SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Vascular Closure Device

Device Trade Name: VASCADE® MVP Venous Vascular Closure System (VVCS)

Device Procode: MGB

Applicant's Name and Address: Cardiva Medical, Inc.
2900 Lakeside Dr. #160
Santa Clara, CA 95054

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P120016/S024

Date of FDA Notice of Approval: November 27, 2018

The original PMA (P120016) for the VASCADE® Vascular Closure System (VCS) was approved on January 31, 2013 and is indicated for femoral arterial access site closure while reducing times to hemostasis and ambulation in patients who have undergone diagnostic or interventional endovascular procedures using a 5F, 6F, or 7F procedural sheath. The VASCADE VCS is also indicated to reduce time to discharge eligibility in patients who have undergone diagnostic endovascular procedures using a 5F, 6F, or 7F procedural sheath. The SSED to support the indication is available on the CDRH website (https://www.accessdata.fda.gov/cdrh_docs/pdf12/P120016b.pdf) and is incorporated by reference here. The current supplement was submitted for the VASCADE MVP VVCS as a line extension for the VASCADE VCS product family.

II. INDICATIONS FOR USE

The VASCADE MVP Venous Vascular Closure System (VVCS) Model 800-612C is indicated for the percutaneous closure of femoral venous access sites while reducing time to ambulation, total post-procedure time, time to hemostasis, and time to discharge eligibility in patients who have undergone catheter-based procedures utilizing 6-12F inner diameter procedural sheaths, with single or multiple access sites in one or both limbs.

III. CONTRAINDICATIONS

The VASCADE MVP VVCS should not be used in patients with a known allergy to bovine derivatives.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the VASCADE MVP VVCS labeling.

V. DEVICE DESCRIPTION

A. Materials and Configuration

The VASCADE MVP VVCS Model 800-612C is intended to seal the femoral vein access site(s) at the completion of a catheter-based procedure. The system is designed to deliver a resorbable Collagen Patch, extravascularly, at the venotomy site to aid in achieving hemostasis. The device can be used in 6F to 12F, 12cm introducer sheaths. The system consists of a sterile disposable Vascular Closure Catheter which houses a resorbable Collagen Patch, and the VASCADE MVP VVCS Clip (refer to Figure 1).

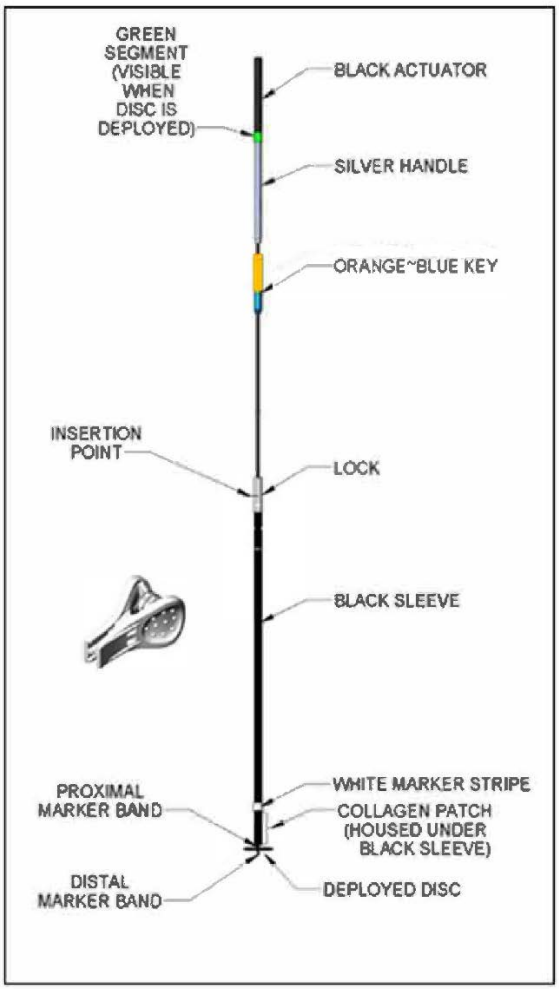

Figure 1: VASCADE MVP VVCS

The collagen patch is composed of Type I Bovine collagen and is delivered in a compressed form that is approximately 15mm in length. The dry weight of the collagen is 12mg ± 3mg. The patch expands as a result of rehydration in the presence of blood in the tissue tract to provide an extravascular seal. A radiopaque proximal marker band on the Catheter provides means to aid in verifying placement of the patch in the tissue tract adjacent to the femoral venotomy site prior to the release of the patch. A second distal marker band locates the distal tip of the VASCADE MVP VVCS Disc.

