pac Islander	0.0% (0/96)	0.0% (0/114)
Am Indian/Alaska Nat	0.0% (0/96)	0.0% (0/114)
Other	3.1% (3/96)	2.6% (3/114)
Not Provided	6.3% (6/96)	5.3% (6/114)

2. Medical History

   The patients in the study had prior medical histories that included coronary artery disease (CAD) in 60.0% (57/95) of the pivotal safety cohort and 58.4% (66/113) of the pivotal effectiveness cohort, coronary artery bypass graft (CABG) surgery in 15.6% (15/96) of the pivotal safety cohort and 14.9% (17/114) of the pivotal effectiveness cohort, and peripheral vascular disease in 13.8% (13/94) of the pivotal safety cohort and 12.5% (14/112) of the pivotal effectiveness cohort. A full accounting of all medical history collected is presented in **Table 7** below.

Table 7: Medical History

Characteristic	Pivotal Safety Cohort (N=96)	Pivotal Effectiveness Cohort (N=114)
History of Smoking	58.3% (56/96)	59.6% (68/114)
Diabetes Mellitus	25.0% (24/96)	24.6% (28/114)
History of CAD	60.0% (57/95)	58.4% (66/113)

History of MI	9.4% (9/96)	8.9% (10/112)
History of CABG	15.6% (15/96)	14.9% (17/114)
History of CHF	46.3% (44/95)	45.1% (51/113)
History of PVD	13.8% (13/94)	12.5% (14/112)
History of Hypertension	89.6% (86/96)	88.6% (101/114)
Hyperlipidemia	84.4% (81/96)	85.1% (97/114)
Bleeding Disorder	0.0% (0/96)	0.0% (0/114)
Cerebrovascular Disease	8.4% (8/95)	8.0% (9/113)
Aortic Aneurysm	46.9% (45/96)	46.5% (53/114)
Rutherford Category		
0	69.2% (9/13)	71.4% (10/14)
1	7.7% (1/13)	7.1% (1/14)
2	7.7% (1/13)	7.1% (1/14)
3	15.4% (2/13)	14.3% (2/14)
4	0.0% (0/13)	0.0% (0/14)
5	0.0% (0/13)	0.0% (0/14)
6	0.0% (0/13)	0.0% (0/14)
Prior Target Artery Closure	8.7% (8/92)	10.1% (11/109)

3. Interventional Procedure Characteristics
   Table 8 below describes key procedural characteristics for the analysis cohorts. Notably, the mean femoral artery diameter was 8.2 mm for both the pivotal safety and effectiveness cohorts, mean procedural sheath size was 15.5Fr ± 1.81Fr for both the pivotal and effectiveness cohorts, and ACT prior to sheath removal was 238.3 ± 58.51 seconds for the pivotal safety cohort and 233.7 ± 58.75 seconds for the pivotal effectiveness cohort.

Table 8: Interventional Procedure Characteristics

Characteristic	**Pivotal Safety (N=96)**	**Pivotal Effectiveness (N=114)**
Target Artery Access		
Left CFA*	41.7% (40/96)	41.2% (47/114)
Right CFA	58.3% (56/96)	58.8% (67/114)
Femoral Artery Diameter (mm)		
N	96	111
Mean ± SD	8.2 ± 1.34	8.2 ± 1.35

Characteristic	Pivotal Safety (N=96)	Pivotal Effectiveness (N=114)
Median (IQR)	8 (7 - 9)	8 (7 - 9)
Min, Max	5, 13.9	5, 13.9
Type of Interventional Procedure		
EVAR	44.8% (43/96)	43.9% (50/114)
TAVR/TAVI	53.1% (51/96)	53.5% (61/114)
TEVAR	2.1% (2/96)	2.6% (3/114)
Largest Procedural Sheath Size (inner diameter in Fr)		
N	94	111
Mean ± SD	15.5 ± 1.81	15.5 ± 1.81
Median (IQR)	16 (14 - 16)	16 (14 - 16)
Min, Max	9, 20	9, 20
Systolic Blood Pressure (mm Hg)		
N	94	111
Mean ± SD	130.0 ± 20.88	128.3 ± 20.63
Median (IQR)	129.5 (115 - 145)	128 (112 - 143)
Min, Max	91, 174	91, 174
Diastolic Blood Pressure (mm Hg)		
N	94	111
Mean ± SD	61.5 ± 13.02	60.6 ± 12.98
Median (IQR)	59 (52 - 71)	59 (51 - 70)
Min, Max	32, 98	32, 98
ACT Prior to Sheath Removal (sec)		
N	94	111
Mean ± SD	238.3 ± 58.51	233.7 ± 58.75
Median (IQR)	239 (192 - 285)	235 (191 - 283)
Min, Max	100, 346	98, 346

