Summary of Safety and Clinical Performance

FemoSeal™ Vascular Closure System

Manufacturer	Terumo Medical Corporation 265 Davidson Ave, Suite 320 Somerset, NJ 08873 USA
Manufacturer's SRN	US-MF-000019594
Basic UDI-DI	38970FS79
EMDNnumber	C900199 – Haemostasis Systems-Other
Device Class	Class III
Year Device was First CE Marked	2005
EU Representative	Terumo Europe, N.V. lnterleuvenlaan 40, 3001 Leuven Belgium SRN: BE-AR-000001433
Notified Body	NSAI CE 0050

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This Summary of Safety and Clinical Performance (SSCP) is intended to provide public access to an updated summary of the main aspects of the safety and clinical performance of the FemoSeal™ Vascular Closure System (VCS).

A summary of the safety and clinical performance of the device, intended for users / healthcare professionals, is provided below, in **Section 1.0**.

1.0 SUMMARY FOR USERS / HEALTHCARE PROFESSIONALS

The SSCP is not intended to replace the Instructions for Use as the main document to ensure the safe use of the device, nor is it intended to provide diagnostic or therapeutic suggestions to intended users or patients.

1.1 Intended Use of the Device

1.1.1 Intended Use

FemoSeal™ Vascular Closure System is a medical device intended for closure of an arterial puncture after percutaneous catheterization through the common femoral artery.

1.1.2 Indications for Use

FemoSeal™ Vascular Closure System is indicated for use in closing the common femoral arterial puncture (arteriotomy) in patients who have undergone percutaneous catheterization using a 7F (2.33 mm) or smaller procedural sheath.

1.1.3 Contraindications and/or Limitations

FemoSeal™ Vascular Closure System is contraindicated in patients with arteriotomies in which sheaths or devices larger than 7F (2.33 mm) have been used.

1.1.4 Target Patient Populations

The safety and effectiveness of FemoSeal™ Vascular Closure System has been established in patients 18 years of age and older who have undergone percutaneous catheterization using a 7F (2.33 mm) or smaller procedural sheath.

1.1.5 Special Patient Populations

The safety and effectiveness of FemoSeal™ Vascular Closure System has not been established in the following patient populations:

- Patients with pre-existing autoimmune disease.
- Patients undergoing therapeutic thrombolysis.
- Patients with clinically significant peripheral vascular disease.
- Patients with uncontrolled hypertension (> 220 mmHg systolic or > 110 mmHg diastolic).
- Patients with a bleeding disorder, including thrombocytopenia (< 100,000 platelet count), or anemia (Hgb < 10 mg/dl).
- Patients having an inner lumen of the common femoral artery smaller than 5 mm.

- Patients with renal and/or hepatic impairment.
- Patients with other relevant co-morbidity.
- Population with specific racial and/or ethnic origins.
- Patients with myocardial infarction within 72 hours.
- Patients with a vascular graft or stent at the puncture site.
- Patients who are pregnant or lactating.
- Patients below the age of 18 years.

1.1.6 Intended Users

FemoSeal Vascular Closure System's intended users are physicians with training qualifying them to perform arterial access and closure for endovascular procedures through the common femoral artery and have participated in a Terumo Medical Corporation FemoSeal physician instruction program

1.2 Device Description

1.2.1 Description of the Device

FemoSeal™ Vascular Closure System, manufactured by Terumo Medical Corporation (TMC), is a resorbable vascular closure device designed to achieve femoral arterial hemostasis after percutaneous catheterization through the common femoral artery.

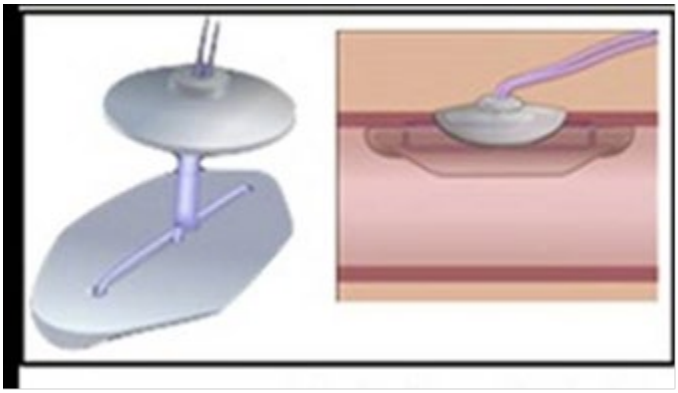
FemoSeal™ closure elements consist of two resorbable polymer discs, the inner seal and the outer locking disc, which are held together by a resorbable multifilament, thereby mechanically sealing the arteriotomy (see **Figure 1.1** and **Figure 1.2**). After being deployed through the cone housing sheath, the outer locking disc is tamped onto the multifilament shaft resulting in mechanical closure of the puncture site between the inner and outer locking disc. The inner seal and outer locking disc are held in place via friction on the multifilament shaft. Hemostasis is achieved by mechanical means. The closure elements are degraded by hydrolysis.

The implantable closure components, inner seal and outer locking disc, are degraded in eighteen (18) months while the multifilament is estimated to be degraded and absorbed via hydrolysis by surrounding tissue after two (2) to three (3) years. The ability of the implantable closure components to maintain compression on the arteriotomy has been tested at up to eight (8) hours. The degradation products are metabolized and excreted in the urine or expired as carbon dioxide via the lungs. No accumulation effects have been observed in animal studies. The additional

components of FemoSeal™ that will come in contact with living tissue or blood during the procedure are the cone housing sheath, dilator, tamping tube, pusher and the guidewire.

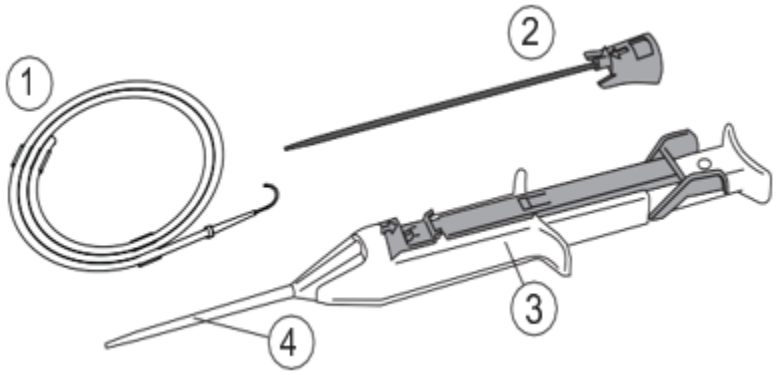
Figure 1.1 Inner Seal and Outer Locking Disc, Respectively

Figure 1.2 Inner Seal and Outer Locking Disc Deployed



The FemoSeal™ unit is packaged together with a dilator and a 0.038” (0.97 mm) OD, 27.5” (70 cm) length guidewire and a J-straightener, see **Figure 1.3** below. The guidewire is contained within a polyethylene tube. All parts are packaged in a fixed paper tray. The packaging also includes the patient implant card. The FemoSeal Vascular Closure System does not require additional accessories for the device to function as intended and the device is only intended to be used with the dilator and guidewire included within the product’s packaging.