B. Operation

After completion of the procedure, the VASCADE MVP VVCS Catheter is inserted through the introducer sheath. The VASCADE MVP Disc is then deployed within the vessel and the introducer sheath is removed over the VASCADE MVP Catheter. After the introducer sheath is removed, the VASCADE MVP Disc is positioned against the intimal aspect of the venotomy, providing both temporary hemostasis and protection from intravascular placement of the Collagen Patch, and the VASCADE MVP Clip is applied at skin level to maintain the position of the Disc. After confirming the position of the Collagen Patch either fluoroscopically or by ultrasound, the Black Sleeve is unlocked and retracted to expose the Collagen Patch to the tissue tract. The system is left in place for a brief dwell period to allow the patch to swell, after which the Disc is collapsed and the VASCADE MVP Catheter is removed from the vein leaving the resorbable, extra-vascular, hemostatic Collagen Patch at the venotomy site providing hemostasis.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for attaining hemostasis at a venous puncture site post- catheterization, including manual or mechanical compression, percutaneous suture delivery, and PEG- based hemostatic devices. Pressure dressings and sandbags are routinely used in combination with compression methods to control oozing. 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

The VASCADE MVP VVCS 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.

- Allergic response
- Vascular occlusion

- Venous thrombus
- Arterio-venous fistula
- Bleeding from the puncture site
- Oozing from the puncture site
- Bruising at the puncture site
- Death
- Device failure/malfunction
- Edema
- Embolization tissue, (thrombus, air, calcific debris device)
- Pulmonary Embolism
- Hematoma
- Infection
- Inflammatory response
- Intimal tear / dissection
- Lower extremity ischemia
- Perforation of the vessel wall
- Laceration of the vessel wall
- Peripheral nerve injury
- Pseudoaneurysm
- Retroperitoneal bleeding
- Deep vein thrombosis
- Vascular injury
- Vasovagal response
- Wound dehiscence
- Puncture site pain
- Superficial vein thrombosis

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

IX. SUMMARY OF PRECLINICAL STUDIES

A series of *in vitro* tests were conducted to verify the performance of the VASCADE MVP VVCS. Testing was referenced from PMA submission P120016 for those evaluations that could be leveraged from previous testing. A summary of previously reported preclinical studies can be found in the Summary of Safety and Effectiveness Data (SSED) for the original PMA (https://www.accessdata.fda.gov/cdrh_docs/pdf12/P120016b.pdf).

A. Laboratory Studies

For the *in vitro* tests not leveraged, VASCADE MVP VVCS devices were tested in accordance with the acceptance criteria defined in the VASCADE MVP VVCS product specifications or as specified in the design verification test protocols. All of the test results met or exceeded the specified requirements in the product specification and test protocols. A summary of device testing (Table 1) includes the following:

Table 1. Summary of Device Testing

Test	Purpose	Acceptance Criteria	Results
Tip Outer Diameter at Proximal Sleeve	Device must be compatible with commercially available introducer sheaths	≤0.070 inch	Pass
Catheter Working Length	Device must be able to reach the arterial access site it intends to seal	15.0 ± 0.5 cm (5.9" ± 0.2")	Pass
Catheter Overall Length		38.0 ±1.0 cm (15.0" ± 0.4")	Pass
Disc deployment force	Device should be easy to use, simple to deploy, and simple to de-deploy.	≤ 3.0 lb	Pass
The sleeve retraction force		Inner Sleeve Retraction Force: < 10 oz Outer Sleeve Retraction Force: < 10 oz	Pass
Deployed Disc Diameter	Device should maintain position when the disc is deployed in the artery and maintain temporary hemostasis	0.2875" ± 0.0275" (21 Fr +3/-1 Fr)	Pass
Catheter Pull Through Force		> 8 oz	Pass
Multiple Disc Deployment	Device shall be able to withstand multiple deployment and de-deployment attempts	Should withstand at least 5 consecutive times without failure	Pass
Prolonged deployment	Sterilized membrane shall be able to withstand prolonged deployment	Deployment time for a period of 1 hour without failure	Pass
Device Integrity	Device integrity should be maintained during the procedure.	The catheter tip should be inserted and removed from the introducer sheath consecutively for 5 times without damage to the membrane or compromising the integrity of the membrane joint.	Pass
Joint between actuator and the inner handle	Device should maintain strength throughout the procedure.	≥ 3.00 lb (13.34 N)	Pass
Joint between tip of the braid and the pull wire		≥ 3.00 lb (13.34 N)	Pass

Test	Purpose	Acceptance Criteria	Results
Proximal braid attachment to the catheter shaft and sleeve		≥ 2.25 lb (10.01 N)	Pass
Collagen hydrated weight post simulative conditioning	Collagen should be of a consistent weight during and after the procedure.	≤ 28 mg	Pass
Collagen displacement post inner sleeve retraction when the device tip is dipped in saline and subjected to 5 seconds of pressurized saline followed by 2 minute of pressurized blood	Implant functionality and position should be maintained until it is ready for deployment.	≤ 2.5mm (0.10 inch) from initial position	Pass

