CARDIVA MEDICAL, INC.

VASCADE® Vascular Closure System (VASCADE VCS)

INSTRUCTIONS FOR USE
5F and 6/7F

CAUTION – Federal (USA) law restricts this device to sale by or on the order of a physician

DESCRIPTION

The VASCADE VCS is intended to seal the femoral arterial or femoral venous access site at the completion of an endovascular procedure. The system is designed to deliver a resorbable Collagen Patch, extra-vascularly, at the arteriotomy or venotomy site to aid in achieving hemostasis. There are two versions of products in the VASCADE product family. One is for use in 5F 12cm[1] introducer sheaths, and the other device is for use in 6F or 7F 12cm[1] introducer sheaths. The system consists of a sterile disposable Vascular Closure Catheter which houses a resorbable Collagen Patch, and the VASCADE Clip (refer to Figure 1). 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 in VASCADE 5F is 8.5mg ± 2mg and in VASCADE 6/7F it 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 verify placement of the patch in the tissue tract adjacent to the femoral arteriotomy or venotomy site prior to the release of the patch. A second distal marker band locates the distal tip of the VASCADE Disc. After completion of the catheterization procedure, the VASCADE VCS Catheter is inserted through a commercially available 5F, 6F, or 7F introducer sheath. The VASCADE Disc is then deployed within the vessel and the introducer sheath is removed over the VASCADE VCS Catheter. After the introducer sheath is removed, the VASCADE Disc is positioned against the intimal aspect of the arteriotomy or venotomy, providing both temporary hemostasis and protection from intravascular placement of the Collagen Patch, and the VASCADE Clip is applied at skin level to maintain the position of the VASCADE Disc. After confirming the position of the Collagen Patch fluoroscopically, 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 VASCADE Disc is collapsed and the VASCADE VCS Catheter is removed from the artery or vein leaving the resorbable, extra-vascular, hemostatic Collagen Patch at the arteriotomy or venotomy site providing vessel hemostasis.

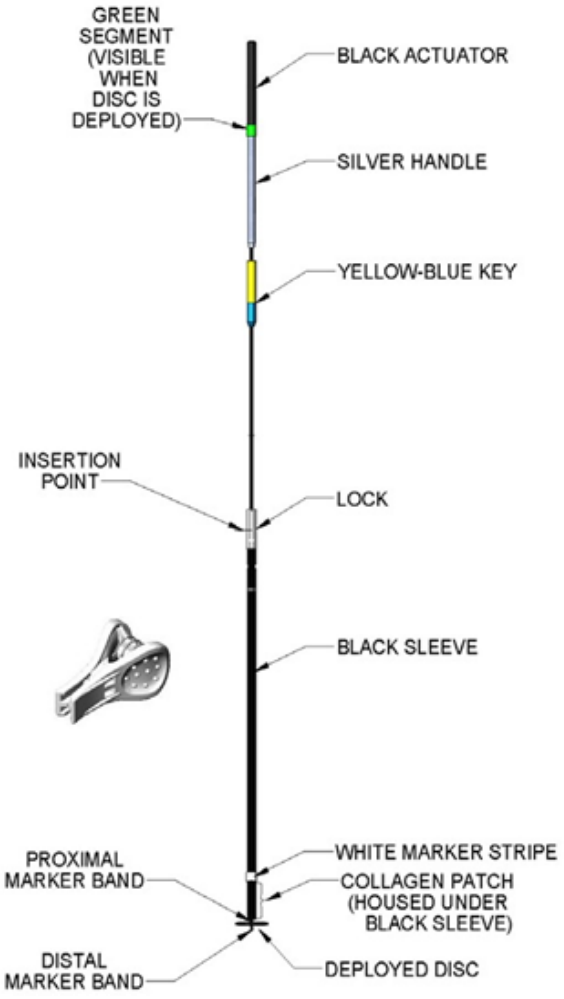


Fig. 1 – VASCADE Vascular Closure System (VCS)

INDICATIONS FOR USE

The VASCADE™ Vascular Closure System (VCS) is indicated for femoral arterial or femoral venous 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 when used for femoral arterial closure in patients who have undergone diagnostic endovascular procedures using a 5F, 6F, or 7F procedural sheath.

[1] Overall length of the sheath (including the hub) needs to be less than 15cm.

CONTRAINDICATIONS

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

WARNINGS

- Do not reuse or re-sterilize. The VASCADE VCS is intended to be used once only for a single patient. Product reuse or re-sterilization, may result in transmission of infectious or blood borne diseases and/or death.
- Do not use if components or packaging appear to be damaged or defective or if any portion of the packaging has been previously opened. Damaged or opened packages may compromise product functionality.
- Do not use if product is beyond the expiration date. Product performance has not been established beyond the labeled shelf life.
- Do not deploy the VASCADE Disc in a stent. Do not pull the deployed VASCADE disc through a stent. Damage to the product may occur.
- Do not use VASCADE if access is through a previously placed permanent closure device such as a metal clip and/or permanent suture. Interference between the two closure devices may result.
- Do not deploy the Collagen Patch if there is a suspicion that the VASCADE Vascular Closure Disc is not seated against the intimal aspect of the arteriotomy or venotomy site. Partial or complete obstruction of blood flow may result.
- Do not deploy a second collagen patch at the same access site within 30 days. The previously implanted collagen plug may be inadvertently introduced into the femoral vessel.

PRECAUTIONS

- The VASCADE VCS should only be used by a trained licensed physician or healthcare professional.
    - Note the training referred to here is previous training for accessing vessels, and positioning and using catheters. The VASCADE VCS device does not require formal training beyond review of the content provided in this IFU
- Do not use in access sites where there is suspicion of a "backwall" stick. Increased bleeding risk may occur.
- Do not use if arteriotomy or venotomy is noted to be a "side stick." Bleeding risk may increase.
- Do not use if arteriotomy or venotomy site is noted to be "high," above the Inguinal Ligament (cephalad to lower half of the femoral head or the inferior epigastric artery origin from the external iliac artery/ inferior epigastric vein entry into the external iliac vein). This may increase the risk of bleeding.
- Do not use in an artery with suspected intraluminal thrombus, hematoma, pseudoaneurysm, or arteriovenous fistula. These conditions may complicate proper device use and performance.
- Do not use if intra-procedural bleeding around the introducer sheath is noted including hematoma formation (sign of possible multiple wall stick). This may suggest problems with the access site.
- Do not use in a procedural sheath > 12cm in length (or >15cm in overall length) or with a diameter other than 5F for VASCADE 5F, or 6F or 7F for VASCADE 6/7F. This may complicate disk deployment.