Figure 1.3 FemoSeal™ VCS Unit with the Guidewire and Dilator



1.2.2 Raw Materials & Components

Table 1.1 below list the components of the FemoSeal™ VCS.

Table 1.1 FemoSeal™ VCS Raw Materials and Components

Part Number	Description		Materials
1	0.038" (0.97 mm) Guidewire with a guidewire J-straightener		Guidewire: Stainless Steel J-Straightener: Polypropylene, white pigment Clip: Polyethylene Tubing: Polyethylene
2	FemoSeal Dilator		Hub: Tetrahydrofuran, Blue pigment, Polybutylene terephtalate (PBT) Tube: High density polyethylene (HDPE), black pigment Lubricant: Silicone oil
3/4	FemoSeal Unit	Molded RD7 – Inner Seal and Outer locking Disc*	Copolymer between glycolide, trimethylene carbonate,ε-caprolactone, and TMP: trimethylolpropane (initiator)
		Multifilament *	Segmented copolymer between L,L-Lactide, trimethylene carbonate, ε-caprolactone, and 1,3 propanediol (initiator) Coating is copolymer between glycolide, ε-caprolactone, and L-lysine

		Tamping Tube	Polypropylene
		Pusher	Stainless steel
		Slider	Polybutylene terephthalate (PBT)
		Housing	Polybutylene terephthalate (PBT)
		Button	Polybutylene terephthalate (PBT)
		Button Lid	Polyoxymethylene (POM)
		Sleeve	Polybutylene terephthalate (PBT)
		Spacer	Polybutylene terephthalate (PBT)
		Cone	Polypropylene
		Housing Lid	Polybutylene terephthalate (PBT)
		Safety Catch	Polybutylene terephthalate (PBT), blue pigment
		Sleeve Lid	Polybutylene terephthalate (PBT)
		Tube Gasket	Silicone shore A 70
		Housing Gasket	Silicone shore A 70
		Spring	Stainless Steel
		Cone Housing Sheath	Polypropylene Silicone Dow Corning 360, Hexane

* Implantable portion of device; implantable components are MRI safe

FemoSeal™ VCS is sterilized via Ethylene Oxide (EO) and is a single-use medical device. The FemoSeal™ VCS device is designed in such a manner that it cannot be re-used.

Mode of Action

The FemoSeal™ VCS promotes mechanical hemostasis by deploying implantable closure elements inside and outside the common femoral artery. The mechanism that prevents bleeding is provided by the inner seal which seals the puncture site, and the outer locking disc which holds the inner seal in position.

1.2.3 Clinical Benefit

FemoSeal™ VCS provides the following clinical benefits relative to vascular closure after common femoral arterial puncture:

- Reduction in time to hemostasis[1]
- Reduction in time to ambulation[1]

1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international, 27, 32–44.

1.2.4 Previous Generation(s) or Variants

- The first version of FemoSeal™ VCS (#11200) was sold on the European market during the year 2005 and part of 2006.
- The current FemoSeal™ VCS (#11202), with an improved delivery system, has been on the market since March 28, 2006.

1.2.5 Accessories Intended to Be Used in Combination with the Device

The FemoSeal unit is packaged together with a dilator, a 0.038" (0.97 mm) OD, 27.5" (70 cm) length guidewire and a J-straightener. The guidewire is an accessory of the FemoSeal™ unit. The J-straightener is a component of the guidewire, while the dilator is a component of the FemoSeal unit. The guidewire is the only considered accessory. The guidewire is contained within a polyethylene tube. All parts are packaged in a fixed paper tray. The packaging also includes the patient implant card. The FemoSeal Vascular Closure System does not require additional accessories for the device to function as intended and the device is only intended to be used with the dilator and guidewire included within the product's packaging.

1.2.6 Other Devices and Products Intended to Be Used in Combination with the Device

The FemoSeal™ VCS does not require additional devices to function as intended.

1.3 Risks and Warnings

1.3.1 Residual Risks and Undesirable Effects

Known or foreseeable adverse events, harms and complications associated with the use of the FemoSeal™ VCS as a result of residual risks are listed in **Table 1.2**. Occurrence rate is based on an analysis of the Risk Documentation and calculated based on post market surveillance data from January 01, 2019 through December 31, 2023.

Table 1.2. FemoSeal Adverse Events/Complications

Harm	N=number of adverse events	Occurrence Rate (%)	Mitigating Factors
Allergic reaction	0	0.000	

Harm	N=number of adverse events	Occurrence Rate (%)	Mitigating Factors
Aneurysm	0	0.000	Actions and plans to reduce risk as far as possible have been addressed by product design features, manufacturing guidelines, product labeling, and physician training.
AV fistula	0	0.000	
Blood loss / bleeding	285	0.027	
Death	3*	0.000	
Ecchymosis	0	0.000	
Embolism	0	0.000	
Foreign body reaction	1	0.000	
Hematoma	14	0.001	
Hemorrhage	2	0.000	
Infection	3	0.000	
Inflammatory reaction	0	0.000	
Numbness	0	0.000	
Pain	1	0.000	
Patient discomfort	2	0.000	
Procedure delay	143	0.014	
Pseudoaneurysm	1	0.000	
Retroperitoneal bleed	2	0.000	
Sepsis	2	0.000	
Thromboembolism	0	0.000	
Thrombosis	0	0.000	
Vessel occlusion/lower limb ischemia	2	0.000	
Vessel perforation	0	0.000	
Vessel tissue dissection/laceration	2	0.000	

* *There were 3 reported deaths. The harms for these three incidents have been captured appropriately.*

1.3.2 Warnings and Precautions

Warnings

1. Do not use if the package has been damaged or any sterile barrier is not intact.

2. Do not use after expiry date – the biodegradable components may not perform adequately.
3. Do not use if any items appear damaged or defective in anyway.
4. Use of FemoSeal™ Vascular Closure System where bacterial contamination of the procedural sheath or the surrounding tissue may have occurred, may cause infection.
5. If it is suspected that the posterior arterial wall has been punctured or more than one arterial puncture has been made, do not rely solely on FemoSeal™ Vascular Closure System to achieve arterial hemostasis. Use additional manual or mechanical compression.
6. If the puncture site is at, or distal to the bifurcation of the femoral artery, FemoSeal™ Vascular Closure System should not be used due to the risk of the Inner Seal being positioned incorrectly. This event may result in bleeding complications and/or disruption to normal blood flow.
7. If there is persistent arterial bleeding from the incision site, do not cut the multifilament until hemostasis is achieved. If hemostasis is not achieved, fasten the multifilament with a sterile wound dressing and apply supplementary compression until hemostasis is achieved. In the case of persistent arterial bleeding, significant bleeding complications may occur which could result in patient injury or death.
8. Do not use the FemoSeal™ Vascular Closure System if the puncture site is proximal to the inguinal ligament as this may result in a retroperitoneal hematoma.
9. Patients at a higher risk for bleeding may suffer increased blood loss, requiring a transfusion.