* CFA - Common femoral artery. ACT- Activated clotting time. Numbers are in % (counts/sample size) unless otherwise stated.

D. Safety and Effectiveness Results

1. Safety Results

Of the 96 patients in the primary safety cohort, 8 were not evaluable for the 30-day primary endpoint, leaving a pivotal safety cohort of 88 patients available for the 30-day evaluation. The key safety outcomes for this study are presented below in **Tables 9** and **10**.

The results for the primary safety endpoint of freedom from major complications within 30 days post-procedure are presented in **Table 9.** In the pivotal safety cohort, the primary safety endpoint of 30-day freedom from major complications was 94.3% (83/88) with a lower one-sided 95% confidence limit of 88.4%, which compared favorably to the performance goal of 85.2%. Thus, the primary safety endpoint was met. There were 6 major complications in 5 patients (patient-based rate 5/88, 5.7%). All safety analyses were done using a patient-based analysis, such that patients with more than one event were counted only once in each analysis.

Table 9: Incidence of Major Complications

Endpoint	**Pivotal Safety**
Freedom from Major Complications through 30 days	94.3% (83/88)
Subjects with any Major Complication	5.7% (5/88)
Lower one-sided 95% confidence limit (Performance Goal > 85.2%)	88.4%
Types of Major Complications:	
Vascular injury that requires surgical repair, stent-graft, or balloon angioplasty	4.5% (4/88)
Access site-related bleeding that requires transfusion	1.1% (1/88)
Ipsilateral lower extremity ischemia documented by subject symptoms, physical exam, and/or decreased or absent blood flow on lower extremity angiogram	1.1% (1/88)
Access site-related nerve injury that requires surgery	0.0% (0/88)
Permanent (lasting > 30 days) access site-related nerve injury	0.0% (0/88)
Access site infection requiring intravenous antibiotics and/or extended hospitalization	0.0% (0/88)

The results for the secondary safety endpoint of minor complications within 30 days post-procedure are presented in **Table 10**. Freedom from minor complications was 95.5% (84/88) in the pivotal safety cohort. There were 4 minor complications in 4 patients (patient-based rate 4/88, 4.5%). Among the individual components of the minor access site complication composite endpoint, treated pseudoaneurysms were reported in 2.3% (2/88), and hematomas ≥ 10 cm in diameter were reported in 1.1% (1/88). There were no minor complications determined to have occurred at the 60-day evaluation.

Table 10: Incidence of Minor Complications

Endpoint	Pivotal Safety
Freedom from Minor Complications through 30 days	95.5% (84/88)
Subjects with any Minor Complication	4.5% (4/88)
Types of Minor Complications	
Non-treated pseudoaneurysm attributable to the investigational device and documented by DUS	0.0% (0/88)
Pseudoaneurysm attributable to the investigational device and treated with ultrasound-guided compression, ultrasound-guided thrombin injection or ultrasound-guided fibrin adhesive injection	2.3% (2/88)
Non-treated or treated arteriovenous (AV) fistula attributable to the investigational device and documented by DUS	0.0% (0/88)
Access site hematoma greater than or equal to 10 cm in diameter, attributable to the investigational device, and confirmed by DUS	1.1% (1/88)
Late (following hospital discharge) access site-related bleeding in target limb	0.0% (0/88)
Lower extremity arterial emboli attributable to the investigational device	0.0% (0/88)
Vein thrombosis attributable to the investigational device	0.0% (0/88)
Transient access site-related nerve injury attributable to the investigational device	0.0% (0/88)
Access site infection treated with intramuscular or oral antibiotics	0.0% (0/88)
Other Complication [1]	1.1% (1/88)
Device-Related Complications within 30 days post-procedure	4.5% (4/88)
Procedure-Related Complications within 30 days post-procedure	4.5% (4/88)