SPECIAL PATIENT POPULATIONS

NOTE: The safety and effectiveness of VASCADE VCS have not been evaluated in the following patients who are/have:

- Less than 18 years of age;
- Pregnant and/or lactating women;
- Pre-existing immunodeficiency disorder and/or chronic use of systemic steroids;
- Known significant coagulopathy/bleeding disorder such as thrombocytopenia (platelet count <100,000/mm^3), thrombasthenia, hemophilia, von Willebrand's disease or anemia (Hemoglobin <10g/dL, Hematocrit <30%);
- Previous vascular grafts or surgery at the target vessel access site;
- Symptomatic ipsilateral lower extremity ischemia;
- Fluoroscopically visible calcium or atherosclerotic disease within 1 cm of the puncture site;
- Femoral artery or vein lumen less than 6 mm;
- Length of the tissue tract, the distance between the anterior arterial or venous wall and skin, is estimated to be less than 2.5cm;
- INR ≥1.8 if patient received warfarin;
- Fibrinogen level < 150 mg/dl if patient received fibrinolytic agent;
- Extreme morbid obesity (BMI > 45 kg/m2) or underweight (BMI < 20 kg/m^2);

- Uncontrolled hypertension (BP > 180/110);

Adverse Events

Complications may occur and may be related to the endovascular procedure or the vascular closure. They include, but are not limited to:

- Allergic response
- Vessel occlusion
- Vessel 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
- Laceration of the vessel wall
- Lower extremity ischemia
- Perforation of the vessel wall
- Peripheral nerve injury
- Pseudoaneurysm
- Retroperitoneal bleeding
- Deep vein thrombosis
- Superficial vein thrombosis
- Vascular injury
- Vasovagal response
- Vasospasm
- Wound dehiscence
- Puncture site pain

VASCADE 6/7F VCS was evaluated in a prospective, multi-center, randomized (2:1) clinical trial (the RESPECT Trial) in 20 sites in the United States and one site in Australia, comparing VASCADE VCS to Manual Compression (MC). The trial involved 420 patients undergoing diagnostic (n=211) or interventional (n=209) endovascular procedures. **Table 1**, **Table 2**, and **Table 3** summarize the reported major and minor complications in the trial for all patients, diagnostic patients, and interventional patients, respectively.

Table1: Reported Major and Minor Complications - All Patients

Access Site-Related Complications at 30 Days by Event	Total (N=417)				
	VASCADE (N=275)		Manual Compression (N=142)		p-value*
Any access-site-related major complication	**0**	**0.0%**	**0**	**0.0%**	1.00
Access site-related bleeding requiring transfusion	0	0.0%	0	0.0%	1.00
Vascular injury requiring repair	0	0.0%	0	0.0%	1.00
New ipsilateral lower extremity ischemia causing a threat to the viability of the limb	0	0.0%	0	0.0%	1.00
Access site-related infection requiring intravenous antibiotics and/or extended hospitalization	0	0.0%	0	0.0%	1.00
New onset access site-related neuropathy in the ipsilateral lower extremity requiring surgical repair	0	0.0%	0	0.0%	1.00
Permanent access site-related nerve injury (> 30 days)	0	0.0%	0	0.0%	1.00
Any Access Site-Related Minor Complication	**3**	**1.1%**	**10**	**7.0%**	**0.002**
Access site-related bleeding requiring > 30 minutes to achieve hemostasis	1	0.4%	10	7.0%	0.0001
Access site-related hematoma > 6 cm	1	0.4%	0	0%	1.00
Late access site-related bleeding (following hospital discharge)	0	0%	0	0%	1.00
Ipsilateral lower extremity arterial emboli	0	0%	0	0%	1.00
Ipsilateral deep vein thrombosis**	4	1.5%	0	0%	NA
Access site-related vessel laceration	0	0%	0	0%	1.00
Access site wound dehiscence	0	0%	0	0%	1.00
Localized access site infection treated with intramuscular or oral antibiotics	0	0%	0	0%	1.00
Arteriovenous fistula not requiring treatment**	1	0.4%	0	0%	NA
Pseudoaneurysm requiring thrombin injection or fibrin adhesive injection**	1	0.4%	0	0%	NA
Pseudoaneurysm not requiring treatment**	4	1.5%	0	0%	NA
New onset access site-related neuropathy in the ipsilateral lower extremity not requiring surgical repair	1	0.4%	0	0%	1.00

Ipsilateral pedal pulse diminished by two grades or transiently lost	0	0%	0	0%	1.00

*Two-sided Fisher's exact test

**Due to different complication-detecting methods between study arms (100 VASCADE patients and no other study patients underwent a femoral ultrasound exam in an ultrasound sub-study), rates for pseudoaneurysm requiring or not requiring treatment, arteriovenous fistula not requiring treatment, and ipsilateral deep vein thrombosis (which were detected by ultrasound exam) are presented but not compared between arms, nor are they included in the computation of the VASCADE overall minor complication rate (top row).

Table2: Reported Major and Minor Complications Diagnostic Patients

Access Site-Related Major Complications at 30 Days by Event	Diagnostic (N=210)				
	VASCADE (N=136)		Manual Compression (N=74)		p-value*
Any access-site-related major complication	**0**	**0.0%**	**0**	**0.0%**	**1.00**
Access site-related bleeding requiring transfusion	0	0.0%	0	0.0%	1.00
Vascular injury requiring repair	0	0.0%	0	0.0%	1.00
New ipsilateral lower extremity ischemia causing a threat to the viability of the limb	0	0.0%	0	0.0%	1.00
Access site-related infection requiring intravenous antibiotics and/or extended hospitalization	0	0.0%	0	0.0%	1.00
New onset access site-related neuropathy in the ipsilateral lower extremity requiring surgical repair	0	0.0%	0	0.0%	1.00
Permanent access site-related nerve injury (> 30 days)	0	0.0%	0	0.0%	1.00
Any Access Site-Related Minor Complication	**2**	**1.5%**	**2**	**2.7%**	**0.61**
Access site-related bleeding requiring > 30 minutes to achieve hemostasis	0	0%	2	2.7%	0.12
Access site-related hematoma > 6 cm	1	0.7%	0	0%	1.00
Late access site-related bleeding (following hospital discharge)	0	0%	0	0%	1.00
Ipsilateral lower extremity arterial emboli	0	0%	0	0%	1.00
Ipsilateral deep vein thrombosis**	3	2.2%	0	0%	NA
Access site-related vessel laceration	0	0%	0	0%	1.00
Access site wound dehiscence	0	0%	0	0%	1.00
Localized access site infection treated with intramuscular or oral antibiotics	0	0%	0	0%	1.00
Arteriovenous fistula not requiring treatment**	0	0%	0	0%	NA
Pseudoaneurysm requiring thrombin injection or fibrin adhesive injection**	0	0%	0	0%	NA
Pseudoaneurysm not requiring treatment**	1	0.7%	0	0%	NA
New onset access site-related neuropathy in the ipsilateral lower extremity not requiring surgical repair	1	0.7%	0	0%	1.00
Ipsilateral pedal pulse diminished by two grades or transiently lost	0	0%	0	0%	1.00