If the inner disc becomes detached it can potentially cause a thrombotic and/or embolic event.

Precautions

1. FemoSeal™ Vascular Closure System deployment procedure should be performed by physicians with adequate training in the use of the device.
2. Perform a limited femoral angiogram or an ultrasound-guided femoral puncture prior to FemoSeal™ Vascular Closure System deployment.
3. Discontinue procedure if:
    - Lumen diameter of common femoral artery < 5 mm.
    - Stenosis and/or significant plaque present in the vicinity of the common femoral arterial puncture site.
    - Arterial puncture is at, or distal to, the femoral artery bifurcation.

- Anomalous branches or vessel abnormalities present in the vicinity of the common femoral arterial puncture site.

4. If any hematoma is present, extra care must be taken for correct insertion of the cone housing sheath into the artery.
5. Use a single wall puncture technique. Do not puncture the posterior wall of the artery.
6. Observe sterile technique at all times when using FemoSeal™ Vascular Closure System.
7. FemoSeal™ Vascular Closure System is for single use only and should not be resterilized or reused in any manner. The FemoSeal™ unit is designed in such a manner, that it cannot be re-used.
8. If deployment of the Inner Seal meets unexpected resistance, discontinue the procedure.
9. For correct deployment of Inner Seal, reposition your thumb so that the button can spring back freely.
10. Ensure the tip of the cone housing sheath of FemoSeal™ Unit is under the skin surface before deployment of the Outer Locking Disc. The Outer Locking Disc may inadvertently be deployed above skin level in patients with a short distance between the femoral artery and the skin level.
11. For correct deployment, a skin incision may be necessary before deployment.
12. If the Inner Seal is inside the artery, but it is not possible to fully depress the button and deploy the Outer Locking Disc, surgery may be required to remove FemoSeal™ Closure Elements.
13. If repuncture of the same femoral artery becomes necessary within 18 months, repuncture should be made at least one centimeter proximal to the previous FemoSeal™ Vascular Closure System access site.
14. Instruct the patient to follow physician's orders regarding closure site inspection.
15. Instruct the patient to carry the Patient Information Card for the next 18 months

Precautions at time of discharge

Before considering discharge, assess the patient for the following clinical conditions:

1. Bleeding and/or hematoma at the closure site.
2. Pain while walking.
3. Signs of infection at the closure site.

1.3.3 Field Safety Corrective Actions

There was one Field Safety Corrective Action involving FemoSeal™ VCS during the period from 01 January 2019 through 31 December 2023.

In 2022, Terumo voluntarily recalled FemoSeal VCS due to complaints alleging the failures in process and lot release testing of Elkton manufactured FemoSeal product for Tamping Force Measurement and Retraction Force. A total of 950 units were recalled from South Korea.

1.4 Clinical Evaluation and Post-Market Clinical Follow-Up

Table 1.3 includes a list of pivotal studies included to bring FemoSeal™ VCS to market as well as post-market studies and post-market clinical follow up activities. Device version utilized in the study is included in the table below. The first version of FemoSeal™ VCS (#11200) was on the market until 2006, while the next version (#C11202) was released to the market in 2006 and is what is currently in the marketplace today.

Table 1.3 Summary of Pivotal Studies

Pre-Market Functional Animal Testing	**Device Version**
Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France).	11200
Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France).	11200
Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France).	11200
First In Human Clinical Study	
Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB.	11200
Completed Post-Market Clinical Studies	
PMS FemoSeal® VCS #11202 (R1756-01) (2006)	C11202 (current device)
Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)	C11202 (current device)
Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)	C11202 (current device)
The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe	C11202

	(current device)
Planned / Ongoing Post-Market Clinical Studies	
None	
Post Market Clinical Follow Up Activities	
20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2020)	C11202 (current device)
20210298 – Guidewire Clinical Survey Report (2020)	C11202 (current device)
FemoSeal™ Vascular Closure System PMCF Clinical Survey Protocol: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022	C11202 (current device

1.4.1 Summary of Data from Pre-Market Animal Testing and Clinical Investigations

Table 1.4 below describes all pre-market studies, both animal testing and clinical investigations.

Table 1.4 Summaries of Pre-market Studies

Pre-Market Functional Animal Testing					
Name of Study	**Year / CI**	**Study Type**	**Objectives**	**Milestones**	**Potential Acceptance Criteria**
Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France).	2000 Radi Medical System AB Performed by Biomatech, France	Animal study; Exploratory investigation	The aim of the study was to evaluate the biocompatibility and biofunctionality of a biodegradable implant designed to achieve hemostasis in the vascular system. Report addresses reserve animals from Study Number 862 (Document # 1051-01)	N = 3 adult female sheep, 1 animal per time point Follow up for histopathologic analysis, macroscopic grading, and ultrastructural analysis • 12 months • 15 months • 18 months Color doppler ultrasound follow up – 30 days at carotid and femoral arterial access sites	Arterial patency • Post deployment blood flow assessment – 2/3 blood flow reduction associated with temporary arterial vasospasm that was attributed to procedure, both occurred at left common carotid artery • Color doppler ultrasound assessment (4 weeks) – 3/3 (100%) without major blood flow reduction 30 days after implantation Macroscopic observations • 12 months – patency confirmed macroscopically by absence of anatomically visible occlusion; no macroscopic local intolerance lesions (hemorrhage, necrosis, or neovascularization); encapsulation of internal

					disc appeared to be marked • 15 months - macroscopic observation showed no signs of inflammation; no residues of inner or outer discs identified; encapsulation tissue located in area of outer disc appeared the same as 12-month observation • 18 months – macroscopic observation showed no signs of local intolerance, outer disc visible (3/3 cases), degradation of inner disc complete; 1/3 (Left common carotid artery) – depression of artery wall observed at implant site (could be related to device deployment) Conclusions • Macroscopically, 12, 15 and 18 months after implantation, no necrotic, degenerative, or thrombotic signs were detected. • The degradation process of the inner and outer discs appeared to progress between 12 and 18 months and seamed complete at 18 months, with a whitish tissue covering the implanted area. • Histologically, after 18 months, polymer material was no longer visible but an endoluminal fibrous tissue was present. No necrotic, degenerative, or thrombotic lesions were noted.
Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and	2002 Radi Medical System AB Performed by Biomatech, France	Animal study; Exploratory investigation	The aim of the study was to evaluate the biocompatibility of a biodegradable implant deigned to achieve hemostasis in the vascular system.	Follow up (after implantation) • 12 weeks • 24 weeks • 36 weeks N = 12 sheep, 3 animals per time point, 3 reserve animals	<u>Patency of carotid and femoral arteries after 4 weeks</u> • Major blood flow reduction 0/12 (0%) <u>No major blood flow reduction</u> • Severe blood flow impairment related to