B. Animal Studies

An acute animal study was performed in a porcine model to evaluate the effect of changing the deployed Disc diameter of the VASCADE MVP VVCS device from 21 F to 23 F to reduce the risk of pulling the Disc through the venotomy. A 14F sheath along with a 9F indwelling sheath was used for venous access to simulate the additional dilation that occurs during a cryo case procedure with 12F sheath access. On average, there was 23.8% increase in the pull through force as the result of the increase in the disc diameter. Temporary hemostasis was obtained in all cases as was evident by lack of any extravasation of contrast in the surrounding tissue. The data demonstrate that the 23 F Disc maintains adequate functionality of the device.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of percutaneous closure of femoral venous access sites with the VASCADE MVP VVCS in patients who have undergone catheter-based procedures utilizing 6-12F inner diameter procedural sheaths, with single or multiple access sites in one or both limbs in the US under IDE # G170144. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

Patients were treated between September 2017 and March 2018. The database for this Panel Track Supplement reflected data collected through April 2018 and included

204 patients and an additional 41 roll-in patients. There were 13 investigational sites, all sites were in the U.S.

The study was a prospective, randomized, controlled multi-center clinical study. Only patients with multiple access sites were enrolled to support the desired indication. Randomization was stratified to account for patients with varying numbers of access sites in a 1:1 treatment device to control arm ratio to ensure treatment and control arms have the same proportion of access sites/patient, i.e. 3 access sites/patient vs. 4 access sites/patient. All of the randomized patients in the study were patients undergoing interventional electrophysiology procedures for the ablation of cardiac arrhythmias which included atrial fibrillation, atrial flutter, atrial fibrillation-flutter, supraventricular tachycardia, and ventricular tachycardia.

A total of 50 consecutive patients were enrolled into an Ultrasound Sub-Study evaluated by a core lab.

The control group consisted of patients receiving manual compression.

1. Clinical Inclusion and Exclusion Criteria

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

   - age ≥ 18 yrs
   - undergoing elective, non-emergent, catheter-based procedures via the common femoral vein(s) using a 6F to 12F inner diameter introducer sheath
   - minimum of 3 and maximum of 4 femoral venous access sites, and a maximum of 2 access sites per leg

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

   - active systemic or cutaneous infection or inflammation in vicinity of the groin
   - any pre-existing immunodeficiency disorder; chronic use of high dose systemic steroids
   - history of bleeding diathesis, coagulopathy, hypercoagulability; platelet count < 100,000 cells/mm^3
   - severe comorbidities with life expectancy less than 12 months in the opinion of the site investigator
   - history of femoral arteriotomy or venotomy within the past 10 days, experienced previous vascular complications or residual hematoma, had been treated with an intravascular closure device within the previous 30 days, or scheduled for femoral venous or arterial access within the next 30 days.
   - history of DVT, pulmonary embolism; thrombophlebitis, significant anemia or renal insufficiency
   - BMI > 45 kg/m^2 or < 20 kg/m^2

- inability to routinely walk at least 20 ft. without assistance; use of low molecular-weight heparin (LMWH) within 8 hours before or after the procedure
- concomitant procedures or conditions that would interfere with an ambulation attempt at 2-3 hours post-procedure.

If participants met the eligibility criteria, then they were consented for the study prior to their electrophysiology procedure. At the end of the study, participants were excluded if any of the following occurred during the electrophysiology procedure:

- any attempt at femoral arterial access; procedural complications that would interfere with routine recovery, ambulation, or discharge times
- difficulty with needle puncture or insertion of the introducer sheath
- sheath placement cephalad to lower half of the femoral head or the inferior epigastric vein origin from the external iliac vein
- obvious intraprocedural bleeding or thrombotic complications; any sheath use < 6 or > 12F inner diameter; or tissue tract < 2.5 cm deep)

2. Follow-up Schedule

All patients were scheduled to return for follow-up examinations at 30 ± 7 days post-procedure. A subset of 50 patients were also enrolled in an Ultrasound Sub-Study, with exams performed at the 30 ± 7 day follow-up visit.

Post-procedure, patients were evaluated for any major or minor complications or adverse event including bleeding, neurological and other potential device or procedure-related adverse effects. Adverse events and complications were recorded at all visits.

3. Clinical Endpoints

With regards to safety, the primary endpoint was the rate of combined major access site closure-related complications, analyzed on a per-limb basis. The secondary safety endpoint was the rate of combined minor access site closure-related complications, analyzed on a per-limb basis.