*Two-sided Fisher's exact test

**Due to different complication-detecting methods between study arms (100 VASCADE patients and no other study patients underwent a femoral ultrasound exam in an ultrasound sub-study), rates for pseudoaneurysm requiring or not requiring treatment, arteriovenous fistula not requiring treatment, and ipsilateral deep vein thrombosis (which were detected by ultrasound exam) are presented but not compared between arms, nor are they included in the computation of the VASCADE overall minor complication rate (top row).

Table 3: Reported Major and Minor Complications
Interventional Patients

Access Site-Related Major Complications at 30 Days by Event	Interventional (N=207)				
	VASCADE (N=139)		Manual Compression (N=68)		p-value*
Any access-site-related major complication	**0**	**0.0%**	**0**	**0.0%**	**1.00**
Access site-related bleeding requiring transfusion	0	0.0%	0	0.0%	1.00
Vascular injury requiring repair	0	0.0%	0	0.0%	1.00
New ipsilateral lower extremity ischemia causing a threat to the viability of the limb	0	0.0%	0	0.0%	1.00
Access site-related infection requiring intravenous antibiotics and/or extended hospitalization	0	0.0%	0	0.0%	1.00
New onset access site-related neuropathy in the ipsilateral lower extremity requiring surgical repair	0	0.0%	0	0.0%	1.00
Permanent access site-related nerve injury (> 30 days)	0	0.0%	0	0.0%	1.00
Any Access Site-Related Minor Complication	**1**	**0.7%**	**8**	**11.8%**	**0.001**
Access site-related bleeding requiring > 30 minutes to achieve hemostasis	1	0.7%	8	11.8%	0.001
Access site-related hematoma > 6 cm	0	0%	0	0%	1.00
Late access site-related bleeding (following hospital discharge)	0	0%	0	0%	1.00
Ipsilateral lower extremity arterial emboli	0	0%	0	0%	1.00
Ipsilateral deep vein thrombosis**	1	0.7%	0	0%	NA
Access site-related vessel laceration	0	0%	0	0%	1.00
Access site wound dehiscence	0	0%	0	0%	1.00
Localized access site infection treated with intramuscular or oral antibiotics	0	0%	0	0%	1.00
Arteriovenous fistula not requiring treatment**	1	0.7%	0	0%	NA
Pseudoaneurysm requiring thrombin injection or fibrin adhesive injection**	1	0.7%	0	0%	NA
Pseudoaneurysm not requiring treatment**	3	2.2%	0	0%	NA
New onset access site-related neuropathy in the ipsilateral lower extremity not requiring surgical repair	0	0%	0	0%	1.00
Ipsilateral pedal pulse diminished by two grades or transiently lost	0	0%	0	0%	1.00

*Two-sided Fisher's exact test

**Due to different complication-detecting methods between study arms (100 VASCADE patients and no other study patients underwent a femoral ultrasound exam in an ultrasound sub-study), rates for pseudoaneurysm requiring or not requiring treatment, arteriovenous fistula not requiring treatment, and ipsilateral deep vein thrombosis (which were detected by ultrasound exam) are presented but not compared between arms, nor are they included in the computation of the VASCADE overall minor complication rate (top row).

VASCADE 6/7F VCS Clinical Trial

The RESPECT Study was a prospective, randomized, controlled multi-center clinical trial designed to evaluate the safety and effectiveness of the study device in sealing common femoral arterial access sites and providing reduced times to hemostasis and ambulation compared with Manual Compression (MC) at the completion of diagnostic or interventional endovascular procedures (cardiac or peripheral vascular catheterizations) performed through 6F or 7F introducer sheaths. Patients were randomized in a 2:1 treatment device to control ratio. The trial was conducted at 20 sites in the United States and one site in Australia. In an ultrasound sub-study, images of the access site were obtained from 100 consecutively randomized, treated, VASCADE patients at 5 sites prior to hospital discharge.

To be eligible for the trial, patients were required to be between 18 and 80 years of age; able and willing to sign an Informed Consent Form; acceptable candidates for an elective, non-emergent diagnostic or interventional endovascular procedure via the common femoral artery using a 6F or 7F introducer sheath who were also acceptable candidates for post-procedure manual compression; and able and willing to complete a 30-day ± 7 days follow-up evaluation. Patients were excluded if they had clinically significant peripheral vascular disease; bleeding disorder; ipsilateral femoral arteriotomy within the previous 30 days; planned endovascular procedure within the next 30 days; previous vascular grafts at target access site; extreme morbid obesity (BMI greater than 45 kg/m2) or were underweight (BMI less than 20 kg/m2); known allergy/adverse reaction to bovine derivatives; planned extended hospitalization; administration of low molecular weight heparin (LMWH) within 8 hours of the procedure; femoral artery diameter less than 6mm at access site; multi arterial sticks; received unfractionated heparin with an ACT greater than 300 seconds in the absence of a glycoprotein (GP) IIb/IIIa inhibitor or greater than 250 seconds in the presence of a glycoprotein IIb/IIIa inhibitor; intra-procedural bleeding around sheath or suspected intraluminal thrombus, hematoma, pseudoaneurysm, or AV fistula; uncontrolled hypertension; or length of tissue tract estimated to be less than 2.5cm.

A total of 420 patients, 211 diagnostic and 209 interventional patients, were enrolled. The mean age was 62 years and mean BMI was 30kg/m2. Twenty-nine percent (29%) of patients were female. The study also included 69 roll-in cases, consisting of 45 diagnostic and 24 interventional patients. The randomized VASCADE arm included 137 diagnostic and 141 interventional patients, while the manual compression arm included 74 diagnostic and 68 interventional patients. Seventy-seven percent (77%) of the VASCADE interventional patients received bivalirudin, 27% received heparin, 60% received clopidogrel, and 8% received GP IIb/IIIa inhibitors. The mean Activated Clotting Time (ACT) in patients receiving unfractionated heparin for diagnostic patients was 221 seconds vs. 172 seconds in the VASCADE and manual compression groups, respectively. The mean ACTs in interventional patients were similar among groups, with the VASCADE group reporting 289.5 ± 136.9 seconds vs. 289.0 ± 100.7 seconds in the manual compression group.