36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France).				sacrificed at 12, 15, and 18 months Implantation sites – right and left femoral arteries, right and left common carotid arteries Color doppler ultrasound analysis	device insertion 0/12 (0%) • Blood flow reduction in left common carotid 2/12 (16.6%) due to temporary arterial vasospasm (attributed to surgery, not device) <u>*Blood flow impairment by follow up*</u> 12 weeks – 0/12 (0%) 24 weeks – 0/12 (0%) 36 weeks – 0/12 (0%) Blood pressure measurements (3 sheep – 36 weeks) • No major blood flow reduction detected Macroscopic data for integration and degradation (Grade 0-4) <u>*Carotid* sites</u> *Internal side* -encapsulation 12 week 1.3 24 week 0.8 36 week 0.7 -material degradation 12 week 2.2 24 week 2.3 36 week 0.7 *External side* -encapsulation 12 week 2.0 24 week 1.0 36 week 0.8 -material degradation 12 week 2.0 24 week 2.7 36 week 3.2 <u>*Femoral sites*</u> *External side* -encapsulation 12 week 1.0 24 week 2.7 36 week 1.0 -material degradation 12 week 2.0

					24 week 2.4 36 week 3.0 *Internal side* -encapsulation 12 week 2.0 24 week 1.2 36 week 1.0 -material degradation 12 week 1.0 24 week 2.2 36 week 3.0 Histological data for integration, degradation, and inflammatory parameters (mean of relevant values, Index 0-4) n=6 *Carotid sites* External fibrosis 12 weeks – 2.3 24 weeks – 2.3 36 weeks – 1.8 Internal neointima 12 weeks – 3.0 24 weeks – 2.7 36 weeks – 3.3 Material degradation 12 weeks – 1.7 24 weeks – 3.0 36 weeks – 3 + Inflammatory parameters (macrophages) 12 weeks – 3.0 24 weeks – 1.7 36 weeks – 1.7 *Femoral sites* External fibrosis 12 weeks – 1.3 24 weeks – 1.5 36 weeks – 1.7 Internal neointima 12 weeks – 3.7 24 weeks – 3.3 36 weeks – 3.8 Material degradation 12 weeks – 2.0 24 weeks – 3.0 36 weeks – 3+

					Inflammatory parameters (macrophages) 12 weeks – 3.5 24 weeks – 1.8 36 weeks – 1.8 <u>Histomorphological patency values</u> Carotid sites 12 week 74.0% 24 week 81.9% 36 weeks -89.43% Femoral sites 12 week – 42.2% 24 week – 73.21% 36 weeks – 78.71% <u>US vessel patency (mean %)</u> Carotid site 12 week 94.6% 24 week – 96.7% 36 week – 94.7% Femoral sites 12 week – 66.9% 24 week – 63.6% 36 week – 75.1% Conclusions • No significant local intolerance sign was detected (absence of visible inflammatory, necrotic, or degenerative lesions) at 12 24, or 36 weeks • No significant adverse tissular reaction recorded with regard to host and device • Degradation of implant was nearly complete at 36 weeks
Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks,	2002 Radi Medical System AB Performed by Biomatech, France	Animal study	The purpose of the study was to evaluate the biocompatibility and biofunctionality of a biodegradable implant designed to achieve haemostasis in the vascular system. The tested device was intended	Implantation period / follow up is 5 weeks for all animals 4 sheep, 1 pig 14 closure elements	Any adverse signs criteria (inflammation, necrosis, hemorrhage, or any other lesion) or any thin pseudo-intimal layer formation were recorded. Particular attention was devoted to initial tissular integration of the device, with a special emphasis on the

(R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France).			to enter the puncture hole in arteries to achieve haemostasis. One disc entered the puncture hole in the artery and the other tightened the internal disc from outside the artery. Both discs were inserted through an introducer sheath. The discs were designed to prevent bleeding, to heal into the vessel wall and finally degrade and be absorbed. The study was designed to collect and analyze data after functional implantation in the sheep and pig to evaluate the capacity of the implant to maintain physiologic function when used in the circulatory system, to determine the response of the host and the response of the device (physical integrity, tissular encapsulation at sacrifice) and to evaluate the degradation of the implant	8 closure elements implanted in 2 sheep, 2 closure elements implanted in 1 pig When two closure elements were implanted into same femoral artery, they were implanted at a distance > 30 mm	internal disc encapsulation. Macroscopically, no significant signs of local intolerance or thrombus formation were observed. The macroscopic observation did not reveal any difference between the sheep or the pig after implantation of the closure elements in the femoral arteries. Macroscopically, no significant signs of local intolerance or thrombus formation were observed. The macroscopic observation did not reveal any difference between the sheep or the pig after implantation of the closure elements in the femoral arteries. The histopatological analysis of the implantation site in sheep showed no local adverse reactions. The inner and outer discs showed signs of degradation and were in some cases broken into smaller parts. The inner discs were completely integrated into neointimal tissue. In the pig the histopatological analysis showed slightly more inflammatory signs around the inner and outer discs. In both animals, the multifilament exhibited slightly more inflammatory signs than in the disc material, which is normal for braided sutures due to the larger surface area.

					The vessel patency was measured after 5 weeks using three different methods, histomorphometric, histomorphometric in combination with measurement of vessel diameter by use of caliper and by the use of color doppler ultrasonography. The mean vessel patency in sheep was between 60 and 80 % depending on method (12 observations). In the pig, the mean vessel patency was between 40 and 80 % (2 observations).
First In Human Clinical Study					
Name of Study	**Year / CI**	**Study Type**	**Objectives**	**Milestones**	**Potential Acceptance Criteria**
Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB.	2004 Radi Medical Systems AB	Open label, single arm, multi-centre trial	The objectives of the study were to determine the safety, performance, and effectiveness of the FemoSeal Vascular Closure System (FemoSeal System) in general, and specifically the Closure Elements, in patients undergoing cardiac diagnostic or interventional cardiology procedures using femoral artery access.	2-part study Total n = 80 Part 1 n = 20 Part 2 n = 60 Indications: Part 1 – diagnostic cardiac catheterization using femoral artery as site of access Part 2 – patients undergoing diagnostic and interventional cardiac procedures using femoral artery as the site of access 30 day follow up	Outcomes <u>-hemostasis achieved with FS without compression</u> - Part 1 20/20 (100%) - Part2 58/60 (97%) Median time to hemostasis at time of procedure (part 2) – 1.0 minutes (Range immediate – 8 minutes) <u>Time to ambulation (minutes)</u> Part 1 – Median: 33.0 mean: 67.8 Part 2 – median: 45 mean: 87.5 <u>Incidence of major vascular complications – 30 day follow up</u> Part 1

					-Free of vascular complications 20/20 (100%) Part 2 Pseudoaneurysm - 1/59 (1.69%) <u>Treatment failure</u> Part 1 – 0/20 (0%) Part 2 – 3/60 (5%) • 2 due to the failure to achieve hemostasis without use of compression • 1 due to major vascular complication, pseudoaneurysm <u>Persistent oozing</u> Part 1 – 0/20 (0%) Part 2- 8/60 (13%) <u>Hematoma</u> Part 1 – 0/20 (0%) Part 2 – 6/60 (10%)

As part of the premarket development plan for FemoSeal VCS, 3 animal functional tests were completed. In 2000, prior to initiating clinical studies, an animal study was performed to evaluate the bio-functionality of FemoSeal VCS. This study evaluated the capacity of the closure elements to maintain physiologic function and to evaluate their degradation. At 18 months the inner and outer disc material was no longer visible, having been replaced with an endoluminal fibrous tissue. In conclusion, the capacity of the FemoSeal VCS closure element to maintain physiologic function when used in the circulatory system was confirmed.