With regards to effectiveness, the primary endpoint was time to ambulation (TTA), defined as elapsed time between removal of the final VASCADE MVP device (treatment arm) or removal of the final sheath (control arm), and time when subject stands and walks 20 feet without evidence of venous re-bleeding from the femoral access sites. The secondary effectiveness endpoints were total post-procedural time (TPPT), time to hemostasis (TTH), time to discharge eligibility (TTDE), time to hospital discharge (TTD), and time to closure eligibility (TTCE). TPPT was defined as elapsed time between removal of the last procedural device/catheter for the index procedure and when subject is able to successfully ambulate. TTH was defined as elapsed time between removal of the VASCADE MVP device (treatment arm) or removal of the sheath (control arm), and first observed and confirmed venous hemostasis, for each access site. TTDE was

defined as elapsed time between removal of the final VASCADE MVP device (treatment arm) or removal of the final sheath (control arm), and when subject is eligible for discharge based solely on the assessment of the access site, as determined by the medical team. TTD was defined as elapsed time between removal of the final VASCADE MVP device (treatment arm) or removal of the final sheath (control arm), and when subject is discharged from the institution. TTCE was defined as elapsed time between removal of the last procedural device/catheter for the index procedure and the removal of the first VASCADE MVP device (treatment arm) or removal of the first sheath (control arm).

With regards to success/failure criteria, procedure success and device success were evaluated as additional secondary effectiveness measures. Procedure Success was defined as attainment of final hemostasis at all venous access sites and freedom from major venous access site closure-related complications through 30 days (Per-patient analysis, both arms). Device Success was defined as the ability to deploy the delivery system, deliver the collagen, and achieve hemostasis with the VASCADE MVP VVCS.

B. Accountability of PMA Cohort

At the time of database lock, of 204 randomized patients enrolled in the PMA study, 99% (202) patients are available for analysis at the completion of the study, the 30-day post-procedure visit. One patient in each treatment group was lost to follow up and one device patient completed the follow up-visit at 3 days post-procedure. The 30-day post-operative visit was complete for all available patients. As summarized in Table 2 below, of the 204 total randomized patients in the study, 192 patients (94.1%) completed a follow-up office visit, with 178 patients (87.3%) completing the 30-day (± 7 days) follow-up visit per protocol.

Table 2. Patient Accountability Summary Table

	VASCADE MVP (N=100)		Manual Compression (N=104)	
Randomized	100		104	
Completed Study	99	99%	103	99%
Completed 30-day follow-up office visit per protocol	87	87%	91	88%
Completed 30-day follow-up office visit out of window	8	8%	6	6%
Completed 30-day phone call in window	3	3%	4	4%
Completed 30-day phone call out of window	1	1%	2	2%
Lost to follow-up within study period	1	1%	1	1%

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for a vascular closure device study performed in the US. The baseline demographic and clinical characteristics of the 2 treatment groups were very similar. The mean ages in the VASCADE MVP and manual compression groups were 61.5 ± 11.6 years, and 63.4 ± 11.1 years, respectively. The percentage of female subjects was 33% in the VASCADE MVP group and 38% in the manual compression group. The mean BMI was 29.0 in the VASCADE MVP group and 29.3 in the manual compression group. Table 3 provides these demographic results.

Table 3. Patient Demographics and Baseline Characteristics – Randomized Patients

	VASCADE MVP (N=100)		Manual Compression (N=104)	
Age				
Mean	61.5	-	63.4	-
Std Dev	11.6	-	11.1	-
Median	62	-	65.5	-
Minimum	28	-	19	-
Maximum	80	-	79	-
Gender				
Female	33	33%	40	38%
Male	67	67%	64	62%
Ethnicity				
Hispanic or Latino	3	3%	6	6%
Not Hispanic or Latino	97	97%	95	91%
Unknown	0	0%	3	3%
Race				
White	86	86%	93	89%
Black or African American	6	6%	4	4%
American Indian or Alaska Native	3	3%	0	0%
Asian	2	2%	1	1%
Other	3	3%	6	6%
BMI				
Mean	29.0	-	29.3	-
Std Dev	4.6	-	5.2	-
Median	29	-	29	-
Minimum	20	-	19	-
Maximum	43	-	44	-

There were no significant differences ($p \geq 0.05$) between the treatment and control groups for any of the above characteristics.

Medical History

Medical History and Risk Factors are presented in Table 4. There were also no statistically significant differences ($p \geq 0.05$) between the two treatment groups.