Enrolled patients were followed for 30±7 days. Four hundred fifteen (415) randomized patients (98.8%) completed 30-day follow-up. Three patients were prematurely randomized and immediately withdrawn from the study due to ineligibility; one was lost to follow-up and one withdrew consent to participate prior to 30-day follow-up.

Effectiveness Results

Table 4 summarizes the primary efficacy endpoint, Time to Hemostasis (TTH), and secondary efficacy endpoints, Time to Ambulation (TTA), Time to Discharge Eligibility (TTDE), and Time to Discharge (TTD). The primary efficacy endpoint, TTH, was defined as elapsed time between device removal, i.e., device removal for Cardiva VASCADE VCS and sheath removal for manual compression, and first observed and confirmed arterial hemostasis (no or minimal subcutaneous oozing and the absence of expanding or developing hematoma). TTA was defined as the elapsed time between device removal, i.e., device removal for Cardiva VASCADE VCS and sheath removal for manual compression, and when ambulation was achieved (patient standing and walking at least 20 feet without re-bleeding). TTDE was defined as the elapsed time between device removal, i.e., device removal for Cardiva VASCADE VCS and sheath removal for manual compression, and when the patient was eligible for hospital discharge based upon an assessment of the access site.

Table 4: Primary and Secondary Effectiveness

	Diagnostic (N=211)			Interventional (N=209)			Total (N=420)		
	VASCADE (N=137)	Manual Compression (N=74)	p-value*	VASCADE (N=141)	Manual Compression (N=68)	p-value*	VASCADE (N=278)	Manual Compression (N=142)	p-value*
Time to Hemostasis (minutes)									
N	136	74		139	68		275	142	
Mean	4.0	18.2	< 0.0001	5.5	24.9	< 0.0001	4.8	21.4	< 0.0001
Std Deviation	4.2	8.1		6.3	15.1		5.4	12.4	
Median	2.6	18.5	< 0.0001	3.3	20.5	< 0.0001	3.0	20.0	< 0.0001
Min	0.6	4.3		0.8	0.0		0.6	0.0	
Max	24.7	64.6		31.6	97.0		31.6	97.0	
Time to Ambulation (hours)									
N	136	74		139	68		275	142	
Mean	2.6	4.6	< 0.0001	5.0	7.2	0.003	3.8	5.8	< 0.0001
Std Deviation	2.0	1.6		6.7	3.7		5.1	3.1	
Median	2.2	4.4	< 0.0001	4.1	6.4	< 0.0001	3.2	5.2	< 0.0001
Min	1.0	1.7		2.2	2.5		1.0	1.7	
Max	20.1	11.0		78.0	22.8		78.0	22.8	
Time to Discharge Eligibility (hours)									
N	136	74		138	68		274	142	
Mean	3.1	5.0		6.6	8.2		4.8	6.5	
Std Deviation	2.1	1.6		8.4	4.0		6.4	3.3	
Median	2.6	4.8		4.6	7.0		3.6	5.7	
Min	1.4	2.2		2.6	3.0		1.4	2.2	
Max	20.5	11.3		78.4	23.2		78.4	23.2	
Time to Hospital Discharge (hours)									
N	136	74		139	68		275	142	
Mean	12.0	7.3		24.5	20.8		18.3	13.7	
Std Deviation	45.4	7.3		16.2	6.7		34.5	9.8	
Median	3.4	5.3		23.4	19.9		17.2	13.9	
Min	1.7	2.4		3.4	4.9		1.7	2.4	
Max	432.9	55.6		147.6	45.7		432.9	55.6	

*p-value from t-test for comparing means and Wilcoxon's test for comparing medians

Table 5 summarizes the secondary effectiveness endpoint of Procedure Success. Procedure Success was defined as attainment of final hemostasis using any method and freedom from major vascular complications through 30 days. The Procedure Success Rate was 100% for VASCADE and Manual Compression.

Table 5: Secondary Effectiveness, Procedure Success

Procedure	Treatment Assignment	Number of Patients	Number of Successes	Success Rate	95% Confidence Interval*	
Diagnostic	VASCADE	136	136	100%	97%	100%
	Manual Compression	74	74	100%	95%	100%
Interventional	VASCADE	139	139	100%	97%	100%
	Manual Compression	68	68	100%	95%	100%
Total	Cardiva VCS	275	275	100%	99%	100%
	Manual Compression	142	142	100%	97%	100%

*95% Exact Binomial Confidence Interval

**Two-sided Fisher's exact test.

Table 6 summarizes the results of Device Success. Device Success was defined as the ability to deploy the delivery system, deliver the collagen, and achieve hemostasis with the VASCADE Vascular Closure System alone or with adjunctive compression. The overall Device Success Rate for the total patients was 96%.

Table 6: Secondary Effectiveness, Device Success

Procedure	Number of Patients**	Number of Successes	Success Rate	95% Confidence Interval*	
Diagnostic	136	128	94%	88.7%	97.4%
Interventional	139	135	97%	92.8%	99.2%

*95% Exact Binomial Confidence Interval

** Includes 6 instances of failure to follow written Instructions for Use. Excluding these 6 instances, Device success rates are 96% (Diagnostic), 99% (Interventional) and 98% (Total)

Table 7, **Table 8**, **Table 9**, and **Table 10** summarize the cumulative data for TTH, TTA, TTDE, and TTD, respectively.