In 2002 an animal study was performed to evaluate the biocompatibility and biofunctionality of a biodegradable implant, FemoSeal VCS, designed to achieve hemostasis in the vascular system. In summary, the degradation of the implant was nearly complete by 36 weeks and there was no significant adverse tissular reaction.

Another animal study in 2002 evaluated the biocompatibility and biofunctionality of a biodegradable implant, FemoSeal VCS, designed to achieve hemostasis in the vascular system.

After 5 weeks, encapsulation of the disc was complete, and signs of degradation were observed for internal and external discs. In conclusion, the capacity of the implant to maintain physiologic function when used in the circulatory system was confirmed.

As part of the clinical development plan for FemoSeal™ VCS, Radi Medical System AB conducted a pre-market clinical investigation. This clinical investigation is not published or available online. The study with device model #11200 was conducted in 2002-2004 under European Standard EN 540 (Clinical Investigation of Medical Devices for Human Subjects) and in accordance with the ICH General Considerations for Clinical Trials and Guideline for Good Clinical Practice. The details of this study are documented in report EU-SE-001.. The clinical trial was documented in the Final Report from Radi Medical Systems AB, "Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures". The clinical study was performed with FemoSeal™'s first model #11200 and focused on the safety and effectiveness of the implantable closure components. The only difference between the first model #11200 and the current model, C11202, is the French size, 6F and 7F respectively, and the improved delivery system. The clinical benefits, intended use, principles of operation, and the raw materials of the implantable closure elements, inner seal and outer locking disc, remain unchanged.

The intended use of the device was for patients undergoing diagnostic cardiac or interventional cardiac procedures using the femoral artery as an access point. The objective of this study was to determine the safety, performance, and effectiveness of the FemoSeal™ VCS. This was a prospective, multi-center, single arm open-label study with 30-day follow-up.

The primary performance endpoint was time to hemostasis defined as the absence of brisk bleeding. The primary safety endpoint was incidence of major vascular complications through 30-days. Secondary endpoints included time to ambulation, proportion of treatment failures, incidence of adverse events, and device performance characteristics during delivery and deployment.

Patients included in this study were adults able to provide informed consent and with at least one intact pedal pulse. Patients were excluded from the study if they had any of the following conditions:

- History of peripheral vascular disease
- Autoimmune disease
- Known bleeding disorder of severe anemia
- INR >1.5
- Myocardial infarct with 72 hours
- Uncontrolled hypertension despite treatment

- Obesity precluding access with Seldinger technique
- Presence of vascular graft or stent at arteriotomy site
- Previous ipsilateral puncture within 3 months
- Life expectancy < 6 months

Additionally, patients were examined intraoperatively and excluded from the study if any of the following were observed:

- Lumen diameter of common femoral artery <5mm
- Arterial branches within 2 cm proximal to puncture site
- Significant stenosis within 3 cm of puncture site
- Use of primary introducer sheath >6Fr
- Puncture at or distal to femoral bifurcation
- Multiple femoral punctures
- Known or suspected posterior femoral wall puncture
- Large hematoma (2:6 cm) at completion of the procedure
- Difficult primary sheath insertion for procedure due to tortuous tissue or vessel

This single protocol study was conducted in two parts: 20 patients were enrolled during Part 1, then a safety analysis was completed, and then an additional 60 patients were enrolled during Part 2.

In Part 1, mean age of enrolled patients was 65.9 years, 70.0% of patients were male, and 95% of patients were on concomitant medications. In Part 2 of the study, mean age was 63.8 years, 78% were male, and 100% were on concomitant medications.

Patients undergoing diagnostic (Part 1 and Part 2) or interventional (Part 2) cardiac catheterization procedures were eligible for enrollment in the study. The procedures were compliant with standard of care at each of the enrolling hospitals, followed by use of the FemoSeal™ VCS. Patient data was collected at baseline, during the procedure, and at 1-day and 30-days post-procedure. Results are summarized in **Table 1.5** and indicate FemoSeal™ VCS is safe and effective for use in this patient population.

Table 1.5 Clinical Results Reported in Pre-Market Study

	Part 1	**Part 2**
Number of patients	20	60
Mean Time to Hemostasis	1.2 minutes	1.6 minutes[a]

Mean Time to Ambulation	72.2 minutes	87.5 minutes[b]
Incidence of Major Vascular Complications[c]	0 (0%)	1 (2%)
Number of Patients with Adverse Events	5 (25%)	19 (32%)
Treatment failure (defined as major vascular complications, need for manual compression, or both)	0 (0%)	3 (5%)
Device Malfunctions	0 (0%)	6 (10%)

[a]*Based on total sample size of 58 because 2 patients did not reach hemostasis at time of procedure due to previous ipsilateral punctures. Hemostasis was achieved at 7 minutes and 37 minutes for these patients.*

[b]*Based on total sample size of 59: 1 patient was not included because they were placed on ventilator due to pulmonary edema and unable to ambulate for over a week.*

[c]*Defined as vascular complication requiring blood transfusion or surgical repair, or local infection requiring administration of antibiotic, hospitalization or extension of hospitalization, or site debridement*

No major vascular complications were observed in Part 1 of the study. There was 1 major vascular complication reported in Part 2 of the study: pseudoaneurysm that was reported within 1 day post-procedure. The event required ultrasound guided compression and an injection of thrombin into the pseudoaneurysm, and extended the patient's hospitalization.

Of the 5 adverse events reported in Part 1 of the study, there was 1 possibly device-related adverse event: a non-serious event of brisk bleeding at 1-day post procedure. Of the 19 adverse events reported in Part 2 of the study, 3 device-related non-serious adverse events of hematoma were observed, and 6 possibly device-related non-serious events were observed including 3 reports of persistent oozing, 2 hematomas, and 1 leg pain after exercise.