Table 4. Medical History and Risk Factors

	VASCADE MVP (N=100)		Manual Compression (N=104)	
Hypercholesterolemia				
Yes	57	57%	58	56%
No	42	42%	44	42%
Unknown	1	1%	2	2%
Hypertension				
Yes	58	58%	69	66%
No	41	41%	34	33%
Unknown	1	1%	1	1%
Cigarette Smoker				
Never	58	58%	62	60%
Current	6	6%	8	8%
Ex-Smoker	36	36%	34	33%
Diabetes Mellitus				
No	86	86%	86	83%
Yes	14	14%	18	17%
Diabetes Treatment*				
Insulin	5	5%	3	3%
Diet	5	5%	5	5%
Oral Hypoglycemics	11	11%	15	14%
Lower Right Limb Neuropathy				
No	99	99%	102	98%
Yes	1	1%	2	2%
Symptoms				
Localized	0	0%	0	0%
Radiating	1	1%	0	0%
Other	0	0%	2	2%
Present at Enrollment				
Yes	1	1%	2	2%
No	0	0%	0	0%
Severity				
Mild	0	0%	1	1%
Moderate	1	1%	1	1%
Severe	0	0%	0	0%
Lower Left Limb Neuropathy				
No	99	99%	102	98%
Yes	1	1%	2	2%

	VASCADE MVP (N=100)		Manual Compression (N=104)	
Symptoms				
Localized	0	0%	0	0%
Radiating	1	1%	0	0%
Other	0	0%	2	2%
Present at Enrollment				
Yes	1	1%	2	2%
No	0	0%	0	0%
Severity				
Mild	0	0%	1	1%
Moderate	1	1%	1	1%
Severe	0	0%	0	0%
Other Relevant Medical History				
Yes	16	16%	16	15%
No	84	84%	88	85%

*Patients with diabetes may have had more than one treatment.

Anti-Coagulant and Antiplatelet Medications

Pre-procedure anticoagulant / antiplatelet administration within the previous 24 hours was reported in 84% of VASCADE MVP and 85% of manual compression cases. In the randomized cohort, intra-procedural heparin was administered in 85% of VASCADE MVP cases and 90% of manual compression cases. Of those cases, protamine was administered in 92% of VASCADE MVP cases and 91% of manual compression cases.

Activated clotting times (ACTs) were collected at the end of the catheterization procedure in subjects receiving unfractionated heparin, with mean ACT for subjects reported as 298.6 seconds vs. 285.9 seconds in the VASCADE MVP and manual compression groups, respectively.

Anticoagulant administration including heparin, bivalirudin (Angiomax), and glycoprotein IIb/IIIa inhibitors is shown in Table 5 below.

Table 5. Pre- and Peri-Procedure Anticoagulant/Antiplatelet Medication

Medication	VASCADE MVP (N=100)		Manual Compression (N=104)	
Aspirin	29	29%	21	20%
Warfarin (Coumadin)	5	5%	3	3%
Ticlopidine (Ticlid)	0	0%	0	0%
Clopidogrel (Plavix)	0	0%	2	2%
Prasugrel (Effient)	0	0%	0	0%
Ticagrelor (Brilinta)	1	1%	0	0%

Medication	VASCADE MVP (N=100)		Manual Compression (N=104)	
Rivaroxaban (Xarelto)	29	29%	25	24%
Dabigatran (Pradaxa)	3	3%	4	4%
Apixaban (Eliquis)	37	37%	46	44%
Tirofiban (Aggrastat)	0	0%	0	0%
Cilostazol	0	0%	0	0%
Low molecular weight Heparin	1	1%	2	2%
Other SQ Heparin	0	0%	0	0%
Bivalirudin	0	0%	0	0%
GP IIb/IIIa inhibitor	0	0%	0	0%
Any of the above	84	84%	88	85%
None	16	16%	16	15%

Pain Medication

The administration of pain medications during bedrest were also measured. Medication administered for pain or anxiety while the subject was on initial bedrest (i.e., post-procedure through successful TTA) was recorded for all subjects. Medication was administered for pain in 24% of the VASCADE MVP subjects, and in 49% of the manual compression subjects. Medication was administered for anxiety in 4.0% of the VVCS subjects, and in 2.0% of the manual compression subjects. The usage of pain medications was numerically lower for the treatment arm compared to the control (see Table 6).

Table 6. Pain Medication Usage

Pain Medication Usage	VASCADE MVP (N=100)		Manual Compression (N=104)	
Yes	24	24%	51	49%
No	76	76%	53	51%

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on the randomized cohort of 204 patients available for the 30-day post-procedure evaluation. The key safety outcomes for this study are presented below in Tables 7 and 8.

Table 7 provides an event-based analysis, on an Intent-to-Treat (ITT) basis, of the major access site-related complications reported in the AMBULATE trial for the VASCADE MVP and manual compression patients during the 30-day follow-up period.

There were no major complications reported in either the VASCADE MVP group or the manual compression control group.