Table 7: Cumulative Time to Hemostasis (TTH) All Patients

Time point	Total (N=420)			
	VASCADE (N=278)		Manual Compression (N=142)	
N	275		142	
≤ 1 minute	8	3%	1	1%
≤ 2 minutes	51	19%	1	1%
≤ 3 minutes	136	49%	1	1%
≤ 4 minutes	195	71%	1	1%
≤ 5 minutes	221	80%	5	4%
≤ 10 minutes	246	89%	16	11%
≤ 20 minutes	263	96%	85	60%
≤ 30 minutes	274	100%	132	93%

Table 8: Cumulative Time to Ambulation (TTA) All Patients

Time point	Total (N=420)			
	VASCADE (N=278)		Manual Compression (N=142)	
N	275		142	
≤ 1 hour	0	0%	0	0%
≤ 2 hours	22	8%	1	1%
≤ 3 hours	122	44%	12	8%
≤ 4 hours	179	65%	31	22%
≤ 5 hours	255	93%	68	48%
≤ 10 hours	268	97%	131	92%
≤ 15 hours	270	98%	138	97%

Table 9: Cumulative Time to Discharge Eligibility (TTDE) All Patients

Time point	Total (N=420)			
	VASCADE (N=278)		Manual Compression (N=142)	
N	274		142	
≤ 2 hours	10	4%	0	0%
≤ 4 hours	152	55%	20	14%
≤ 6 hours	247	90%	79	56%
≤ 8 hours	257	94%	117	82%
≤ 12 hours	262	96%	131	92%
≤ 24 hours	270	99%	142	100%
≤ 48 hours	272	99%	142	100%

Table 10: Cumulative Time to Discharge (TTD) All Patients

Time point	Total (N=420)			
	VASCADE (N=278)		Manual Compression (N=142)	
N	275		142	
≤ 2 hours	1	0%	0	0%
≤ 4 hours	86	31%	12	8%
≤ 6 hours	123	45%	50	35%
≤ 8 hours	131	48%	66	46%
≤ 12 hours	134	49%	69	49%
≤ 24 hours	207	75%	129	91%
≤ 48 hours	265	96%	141	99%

Evaluation of VASCADE 5F VCS

A. VASCADE 5F Confirmatory Trial

The purpose of the VASCADE 5F study was to confirm the safety and effectiveness of the scaled-down 5F version of the VASCADE 6/7F VCS. The 5F device is virtually identical to the slightly larger 6/7F VCS. The study population was defined as patients undergoing cardiac or peripheral vascular catheterization procedures via the femoral artery approach when using a standard 5F introducer sheath. The study was conducted at a single-center in Australia, and was a prospective, non-randomized, non-blinded, single treatment trial. The inclusion and exclusion criteria were identical to the U.S. IDE RESPECT trial with the exception that patients had to be undergoing a catheterization procedure utilizing a 5F introducer sheath.

Thirty (30) patients were enrolled into the study. All of the patients enrolled in the study underwent diagnostic procedures. Patient demographic characteristics at baseline, such as gender, age, and BMI were comparable between the U.S. IDE trial and the 5F Australian confirmatory study. The safety and effectiveness endpoints for the 5F confirmatory study were identical to the 6/7F study. Identical to the pivotal RESPECT trial, the primary safety endpoint was the rate of combined major access site-related complications within 30 ± 7 days following the catheterization procedure. The secondary safety endpoint was the rate of combined minor access site-related complications within 30 ± 7 days following the procedure. Identical to the IDE RESPECT trial, the primary effectiveness endpoint was TTH. The secondary effectiveness endpoints were TTA, TTDE, TTD, procedure success, and device success.

Results of 5F trial

Table 1: Access Site-Related Major Complications

Access Site-Related Major Complications	5-French (N=30)	
Any access-site-related major complication	**1**	**3.3%**
Access site re-bleeding requiring transfusion	1*	3.3%
Vascular injury requiring repair	0	0.0%
New ipsilateral lower extremity ischemia causing a threat to the viability of the limb	0	0.0%
Access site-related infection requiring intravenous antibiotics and/or extended hospitalization	0	0.0%
New onset access site-related neuropathy in the ipsilateral lower extremity requiring surgical repair	0	0.0%
Permanent access site-related nerve injury (> 30 days)	0	0.0%

One occurrence only.

Table 2: Access Site-Related Minor Complications

Access Site-Related Minor Complications	5-French (N=30)	
Any Access Site-Related Minor Complication	**1**	**3.3%**
Access site-related bleeding requiring > 30 minutes to achieve hemostasis	0	0.0%
Access site-related hematoma > 6 cm	0	0.0%
Late access site-related bleeding (following hospital discharge)	0	0.0%
Ipsilateral lower extremity arterial emboli	0	0.0%
Ipsilateral deep vein thrombosis	0	0.0%
Access site-related vessel laceration	0	0.0%
Access site wound dehiscence	0	0.0%
Localized access site infection treated with intramuscular or oral antibiotics	0	0.0%
Arteriovenous fistula not requiring treatment	0	0.0%
Pseudoaneurysm requiring thrombin injection or fibrin adhesive injection	0	0.0%
Pseudoaneurysm not requiring treatment	0	0.0%
New onset access site-related neuropathy in the ipsilateral lower extremity not requiring surgical repair	1*	3.3%
Ipsilateral pedal pulse diminished by two grades or transiently lost	0	0.0%

*One occurrence only.

Table 3: TTH, TTA, TTDE, and TTD Effectiveness Endpoints

	5 French (N=30)
Time to Hemostasis (minutes)	
N	30
Mean	3.0
Std Deviation	2.4
Median	2.3
Min	0.2
Max	11.8
Time to Ambulation (hours)	.
N	30
Mean	4.1
Std Deviation	5.9
Median	2.3
Min	1.5
Max	25.9
Time to Discharge Eligibility (hours)	.
N	30
Mean	5.6
Std Deviation	9.0
Median	3.1
Min	2.0
Max	46.9
Time to Hospital Discharge (hours)	.
N	30
Mean	11.9
Std Deviation	16.0
Median	3.5
Min	2.0
Max	73.0

B. VASCADE 5F Engineering Analysis

Engineering analysis for the scaled down VASCADE 5F VCS included Collagen Patch size calculations resulting in a proportionally smaller Collagen Patch as compared with the VASCADE 6/7F VCS device. These analyses confirmed equivalent tissue-tract space-filling capability between the 5F and 6/7F versions of the VASCADE device. In addition, fundamentally the same verification and validation testing was completed for the 5F VASCADE VCS device as was completed for the 6/7F VASCADE VCS device.

Conclusions

The results from the RESPECT clinical trial demonstrate that patients who have undergone diagnostic or interventional cardiac or peripheral vascular endovascular procedures using a 6F or 7F introducer sheath and were treated with VASCADE VCS have statistically and clinically significant decreased times to hemostasis and ambulation for diagnostic and interventional procedures, and statistically and clinically significant decreased time to discharge eligibility for diagnostic procedures, when compared to patients treated with manual compression. In addition, the trial demonstrated that patients treated with the VASCADE VCS were noninferior to patients treated with manual compression with respect to major access site-related complications.

A confirmatory clinical study and engineering analysis demonstrated that the VASCADE 5F VCS is equivalent to the VASCADE 6/7F VCS in design and performance.