There were 3 patients in Part 2 considered treatment failures: 2 due to failure to achieve hemostasis without the use of compression and 1 due to the major vascular complication (pseudoaneurysm). There were no treatment failures in Part 1 of the study.

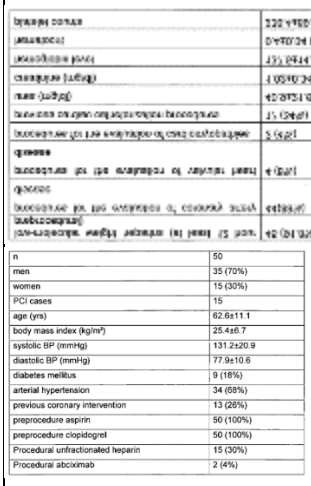
Of the six device malfunctions in Part 2 of the study, three did not interfere with the procedure, one was attributed to user error, one was leakage of the introducer, and one was a broken filament joint. The last two issues were addressed with model updates implemented in C11202.

Part 2 of the pre-market clinical study did not report the 6 month follow-up results due to patient non-compliance. The pre-market clinical study (EU-SE-001) 30-day results, which is in line with the clinical literature's follow-up time period, demonstrates that FemoSeal™ VCS is safe and effective.

1.4.2 Summary of Data from Post-Market Clinical Studies

There were 4 completed post-market clinical studies described in **Table 1.6** below. These clinical investigations are not published or available online.

Table 1.6 Post-Market Studies

Completed Post-Market Clinical Studies					
Name of Study	**Year / CI**	**Study Type**	**Objectives**	**Milestones**	**Potential Acceptance Criteria**
PMS FemoSeal® VCS #11202 (R1756-01) (2006) User Acceptability of New Packaging (SIS)	2006 RADI	Post Market Study, User Acceptability of New Packaging	Post-market study carried out on the model update FemoSeal Vascular® Closure System #11202 which has a modified delivery system compared to the first model, #11200, to document functionality. The objective of the study was to get feedback on the revised Instructions for Use (IFU), the training project for physicians and nurse, to confirm the assessments made in the risk analysis and to give input to any product quality improvements.	100 patients • 63 male / 37 females • Mean age 68 years for female, 65 years for males 2 Swedish hospitals, 6 physicians 112 devices Data captured on patient record forms (CRF) Planned observation time – 30 minutes from time of application	Outcomes 1.Illustrations/Instructions in IFU considered informative and adequate 2. Immediate hemostasis (91/100)
Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)	Dr. Nicolas Moes Innsbruk Medical University, Austria	Post -Market Confirmatory Assessment	The objective of this study was to assess safety and performance of FemoSeal® used during normal clinical routine in patients undergoing diagnostic cardiac catheterization or percutaneous cardiac interventional procedure performed with 7F-sheath.	50 consecutive patients Indication – diagnostic or invasive cardiac catheterization from common femoral artery  n 50 men 35 (70%) women 15 (30%) PCI cases 15 age (yrs) 62.6±11.1 body mass index (kg/m²) 25.4±6.7 systolic BP (mmHg) 131.2±20.9 diastolic BP (mmHg) 77.9±10.6 diabetes mellitus 9 (18%) arterial hypertension 34 (68%) previous coronary intervention 13 (26%) preprocedure aspirin 50 (100%) preprocedure clopidogrel 50 (100%) Procedural unfractionated heparin 15 (30%) Procedural abciximab 2 (4%)	Primary endpoints • Primary efficacy endpoint – TTH (time to hemostasis) with or without oozing but without any additional compression, manual or mechanical. • Safety endpoint - incidence of adverse events - minor and major vascular complications and all other adverse events – serious and non-serious during duration of the study (i.e., until patient discharge). Outcomes • Mean time to hemostasis • Diagnostic - 56.6 ± 29 seconds • Interventional 59.9 ± 16.2 seconds • All patients 57.8 ±26.3 • All patients could be ambulated after 4 hours

					bed rest without any problems. Safety outcomes • 49/50 (98%) free of vascular complications until hospital discharge • Mean time to discharge 2.6 days • 1/50 (2%) minor bleeding next day after uneventful ambulation on day of angiography
Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)	2009 RADI	Post Market Study	The study should inform if the customers/users perceived any problems with the new package, especially the non-sterile outer side of the Tuvek/PET-PE pouch. The study should also give information about if the treating physician perceives any differences in the application/deployment steps of the device compared to previously used devices. The study should also give input to any further needs for product quality improvement.	25 devices 4 Swedish hospitals 16/25 (64%) of patients were PCI patients with heavy anti-coagulation medications	Outcomes 1. Package related problems – 21/25 (84%) applications were successful; 4/25 (16%) were unsuccessful (1 - testing new introducer, 1 inner disc when through arteriotomy at backing step, button came up and outer disc was placed in incision tissue canal, 2 immediate hemostasis was not achieved despite no deployment issues.) 2. Immediate hemostasis 19/25 (76%) patients 3. Bleeding 11/25 (44%) – 9/25 (36%) oozing/bleeding, 2/25 (8%) hematomas Total event rate 19%
The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (T138E4)	2022/Terumo Medical Corporation	Prospective, Multi-center, Observational, Post-market	To further demonstrate the safety and effectiveness of the FemoSeal™ VCS in achieving hemostasis of common femoral artery (CFA) access site in real-world subjects undergoing percutaneous endovascular procedures	• Patient follow-up at 30 days (± 7 days) by hospital visit or telephone call. • Enrollment: December 2021 through July 2022. • 230 enrolled subjects undergoing diagnostic or interventional endovascular procedures in which FemoSeal™ is used. 3 European sites: France (92 patients), Germany (38 patients), Belgium (100 patients).	• **Demographics/comorbidities:** - Gender: 161 males (70 %)/69 females 69 (30%). - Mean age: 70 ± 12. - BMI: 26.1 ± 4.95 kg/m2. - Hypertension: 160 patients (69.6 %). - Dyslipidemia: 128 (55.7 %). - Coronary artery disease: 42 (18.3%). - Current smoker: 86 (37.6 %).