Table 7. Major Venous Access Site Closure-Related Complications, Number of Limbs with Each Event

Major Venous Access Site Closure-Related Complications at 30 Days by Event	VASCADE MVP (N=199)		Manual Compression (N=209)	
Any major venous access site closure-related complication	0	0.0%	0	0.0%
Access site-related bleeding requiring transfusion	0	0.0%	0	0.0%
Vascular injury requiring surgical repair	0	0.0%	0	0.0%
Access site-related infection confirmed and requiring intravenous antibiotics and/or extended hospitalization	0	0.0%	0	0.0%
New onset permanent access site-related nerve injury (i.e., persisting for > 30 days)	0	0.0%	0	0.0%
New onset access site-related nerve injury in the ipsilateral lower extremity requiring surgical repair	0	0.0%	0	0.0%
Pulmonary embolism requiring surgical or endovascular intervention and/or resulting in death	0	0.0%	0	0.0%
Pulmonary embolism NOT requiring surgical or endovascular intervention and/or NOT resulting in death	0	0.0%	0	0.0%

The combined rate of minor complications was the secondary safety endpoint. Protocol established minor complications are listed in Table 8. The minor complication rate for all patients in the VASCADE MVP group was 1.0% (2/199) per limb compared to 2.4% (5/209) per limb in the manual compression control group.

Table 8. Minor Venous Access Site Closure-Related Complications, Reported, Number of Limbs with Each Event

Minor Venous Access Site Closure-Related Complications at 30 Days by Event	VASCADE MVP (N=199)		Manual Compression (N=209)	
Any Minor Venous Access Site Closure-Related Complication	2	1.0%	5	2.4%
Access site-related bleeding requiring > 30 minutes of continual manual compression to achieve initial venous hemostasis	0	0.0%	0	0.0%
Access site-related hematoma > 6 cm documented by ultrasound	0	0.0%	2	1.0%
Late access site-related bleeding (following hospital discharge)	0	0.0%	0	0.0%
Ipsilateral deep vein thrombosis,	0	0.0%	0	0.0%

Minor Venous Access Site Closure-Related Complications at 30 Days by Event	VASCADE MVP (N=199)		Manual Compression (N=209)	
confirmed by ultrasound/imaging				
Localized access site infection confirmed and treated with intramuscular or oral antibiotics	1	0.5%	1	0.5%
Arteriovenous fistula requiring treatment	0	0.0%	0	0.0%
Arteriovenous fistula not requiring treatment	0	0.0%	1	0.5%
Pseudoaneurysm requiring thrombin/fibrin adhesive injection or ultrasound-guided compression	1	0.5%	0	0.0%
Pseudoaneurysm not requiring treatment	0	0.0%	0	0.0%
Access site-related vessel laceration	0	0.0%	0	0.0%
Access site-related wound dehiscence	0	0.0%	0	0.0%
Transient access site-related nerve injury	0	0.0%	1	0.5%

None of the complications in the AMBULATE Trial were considered unanticipated events. There were no deaths during the study.

Adverse effects leading to device modification:

During the AMBULATE study, there was a device modification made (approved in G170144/S004) to the deployed disc diameter from 21F to 23F to better achieve temporary hemostasis without pull-through in the 12F access sites. No adverse events were associated with pull-throughs, only conversion of access site management to manual compression. The change was effective in reducing 12F pull throughs from 12 out of 24 (50%) before the change to 0 out of 12 (0%) after the change.

2. Effectiveness Results

The analysis of effectiveness was based on the 204 evaluable patients at the 30-day post-operative evaluation time point. Key effectiveness outcomes are presented in Table 9.

A total of 204 of the 204 enrolled patients in the AMBULATE Trial were evaluable for effectiveness. Time to Ambulation (TTA), Total Post Procedure Time (TPPT), Time to Hemostasis (TTH), Time to Discharge Eligibility (TTDE), Time to Discharge (TTD), and Time to Closure Eligibility (TTCE) are presented in Table 9 below. Time to Ambulation was reported in hours (h): minutes (mm) as a per-patient analysis.

For the primary ANCOVA model, the VASCADE MVP VVCS treatment effect for TTA compared to manual compression was -3.32 hours, (2.8 ±1.3 hours for VVCS vs. 6.1 ±1.6 hours for manual compression; p<0.0001), indicating VASCADE MVP superiority compared to manual compression. Similarly, superiority of the VASCADE MVP VVCS based on the ANCOVA model was demonstrated for TPPT, TTDE, and TTCE. The VASCADE MVP treatment effect for TPPT compared to manual compression was -3.69 hours (3.1 ± 1.3 hours versus 6.8 ± 1.7; p<0.0001), and the VASCADE MVP treatment effect for TTDE compared to manual compression was -3.41 hours (3.1 ± 1.3 hours versus 6.5 ± 1.9 hours; p<0.0001). The mean TTCE in the group assigned to VASCADE MVP was 10.5 ± 6.0 minutes versus 37.6 ± 33.2 minutes for manual compression. The VASCADE MVP treatment effect for TTD compared to manual compression was -0.04 hours (21.8 ± 13.4 hours versus 21.8 ± 9.5 hours; p=0.98), which did not indicate a significant difference between the VASCADE MVP and manual compression. Independent variables such as types of underlying or additional procedures (e.g., CABG surgery) and overall patient condition, unrelated to access site closure, may impact actual hospital discharge times.