[1] Persistent access site-related bleeding at the time of attempted Cross-Seal deployment that required surgical cut-down to stop the bleeding and close the access site.

The findings that were noted during the ultrasound examinations of the study patients were complications that are expected with large-bore interventional procedures like TAVR/TAVI, EVAR, and TEVAR which the study patients underwent. In the pivotal effectiveness cohort, there were 3 abnormalities noted on the 30-day ultrasounds as reported by the Core Laboratory which evaluated the ultrasound images. These abnormalities were a visible intraluminal thrombus, a pseudoaneurysm, and a dissection. In the pivotal effectiveness cohort, there was 1 abnormality noted on the 60-day ultrasounds as reported by the Core Laboratory, which was a pseudoaneurysm.

2. Effectiveness Results

The analysis of effectiveness was based on the 101 evaluable patients at the index procedure time-point. Key effectiveness outcomes are presented in **Tables 11** and **12**.

The primary effectiveness endpoint of TTH was evaluable in 101/114 subjects in the pivotal effectiveness cohort. The mean TTH was 0.4 ± 1.4 minutes with an upper one-sided 97.5% confidence limit of 0.7 minutes, which compares favorably to the

PG of 15 minutes. Thus, the primary efficacy endpoint was met. Of note, 92.1% of subjects in the pivotal effectiveness analysis dataset had a TTH of 1 minute or less in duration.

Table 11: Primary Effectiveness Results

Effectiveness Parameter	**Result**
Primary Effectiveness Endpoint: Time-to-Hemostasis (minutes)	
N	101
Mean ± SD	0.4 ± 1.40
Median (IQR)	0.05 (0.017 - 0.15)
Min, Max	0, 12.1
Upper One-Sided 97.5% Confidence Limit	0.7

The results of the secondary effectiveness endpoints are summarized in **Table 12**. The secondary effectiveness endpoints are reported as follows: The rates of technical success, access site closure success, and treatment success were 92.7% (102/110), 88.4% (99/112), and 88.4% (99/112), respectively. Adjunctive surgical or endovascular interventions were reported in 7.3% (8/110) of the subjects, and manual compression was used in 27.9% (31/111). The mean to time-to-ambulation was 15.9 ± 14.65 hours and the mean time-to-discharge was reported as 44.8 ± 36.99 hours.

Table 12: Secondary Effectiveness Results

Characteristic	**Result**
Technical Success	92.7% (102/110)
Access Site Closure Success	88.4% (99/112)
Treatment Success	88.4% (99/112)
Device Failures	0.9% (1/114)
Adjunctive Surgical/ Endovascular Intervention	7.3% (8/110)
Surgical	25.0% (2/8)
Endovascular	75.0% (6/8)
Manual Compression Used	27.9% (31/111)
Firm (occlusive)	16.1% (5/31)
Light (non-occlusive)	83.9% (26/31)
Time-to-Ambulation (hours)	
N	108
Mean ± SD	15.9 ± 14.65
Median (IQR)	10.5 (7 - 21)
Min, Max	2, 90

Characteristic	Result
Time-to-Discharge (hours)	
N	110
Mean ± SD	44.8 ± 36.99
Median (IQR)	27 (25 - 51)
Min, Max	18, 246

3. Subgroup Analyses
   The following preoperative characteristics were evaluated for potential association with outcomes: gender, race, and age. With regards to the primary safety analysis, no substantial differences were noted in terms of gender. The few non-white subjects and subjects < 65 years old impeded a meaningful subgroup analysis for race or age, though no substantial differences between these subgroups were noted. For the primary effectiveness analysis, there were no substantial differences noted in time-to-hemostasis in gender, race, or age.