DEVICE PREPARATION AND PROCEDURE

At the time of initial introducer sheath placement, patient body habitus should be evaluated to provide reasonable assurance that the distance between the femoral arteriotomy or femoral venotomy and the skin surface is greater than 2.5cm. After introducer sheath placement, an anterior oblique fluoroscopic image may be digitally recorded and stored, so that the arteriotomy or venotomy site location can be compared to the position of the radiopaque marker just prior to Collagen Patch release. The radiopaque marker is located immediately distal to the Collagen Patch. A single wall, common femoral arteriotomy or venotomy should also be confirmed at this time.

CAUTION: During access care should be taken so that the tissue tract is not pushed laterally or medially prior to accessing the vessel. This is to avoid misalignment of the tissue tract and the Collagen Patch relative to the arteriotomy or venotomy site once the device is removed from the vessel which may result in prolonged time to hemostasis.

1. Use the Cardiva VASCADE VCS only as described below:

Device	Model	Sheath Size	Sheath Length	Disc Size	Collagen Patch Length	Device Working Length	Maximum OD
Cardiva VASCADE 5F VCS	700-500DX	5 French	up to 12 cm	6.5 mm	15 mm	15 cm	1.80 mm
Cardiva VASCADE 6/7F VCS	700-580I	6 or 7 French	up to 12 cm	6.5 mm	15 mm	15 cm	2.1 mm

Note: The Collagen implant is a biological material compatible with Magnetic Resonance Imaging (MRI).

2. Inspect the package for damage (breaks, tears, open seals, water damage, etc.) and verify that expiration date has not passed.

3. Using standard sterile technique[2], remove the tray containing the VASCADE VCS Catheter and Clip from the foil pouch. Carefully remove VASCADE VCS Catheter and Clip from the tray. Examine the device by first verifying that the Black Sleeve is locked in position and the Collagen Patch is not exposed. Also verify that the Yellow-Blue Key **(Figure 2)** is not engaged in the Lock (the Lock is located at the proximal aspect of the Black Sleeve), and the Yellow-Blue Key is located at the proximal end of the Catheter Shaft. Inspect the Catheter further by examining the deployed VASCADE Disc. To deploy the Disc, hold the Silver Handle firmly and pull back on the Black Actuator until it locks in place. When the Disc is locked in the deployed position, the Green Segment will become visible as shown in Figure 3. Examine the Disc, which should appear circular and symmetrical with an intact membrane. **Figure 4** shows the deployed and collapsed Disc. After examination, collapse the Disc by pressing the Black Actuator tip down **(Figure 5)**. The tip of the VASCADE VCS Catheter should return to its original profile.

Fig. 2 – Verify Yellow-Blue Key is not engaged in the Lock and Black Sleeve is locked in position

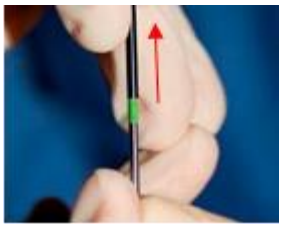


Fig. 3 – Pull back on Black Actuator Tip to deploy the Disc

Fig. 4 – Deployed & Collapsed Disc

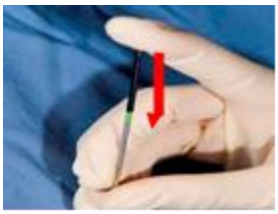


Fig. 5 – Collapse Disc by pressing Black Actuator Tip like a ballpoint pen

4. Verify that the sheath is not positioned in a tortuous vessel. If required, retract the sheath slightly to a non-tortuous location. Verify that the sheath is still positioned within the artery or vein.

WARNING: Verify there is no vessel tortuosity or side branches within 3-4 cm from the distal opening of the sheath and the end of the sheath is not resting against the vessel wall. This is to prevent any vascular injury as a result of advancing the catheter. If required, retract the sheath slightly to a non-tortuous location, being careful not to lose vessel access.

[2] See Aseptic Presentation Section for additional information.

5. Flush the sheath with sterile saline solution prior to insertion of the device.
6. Prior to insertion of device in the introducer sheath, momentarily insert the tip of the VCS Catheter in saline solution up to the White Marker Stripe and quickly remove.

CAUTION: Do not soak the VASCADE VCS Catheter in saline. Momentarily insert only the Catheter tip in saline solution immediately before use to avoid over-hydration of the patch, which may result in Catheter pull through during the sleeve retraction step.

7. Gently insert the VASCADE VCS Catheter (with disc collapsed) into the introducer sheath hub as shown in **Figure 6**. Insert the VASCADE VCS Catheter such that approximately half of the Lock is visible. Make certain that the Lock is NOT fully inserted into the sheath. See **Figure 7** for correct placement.

CAUTION: Do not advance VASCADE VCS Catheter into the patient if resistance is felt due to risk of vascular damage.

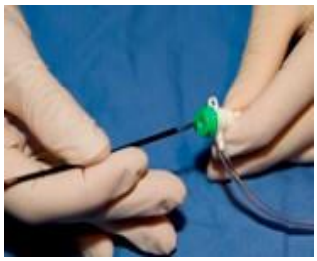


Fig. 6 – Insert device into hub of introducer sheath

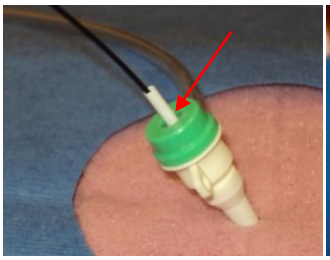


Fig. 7 – Insert device half way of the Lock

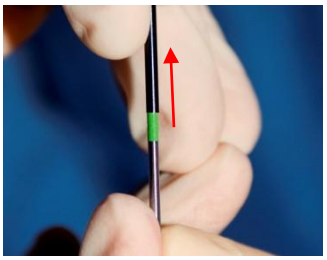


Fig. 8 – Pull back on Black Actuator Tip to deploy the Vascade Disc

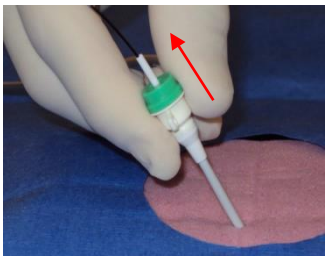


Fig. 9 – Grasp hub of sheath and remove over catheter

8. Deploy the Disc by holding the Silver Handle and pulling back the Black Actuator until it locks in place as shown in **Figure 8.**

CAUTION: Do **not** continue to pull on the Black Actuator once it is locked in place as this may damage the device.