					- Past smoker: 66 (28.8%). - Coronary heart disease: 34 (14%). - Previous myocardial infarction: 18 (7.8%). - Peripheral artery revascularization: 12 (5.2 %) carotid and 83 (37.5%) and low limb artery. - Antiplatelet therapy (at baseline): 211 (91,7 %), including 21 (9.1%) dual antiplatelet therapy (DAPT). - Oral anticoagulation: 40 (17.4%) patients. • **Intervention characteristics:** - Setting: inpatient clinic 162 cases (70.4%), outpatient clinic 68 cases (29.6%). - Prevailing indication: claudication 147 cases (63.9%). - Approach: 35 antegrade (15.3%), 194 retrograde (84.7%). • **Primary Endpoints:** - Combined safety (freedom from major complications of the access site limb within 6 hours post-procedure) and effectiveness (successful puncture site hemostasis) endpoint achieved in 215/226 (95.1%) [95% CI: 91.46; 97.55] patients in the Full Analysis Set and 215/230 (93.5%) [95% CI 89.47, 96.30] in the FemoSeal™ Treated Set. - Effectiveness endpoint was achieved in 219/226 (96.9%) CI [93.7, 98.7] of patients. - Safety endpoint achieved in 220/230 (95.2%) [95% CI: 92.15, 97.90] patients. • **Secondary endpoints:**

					- Freedom from minor access site complications for six hours post-procedure achieved in 225/230 (97.8%) [95% CI: 95.00; 99.29]. - Freedom from major and minor access site complications from six hours to 30 days post-procedure achieved in 219/230 (95.2%) [95% CI:91.60; 97.59] of patients. - Median Time to hemostasis with FemoSeal™ VCD: 0.42 (0.25; 0.50) minutes. - Median Time to ambulation: 5.00 (4.54; 5.50) minutes. - Median length of stay in hospital: 23.98 (22.72, 25.00) hours. - FemoSeal™ VCS usability: 'easy' or 'very easy' to deploy in 98.7% of cases ('easy' to deploy in 21 (9.2%), 'very easy' to deploy in 205 (89.5 %)) with no or low resistance at deployment in 226 (98.3%) of cases. 152/230 (66.1%) of patients treated using guidewire included with the FemoSeal™ kit (GW 0.038") and recommended in the FemoSeal™ without any reported device deficiencies or adverse events.

The 2006 study was conducted to confirm the safety and effectiveness of the current device with an improved delivery system and to get feedback on the FemoSeal VCS IFU and training program. The study included 100 patients and the primary endpoint was whether hemostasis was achieved, or if additional manual or mechanical compressions was needed. This study concluded that the application of FemoSeal VCS was successful in the majority of cases (91% achieved immediate hemostasis).

The 2008 study enrolled 50 patients to assess the safety and performance of FemoSeal VCS when used during normal clinical routine in patients undergoing cardiac catheterization with a 7 Fr sheath. The primary endpoint for the study was to collect data on the time to hemostasis and the time to ambulation without additional compression, manual or mechanical. The study results concluded that the mean time to hemostasis was 57.8 seconds and all patients ambulated after 4 hours of bed rest.

The 2009 study was to evaluate the new FemoSeal VCS packaging. 25 patients were enrolled in the study. The primary endpoint was whether the user experienced any problems with the packaging. The users noted no problems regarding the new FemoSeal VCS packaging. This study also collected data for the time to hemostasis.

The 2022 study was to proactively collect safety and effectiveness data of FemoSeal VCS in achieving hemostasis of common femoral artery (CFA) access site in real-world subjects undergoing percutaneous endovascular procedures. 230 patients were enrolled in the study. The primary endpoints for the registry are procedural success (i.e., successful puncture site hemostasis) and reduction in major complications (e.g., vascular injury, access site-related bleeding, access site infection, repeat manual compression, and new access site-related ipsilateral acute leg ischemia). The study concluded that the FemoSeal VCS performs well in real-world settings and provides effective haemostasis and low rates of access-site complications for patients undergoing peripheral endovascular interventions. It demonstrates a good performance with short time to haemostasis and good operator usability feedback, which makes FemoSeal VCS a valuable device for femoral access closure.

1.4.3 Summary of Clinical Performance and Safety

1.4.3.1 Systematic Literature Review

Terumo Medical Corporation conducts systematic literature reviews to collect and evaluate clinical safety and performance data from published studies on the FemoSeal™ VCS and/or similar devices. The aim of the annual screening of the published literature is to identify previously unknown side-effects, monitor known side effects, identify emergent risks, and identify possible systematic misuse or off-label use of the FemoSeal™ VCS.

The most recent systematic literature review, which covered the period from January 1, 2019 through December 31, 2023, identified 28 published studies that provided clinical safety and performance data on the FemoSeal™ VCS. Overall, the literature review of studies specific to the use of FemoSeal™ VCS shows a population under study that is representative of patients in the EU undergoing percutaneous vascular catheterization procedures. See **Section1.8** for a list of these 28 peer-reviewed publications.

Clinical performance was assessed by the following measures:

- Percentage of patients with complete hemostasis

- Mean time to hemostasis
- Percentage of patients requiring crossover to manual compression
- Percentage of patients in which the device failed

Based on these clinical performance measures, the data in the literature review showed that FemoSeal™ VCS can be used successfully in closing the common femoral arterial puncture (arteriotomy) in patients who have undergone percutaneous catheterization using a 7F or smaller procedural sheath. Performance outcomes identified in the FemoSeal™ VCS literature includes: complete hemostasis 100% (Lee et al., 2019); need of manual compression 2.11%-4.4% (Mayer et al., 2021; Gouëffic et al., 2021); device failure 0.9%-10% (Gmeiner et al., 2022; Mayer et al., 2021; Noory et al., 2023); with a median time to hemostasis of 0.5 min (0.2-1.0 min; Mayer et al., 2021); resumption of ambulation in 86.7% of patients (Gouëffic et al., 2021), technical success 79.65%-100% (Gouëffic et al., 2021; Ha et al., 2021) and closure success in 100% of patients (Gabrielli et al., 2021). No concerns with performance have been identified, the literature reviewed contained use of the Subject Device that was consistent with the manufacturer's intended use. It is worth noting that FemoSeal VCS was superior to Proglide and ExoSeal in achieving hemostasis (Gouëffic et al., 2021; Mayer et al., 2021) and superior to Proglide in achieving early ambulation (Gouëffic et al., 2021). FemoSeal VCS was also associated with fewer device failures compared to other devices (Mayer et al., 2021; Noory et al., 2023).

Clinical safety was assessed by adverse events including, but not limited to:

- Arteriovenous fistula
- Bleeding
- Dissection
- Ecchymosis
- Hematoma
- Infection
- Mortality
- Need for surgical/interventional treatment
- Occlusion
- Pseudoaneurysm
- Retroperitoneal hemorrhage
- Stroke (see explanation below)

- Thrombosis

For each of these adverse events, the rate of occurrence reported for FemoSeal™ VCS in the included studies was less than or comparable to historically reported rates for manual compression and other vascular closure devices.

No adverse events were identified through review of 12 case reports, as no new, unanticipated, emerging, or unacceptable risks were identified.

Overall, the data in this literature review did not identify any performance or safety issues in the clinical setting that were previously unknown, or adverse effects that occurred at higher than anticipated / acceptable rates. Therefore, it can be concluded from this literature review that FemoSeal VCS, when used to provide compression for hemostasis at the arteriotomy following percutaneous catheterization, continues to perform as expected and is not associated with serious safety events.