The mean TTH in the group assigned to the VASCADE MVP was 6.1 ± 3.7 minutes versus 13.7 ± 6.5 minutes in the manual compression group (p <0.0001). A Generalized Estimating Equation (GEE) statistical analysis was performed to evaluate non-inferiority versus manual compression. The VASCADE MVP demonstrated non-inferior to manual compression, and further showed superiority, with a mean difference of -7.6 minutes (95% CI: -8.8, -6.3).

Table 9. Primary and Secondary Effectiveness Endpoints

Outcome	VASCADE MVP			Manual Compression			ANCOVA Analysis	
	Total	3 Access Sites	4 Access Sites	Total	3 Access Sites	4 Access Sites	Parameter Estimate (95% CI)	p-value
TTA, h							-3.32 (-3.71, -2.92)	<0.0001
N	N=100	N=31	N=69	N=104	N=34	N=70		
Mean ± SD	2.8 ± 1.3	2.5 ± 0.8	2.9 ± 1.5	6.1 ± 1.6	5.9 ± 1.2	6.2 ± 1.7		
Median (min, max)	2.2 (2.0, 11.5)	2.2 (2.0, 5.6)	2.3 (2.0, 11.5)	6.1 (3.4, 15.7)	5.3 (4.2, 9.1)	6.2 (3.4, 15.7)		
TPPT, h							-3.69 (-4.10, -3.27)	<0.0001
N	N=100	N=31	N=69	N=104	N=34	N=70		
Mean ± SD	3.1 ± 1.3	2.7 ± 0.8	3.3 ± 1.5	6.8 ± 1.7	6.4 ± 1.3	6.9 ± 1.9		
Median (min, max)	2.6 (2.2, 11.8)	2.4 (2.2, 5.9)	2.7 (2.2, 11.8)	6.4 (4.2, 15.9)	6.2 (4.5, 9.8)	6.6 (4.2, 15.9)		
TTH, min							GEE Model	<0.000

Outcome	VASCADE MVP			Manual Compression			ANCOVA Analysis	
							Parameter Estimate	p-value
N	N=369	N=93	N=276	N=382	N=102	N=280	-7.5 (-8.7, -6.3)	1
Mean ± SD	6.1 ± 3.7	5.4 ± 2.0	6.3 ± 4.1	13.7 ± 6.5	11.4 ± 6.4	14.5 ± 6.4		
Median (min, max)	5.1 (0.4, 33.3)	5.1 (1.3, 23.3)	5.1 (0.4, 33.3)	11.7 (0.6, 37.1)	10.0 (2.9, 32.7)	12.5 (0.6, 37.1)		
TTDE, h								
N	N=100	N=31	N=69	N=104	N=34	N=70	-3.41 (-3.87, -2.96)	<0.0001
Mean ± SD	3.1 ± 1.3	2.7 ± 0.8	3.2 ± 1.5	6.5 ± 1.9	6.2 ± 1.3	6.6 ± 2.2		
Median (min, max)	2.5 (2.3, 11.7)	2.5 (2.3, 5.9)	2.6 (2.3, 11.7)	6.3 (4.3, 21.3)	5.7 (4.6, 9.4)	6.5 (4.3, 21.3)		
TTD, h								
N	N=100	N=31	N=69	N=104	N=34	N=70	-0.04 (-3.25, 3.17)	0.98
Mean ± SD	21.8 ± 13.4	20.5 ± 10.8	22.3 ± 14.5	21.8 ± 9.5	22.7 ± 10.6	21.4 ± 9.0		
Median (min, max)	22.3 (2.3, 96.1)	22.9 (2.3, 48.2)	22.3 (3.5, 96.1)	22.1 (5.7, 72.9)	22.8 (5.7, 71.5)	21.6 (5.8, 72.9)		
TTCE, min								
N	N=100	N=31	N=69	N=104	N=34	N=70	-27.23 (-33.86, -20.60)	<0.0001
Mean ± SD	10.5 ± 6.0	9.0 ± 4.1	11.1 ± 6.6	37.6 ± 33.2	32.2 ± 27.6	40.3 ± 35.5		
Median (min, max)	10.1 (1.7, 47.5)	9.8 (1.7, 17.5)	10.2 (2.0, 47.5)	25.2 (1.8, 132.3)	21.1 (2.0, 108.9)	27.8 (1.8, 132.3)		

Proportions of subjects achieving TTA at various fixed time points during the AMBULATE Trial are shown in Table 10.