NOTE: When the Disc is properly deployed, the Green Segment will become visible distal to the Black Actuator. If the catheter is not properly locked in place, the Black Actuator will slide back to its original position and the Green Segment will disappear (in VASCADE 5F approximately 1mm of the Green Segment remains visible when disc is collapsed) indicating that the Disc is not properly deployed. In this case repeat the step for deploying the Disc by pulling the Black Actuator more firmly until it locks in place.

9. Gently remove sheath, without applying any compression at the access site or holding the VASCADE VCS Catheter**,** as shown in **Figure 9**. As the sheath slides over the VASCADE VCS Catheter, grasp the Catheter proximal to the LOCK as it exits the distal end of the introducer sheath. Continue sliding the sheath over the VASCADE VCS Catheter and discard sheath.

CAUTION: Compressing the access site during sheath removal may not allow the Disc to track back to the arteriotomy or venotomy and may cause Disc deformation. This may lead to inability to achieve temporary hemostasis.

10. Apply gentle tension on the Black Actuator until temporary hemostasis is achieved. Note whether any portion of the White Marker Stripe, which is located near the distal aspect of the Black Sleeve, is visible above the skin. If it is, then the length of the tissue tract is less than 2.5 cm, indicating the tissue tract may not be long enough for the Collagen Patch.

WARNING: If any portion of the White Marker Stripe is showing DO NOT RELEASE the Collagen Patch as this may increase the risk of infection.

NOTE: If any portion of the White Marker Stripe is showing and the collagen patch is not to be deployed continue the procedure as follows:

For diagnostic cases: the VASCADE VCS Catheter should be removed by collapsing the Disc and then manual compression can be applied per institutional protocol.

For anti-coagulated patients: the Clip may be applied to the VASCADE VCS Catheter on the skin surface as shown in **Figure 10** to maintain temporary hemostasis. The device may then stay in dwelling to allow time for the ACT level to normalize. The device can then be removed followed by application of manual compression per institutional protocol to achieve final hemostasis.

11. Once temporary hemostasis is achieved, apply the Clip to the Black Sleeve at skin level as shown in **Figure 10.** Utilize fluoroscopy to verify that the deployed Disc is positioned against the intimal surface of the arteriotomy or venotomy by noting the position of the more proximal radiopaque marker. The marker should be at the arteriotomy or venotomy site which can be verified by comparing its location with the location of the arteriotomy or venotomy documented at the time of the introducer sheath insertion. The Collagen Patch is immediately proximal to this Marker Band. The Distal Marker Band locates the distal end of the Disc.

CAUTION: Applying too much upward tension on the Black Actuator may cause disc to pull out of vessel. Should this occur, convert to your **institution's manual compression protocol.**

WARNING: It is important to ensure that the Disc is in contact with the intimal aspect of the arteriotomy or venotomy before deploying the extra- vascular Collagen Patch to avoid releasing the Collagen Patch in the vessel**.** This step requires fluoroscopy **(Figure 11)**.

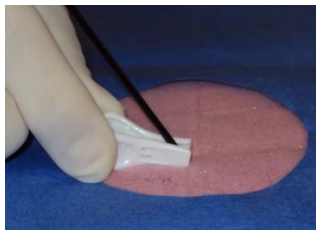


Fig. 10 – Apply Clip to Black Sleeve at skin level

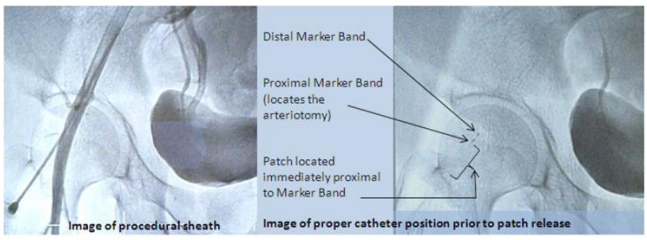


Fig. 11 – Fluoroscopic image demonstrating proper position of Disc against the intima

EXTRA-VASCULAR COLLAGEN PATCH DEPLOYMENT AND DEVICE REMOVAL

12. Once the Disc location is verified, expose the extra-vascular resorbable Collagen Patch by unlocking the Black Sleeve. This is done by grasping the Lock with the left hand, between the thumb and the index finger, and grasping the Yellow-Blue Key with the right hand and then sliding the Yellow-Blue Key into the Lock until no blue color is visible, as shown in Figure 12. Once the Sleeve is unlocked and while still holding on to the Lock, remove the Clip with the right hand, and gently slide the Lock back along the angle of entry to retract the Black Sleeve as shown in Figure 13. The Black Sleeve will move freely after some initial resistance. A second resistance point may be felt after the sleeve is moved approximately 1.6 cm (0.6 inch).

    Proceed to fully retract the Black Sleeve proximally to the Silver Handle. This action exposes the Collagen Patch extra-vascularly, which will swell at the arteriotomy or venotomy site. The Collagen Patch may be allowed to swell for up to 30 seconds prior to removal of the VASCADE VCS Catheter. The Clip should be reapplied during the Collagen Patch swell period with minimal tension on the Catheter (Figure 14).

NOTE: If the Black Sleeve does not retract easily, recheck that the blue end of the Yellow-Blue Key is fully engaged in the Lock.

NOTE: If the Collagen Patch is removed during sleeve retraction, for non-anti-coagulated patients, collapse the Disc, remove the Catheter and apply manual compression, per institutional protocol. If the patient is anti-coagulated, the Clip may be applied to the VASCADE VCS Catheter on the skin surface to maintain temporary hemostasis. The device may then stay in dwelling in order to allow time for the ACT level to normalize. The device can then be removed followed by application of manual compression to achieve final hemostasis.

Fig. 12 – Unlock the Black Sleeve by sliding Yellow-Blue Key into the Lock

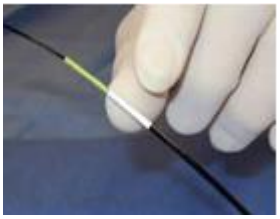


Fig. 13 – Retract the Black Sleeve by grasping the Lock and applying gentle upward tension toward the Silver Handle

Fig. 14 – Reapply Clip during the Collagen Patch swell period

Fig. 15 – Grasp Green Tube prior to collapsing the Disc

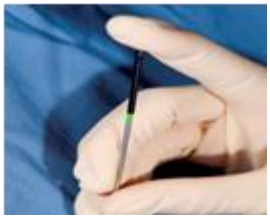


Fig. 16 – Collapse the Disc by pressing on the Black Actuator Tip

13. After patch swell time (≤ 30 seconds) has elapsed, remove the Clip. Rest the palm of the hand on the patient and grasp the green tube between the thumb and the index finger as shown in **Figure 15**. With slack in the catheter, collapse the Disc by pressing on the Black Actuator Tip as shown in **Figure 16**. When the Disc is fully collapsed, the Green Segment should not be visible for 6/7F device, or only a small portion, approximately 1mm, may be visible for the 5F device. While keeping the green tube stationary pull back the VASCADE VCS Catheter proximally. The Catheter Handle will move approximately 1.5cm while the green portion of the catheter remains stationary. This action slides the collapsed catheter Disc by the Collagen Patch while maintaining the position of the Collagen Patch. Once this initial movement has occurred, let go of the Green Tube. Gentle manual compression may be applied at the arteriotomy or venotomy site. Remove the VASCADE VCS Catheter, and apply manual compression.