4. Pediatric Extrapolation
   In this premarket application, existing clinical data were not leveraged to support approval of a pediatric patient population.

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 62 investigators of which none were full-time or part-time employees of the sponsor and two (2) investigators had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: 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. Statistical analyses were conducted by FDA to determine whether the financial interests/arrangements had any impact on the clinical study outcome. The information provided does not raise any questions about the reliability of the data.

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

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory System Devices

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

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The assessment of effectiveness for the Cross-Seal System was based on mean time-to-hemostasis (TTH). In the pivotal cohort, on average, TTH was achieved in 0.4 ± 1.4 minutes with an upper one-sided 97.5% confidence limit of 0.7 minutes. The study met its endpoint, comparing favorably against the established performance goal of 15 minutes. Of note, 92.1% of subjects in the pivotal effectiveness analysis dataset had a TTH of 1 minute or less in duration.

Effectiveness measures were also analyzed in conjunction with the secondary endpoints of the study, and these returned favorable results. The rates of technical success, access site closure success, and treatment success were 92.7%, 88.4%, and 88.4%, respectively. Hemostasis was achieved by the Cross-Seal System alone without the need for adjunctive methods in 92.7% of subjects. Manual compression was used in 27.9% of subjects, and 16.1% received firm, occlusive pressure. The mean time-to-ambulation was 15.9 ± 14.65 hours and the mean time-to-discharge was reported as 44.8 ± 36.99 hours. One instance of a study-defined device failure was observed, representing a rate of 0.9%. In a subgroup analysis of age, gender, and race, there were no statistically significant differences noted in TTH.

B. Safety Conclusions

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

The safety assessments for the Cross-Seal System were based on the primary safety endpoint defined as freedom from major complications of the target limb access site within 30 days post-procedure. The analysis provided to support this PMA indicates that the device met the primary endpoint performance goal of 85.2% with an observed freedom from major complications of 94.3%, with a lower one-sided 95% confidence limit of 88.4%. The secondary safety endpoints provided additional evidence to support Cross-Seal System safety. The observed freedom from minor complications within 30 days was 95.5%, and the rates of device-related complications and procedure-related complications within that same period were both 4.5%. No major or minor complications, as determined by the Clinical Events Committee, occurred past the 30-day evaluation. In subgroup analyses for age, gender, and race, there were no substantial differences noted in safety outcomes in gender. While the number of non-white and younger subjects impeded a meaningful subset analysis by race or age, no differences were noted.

C. Benefit-Risk Determination

The probable benefits of the device are also based on data collected in a clinical study conducted to support PMA approval as described above. The potential benefits of using the Cross-Seal System include hemostasis to be achieved in around one minute for a majority of subjects and a technical success rate of 92.7%. The device performance is associated with an acceptable patient-based rate of major complications through 30 days of 5.7% and an acceptable patient-based rate of minor complications through 30 days of 4.5%.

The probable risks of the device are also based on data collected in a clinical study conducted to support PMA approval as described above. Risks associated with the device include major vascular injury, access site bleeding, ipsilateral lower extremity ischemia, nerve injury, and access site infection. Additional risks include minor pseudoaneurysm, arteriovenous (AV) fistula, access site hematoma, late access site bleeding, lower extremity arterial emboli, vein thrombosis, transient access site nerve injury, access site wound dehiscence, and access site infection.

1. Patient Perspective
   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 closure of the common femoral artery access sites of patients who have undergone diagnostic or interventional catheterization procedures using 8F to 18F introducer sheaths, the probable benefits outweigh the probable risks.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. As discussed in the previous sections, the benefits of potential reduced time-to-hemostasis coupled with low rates of access site-related complications suggest that the benefits of using the Cross-Seal System outweigh the risks.

XIII. CDRH DECISION

CDRH issued an approval order on 9/26/2023.

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 final approved device labeling (Instructions for Use).

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

Post-approval Requirements and Restrictions: See approval order.

XV. REFERENCES

None.