Table 10. Proportion of Patients Achieving Ambulation at Fixed Time Points (per-patient analysis)

Time point	VASCADE MVP (N=100)		Manual Compression (N=104)	
≤ 1 hours	0	0%	0	0%
≤ 2 hours	1	1%	0	0%
≤ 3 hours	78	78%	0	0%
≤ 4 hours	84	84%	1	1%
≤ 5 hours	93	93%	18	17%
≤ 6 hours	98	98%	48	46%
≤ 7 hours	99	99%	87	84%
≤ 8 hours	99	99%	93	89%

Time point	VASCADE MVP (N=100)		Manual Compression (N=104)	
≤ 9 hours	99	99%	100	96%
≤ 10 hours	99	99%	103	99%
≤ 12 hours	100	100%	103	99%
≤ 24 hours	100	100%	104	100%

Device Success

Device success was achieved in 351 of the 363 access sites in which device deployment was attempted (97%). Table 11 shows the proportion of subjects achieving Device Success. Device issues were limited to known device performance issues based on VASCADE MVP product family such as device pull through, inability to deploy disc, inability to achieve temporary hemostasis, and use error. As noted above in the Safety Results section, as a result of pull-throughs during the AMBULATE Trial, mostly with 12F access sites, the deployed disc diameter was increased from 21F to 23F to better achieve temporary hemostasis without pull-through.

Table 11. VASCADE MVP Device Success (Device Arm Only) Per Access Site

Actual Devices Attempted	Number of Access Sites	Successes	Percent
	363	351	97%

Procedure Success

No major access site-related complications were reported in either randomized group; however, there were 2 VASCADE MVP subjects and 1 manual compression subject that did not complete follow-up. Therefore, Procedure Success was achieved in 98% of VASCADE MVP cases and in 99% of manual compression cases.

Table 12. Proportion of Procedure Success

Procedure Success	VVCS (N=100)		Manual Compression (N=104)	
Yes	98	98%	103**	99%
Unknown*	2	2%	1	1%

* VASCADE MVP: subject 03-001 had an office follow-up at 3 days post-procedure and did not return for a later visit; subject 11-007 was lost to follow-up within study period
**MC: subject 03-002 lost to follow-up within study period

3. Subgroup Analyses

The following baseline characteristic was evaluated for potential association with outcomes: sex. There was no statistically significant difference in the rate of major or minor complications for either sex. In addition, there was no statistically significant difference in TTA, TPPT, TTH, TTDE, TTD, or TTCE for either sex.

4. Pediatric Extrapolation

In this premarket application, existing clinical data was 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 33 investigators. None of the clinical investigators had disclosable financial interests/arrangements as defined in sections 54.2(a), (b), (c), and (f). 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 Device 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 clinical data from the AMBULATE study demonstrate that patients treated with the VASCADE MVP VVCS had a lower mean time to ambulation, total post-procedural time, time to hemostasis, time to eligibility for hospital discharge, and time to closure eligibility compared to patients treated with manual compression, and that the differences in these times are statistically and clinically significant.

B. Safety Conclusions

The risks of the device are based on data collected in a clinical study conducted to support PMA approval as described above. There were no major complications in the pivotal study in either arm. Additionally, the rate of overall minor complications was numerically lower in the VASCADE MVP VVCS treatment arm as compared to manual compression.

C. Benefit-Risk Conclusions

The probable benefits of the device are also based on data collected in a clinical study conducted to support PMA approval as described above. In summary, the benefits of the VASCADE MVP VVCS device include significantly reduced mean TTA (54% reduction), mean TPPT (54% reduction), mean TTH (55% reduction) and mean TTDE (52% reduction), as compared with manual compression.

Additionally, there was a numerically lower rate of overall major and minor complications in the VASCADE MVP VVCS device patients as compared to the manual compression patients.

Additional factors to be considered in determining probable risks and benefits for the VASCADE MVP VVCS device included: the design of the study, the conduct of the study, the robustness of the analysis of the study results, and the generalizability of the study results. The availability of alternative treatments, and risk mitigation also factored into the overall risk assessment.

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

In conclusion, given the available information above, the data support that for mid-bore femoral venous access site closure in patients who have undergone interventional catheter-based procedures, 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. The data support the claims of improved time to ambulation, total post-procedural time, time to hemostasis, and time to hospital discharge eligibility in interventional patients when compared to manual compression.

XIII. CDRH DECISION

CDRH issued an approval order on November 27, 2018.

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

XIV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

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

Post-approval Requirements and Restrictions: See approval order.