    Alternative Technique: AFTER 15-30 seconds of patch swell time and PRIOR TO collapsing the Disk, remove the Clip. Rest the palm of the hand on the patient and grasp the green tube between the thumb and the index finger as shown in **Figure 15.** Push the green tube in the proximal direction approximately 1.5 cm while gently pulling back on the VASCADE VCS Catheter to maintain Disk position against artery wall. The green tube may be slid back and forth 2-3 times in order to assure release of the Collagen patch from device. Upon completion of this step, apply proximal compression, collapse the Disc by pressing on the Black Actuator Tip as shown in **Figure 16**. Gentle manual compression may be applied at the arteriotomy or venotomy site. Remove the VASCADE VCS Catheter, and apply manual compression.

14. Observe for vessel hemostasis. Manual compression can be used to decrease or stop any tract ooze until full hemostasis is achieved.

NOTE: Prior to the VASCADE VCS Catheter removal confirm that the Disc is completely collapsed by verifying that the Green Segment is no longer visible for 6/7F device and only a small portion approximately 1mm is visible for the 5F device. Care should be taken not to compress directly over the catheter during the removal step of the device so that the catheter can be easily removed and without displacement of Collagen Patch.

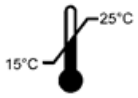
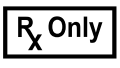
15. Apply sterile dressing to site per institution protocol. Maintain bed rest and periodically check site until patient is ready to ambulate.
16. Complete information on Patient Implant Card and provide to the patient.

Device Disposal:
After use, dispose of the contaminated device and/or packaging materials using standard hospital procedures and universally accepted practices for bio-hazardous wastes.

Additional Information for Step #3 Regarding Aseptic Presentation Steps to Follow:

- Inspect the product packaging. Observe for any breaks, holes, or openings that would compromise the integrity and sterility of the product.
- Read the label. Check the expiration date and verify correct product/size is used.
- Position near the sterile field. Be sure the scrubbed person receiving the product is prepared and ready to receive it with a clear space in the field.
    - All packaging for sterile products has a designated side to open from. Locate this side and slowly peel the package open.
    - Open the packaging with arms extended to avoid accidental contact with the product or the sterile field. Be sure the secondary sterile packaging containing the product does not come in contact with the edges of the external packaging as they are not considered sterile. Create a large enough opening in the package to remove the interior packaging containing the product without touching the non-sterile areas.
- Present the product to the scrubbed person.
- Discard packaging following facility protocol.

GRAPHICAL SYMBOLS ON THE VASCADE VCS PACKAGING

Symbol	Standard / Regulation*	Standard Reference No. / Symbol Title	Definition
	ISO 15223-1	5.1.1 / Manufacturer	medical device manufacturer
	ISO 15223-1	5.1.2 / Authorized representative in the European Community	authorized representative in the European Community
	ISO 15223-1	5.1.4 / Use-By Date	date after which the medical device is not to be used.
	ISO 15223-1	5.1.5 / Batch Code	manufacturer's batch code so that the batch or lot can be identified.
	ISO 15223-1	5.1.6 / Catalogue number	manufacturer's catalogue number so that the medical device can be identified.
	ISO 15223-1	5.2.4 / Sterilized using irradiation	medical device that has been sterilized using irradiation.
	ISO 15223-1	5.2.6 / Do not resterilize	medical device that is not to be re-sterilized.
	ISO 15223-1	5.2.8 / Do not use if package is damaged	medical device that should not be used if the package has been damaged or opened.
	ISO 15223-1	5.3.4 / Keep dry	medical device that needs to be protected from moisture.
	ISO 15223-1	5.3.7 / Temperature limit	temperature limits to which the medical device can be safely exposed.
	ISO 15223-1	5.4.2 / Do not re-use	medical device that is intended for one use, or for use on a single patient during a single procedure.
	ISO 15223-1	5.4.4 / Caution	Indicates the need for the user to consult the instructions for use for important cautionary information such as warnings and precautions that cannot, for a variety of reasons, be presented on the medical device itself.
	ISO 15223-1	5.4.5 / Contains or presence of natural rubber latex B.2 / Negation Symbol	Indicates that there is no presence of natural rubber or dry natural rubber latex as a material of construction within the medical device or the packaging of a medical device.
	21 CFR 801.109	Prescription Device	product is a medical device and Federal Law (USA) restricts this device to sale by or on the order of a physician
	N/A	Package quantity	quantity of systems in package
	ISO 11607-1	Sterile barrier packaging	Identifies the sterile barrier packaging

**Standards and Regulations:*
ISO 15223-1: *Medical devices-Symbols to be used with medical device labels, labelling and information to be supplied*
US FDA Title 21 CFR 801.109*: Prescription Devices*
ISO 11607-1*: Packaging for terminally sterilized medical devices — Part 1: Requirements for materials, sterile barrier systems and packaging systems*

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LIMITED WARRANTY

Cardiva Medical, Inc. warrants that each VASCADE Vascular Closure System is free from defects in workmanship and material under normal use and service, and provided it is used prior to the stated expiration date. Cardiva Medical, Inc. will not be liable for any incidental, special or consequential loss, damage or expense direct or indirect from the use of its product. Liability under this warranty is limited to refund or replacement of any device that has been found by Cardiva Medical, Inc. to be defective at the time of shipment. Damage to the device through misuse, alteration, improper storage or improper handling shall void this limited warranty. The remedies set forth in this warranty and limitation shall be the exclusive remedy available to any person. No employee, agent or distributor of Cardiva Medical, Inc. has any authority to alter or amend this limited warranty, or assume or bind Cardiva Medical, Inc. to any additional liability or responsibility with respect to this device. There is no express or implied warranty, including any implied warranty of merchantability or fitness for a particular purpose, on the Cardiva Medical, Inc. product(s) described herein.