1.4.3.2 Post-Market Surveillance

A proactive PMS system is in place and a review of all complaints is completed on a monthly basis and in compliance with internal manufacturing procedures. Complaint data was analyzed during the time period of January 1, 2019, to December 31, 2023. Overall, there were 29 Medical Device Vigilance (MDV) Reports and 458 customer complaint reports submitted to the manufacturer. Of the 29 MDV reports, there were 3 related to deaths and 26 regarding other adverse events. Among the 458 complaints made to the manufacturer, the most common reasons for complaint were: Bleeding and Procedure Delay.

FemoSeal Vascular Closure System has over 1,053,639 sales globally and 827,833 in the European Economic Area. The calculated frequency of complaints based on global sales is 0.043%. The overall customer complaint rate is very low. No new risks were identified that are not included in the IFU and risk documentation.

The occurrence rates for the undesirable side effects are shown in **Table 1.2**. No previously unknown side effects were identified and there were no significant increases in the frequency or severity of known undesirable side effects.

1.4.3.3 Overall Summary of Clinical Performance and Safety

FemoSeal™ VCS is indicated for use in closing the common femoral arterial puncture (arteriotomy) in patients who have undergone percutaneous catheterization using a 7F (2.33 mm) or smaller procedural sheath. This clinical evaluation is based on a comprehensive analysis of available pre- and post-market clinical data and literature relevant to the intended use of the FemoSeal™ VCS. A comprehensive review of the published literature was conducted covering the period from January 1, 2019, through December 31, 2023. The body of evidence included 28 studies for the FemoSeal™ VCS. The evidence provided in the clinical evaluation concludes that when used as indicated, the subject device is safe and effective and any risks or undesirable side

effects, which may be associated with the device under normal conditions of use, constitute acceptable risks when weighed against the benefits to the patient. The performance outcomes for the subject devices are consistent with those expected for this type of device when used as intended.

The potential undesirable side-effects associated with the use of FemoSeal™ VCS include the adverse events commonly reported with alternative means of arteriotomy closure, e.g., bleeding and hematoma. Overall, the occurrence rates for the adverse events reported with the use of FemoSeal™ VCS are similar to the rates reported with manual compression and similar vascular closure devices. Specifically, for bleeding and hematoma, the reported rates for FemoSeal™ VCS are less than the reported rates for similar vascular closure devices. Each of the reported adverse events, from both the published literature and post-market surveillance, had been previously identified (see **Section 1.3**).

The existing data regarding the clinical safety and performance of FemoSeal™ VCS suggest that patient benefits from use of this vascular closure device outweigh possible risks when it is used in accordance with the Instruction for Use.

1.4.4 Post-market Clinical Follow-Up

1.4.4.1 Completed Post-Market Clinical Follow-Up

Terumo Medical Corporation has recently completed two high quality physician user surveys.

The FemoSeal™ Clinical Surveys collected proactive clinical data in relation to the safety and performance of the FemoSeal™ VCS during clinical use. The survey included questions focused on the overall device and associated accessories including the 0.038” guidewire, and their direct interactions. The Guidewire clinical surveys collected proactive clinical data in relation to safety and performance during clinical use of the 0.038” guidewire supplied with FemoSeal™ VCS. The survey questions focused specifically on the general use of the guidewire ranging from insertion through the procedural sheath into the vasculature through removal of the wire.

The FemoSeal VCS and 0.038” guidewire included with the device received all acceptable ratings and six (6) complaints were filed for the device and nine (9) non-complaints for the guidewire based on evaluation of the comments received from the high-quality clinical surveys. The complaints have been evaluated for both the FemoSeal and the guidewire and were assessed as part of Terumo post-market surveillance process. There were no new risks and or risk levels identified.

1.4.4.2 Ongoing/Planned Post-Market Clinical Follow-Up

TMC has one ongoing/planned post-market clinical follow-up activities. A clinical survey will be completed to prospectively collect feedback related to the use of the guidewire with FemoSeal

VCS distributed in the EU market. The survey will be completed by physicians to study which guidewires they used during the procedure. The feedback includes technical outcomes, clinical performance, and safety pertaining to the performance of the device with different guidewires.

1.5 Possible Therapeutic Alternatives

Manual compression is traditionally used to achieve hemostasis at the arteriotomy site after vascular catheterizations[4]. Manual compression has been associated with the patient being immobilized for long periods of time (up to 8 hours after a procedure) and with substantial discomfort and extended hospital stays. A recent systematic review found that the median time to achieve hemostasis with manual compression was 20.8 minutes.

Alternatives to manual compression include external hemostatic devices that apply mechanical compression to the arteriotomy site. These devices do not shorten the time to hemostasis or time to ambulation but reduce the personnel requirements by replacing manual compression with mechanical compression. Adverse event rates associated with the use of mechanical compression are similar to rates with manual compression[3].

Vascular closure devices, such as FemoSeal™ VCS, are designed to close the arteriotomy. They aim to reduce the time to hemostasis and enable earlier ambulation. A recent systematic review[2], including 13 commercially available devices, found that the median time to achieve hemostasis with a vascular closure device was 5.4 minutes. The median hemostasis time for the individual vascular closure devices ranged from 1 minute (FemoSeal™ VCS) to 14 minutes; with the majority of devices being between 4 and 10 minutes.

Commonly reported adverse events associated with closure of the arteriotomy site, with manual compressions, external hemostatic devices, or vascular closure devices, include hematoma, bleeding at the access site, pseudoaneurysm, arteriovenous fistula, and infection. The same systematic review[2] (34 randomized controlled trials, 14,401 patients) found that the rates of adverse events were similar between manual compression and the use of vascular closure devices, with the exception that bleeding tended to be a little higher with vascular closure devices.

1.6 Suggested User Profile and Training

FemoSeal Vascular Closure System's intended users are physicians with training qualifying them to perform arterial access and closure for endovascular procedures through the common femoral artery and have participated in a Terumo Medical Corporation FemoSeal physician instruction program.

1.7 Relevant Harmonized and Common Standards

Standard Reference	Current Year of Compliance/Rev	Description
ISO 11070	2014/AMD1:2018	Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1
EN ISO 11070	2014/A1:2018	Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1
FDA Guidance	May 20, 2021	FDA Guidance: Testing and Labeling Medical Devices for Safety in Magnetic Resonance (MR) Environment
ASTM F2052	2015	Standard Test Method for Measurement of Magnetically Induced Displacement Force on Medical Devices in the Magnetic Resonance Environment
ASTM F2213	2017	Standard Test Method for Measurement of Magnetically Induced Torque on Medical Devices in the Magnetic Resonance Environment
ASTM F2503	2020	Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment
ASTM F2182	2019	Standard Test Method for Measurement of Radio Frequency Induced Heating On or Near Passive Implants During Magnetic Resonance Imaging
EN ISO 13485	2016/A11:2021	Medical devices - Quality management systems - Requirements for regulatory purposes
ISO 13485	2016	Medical devices - Quality management systems - Requirements for regulatory purposes
ISO 14644-1	2015	Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration
EN ISO 14644-1	2015	Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration
ISO 14644-2	2015	Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of

Standard Reference	Current Year of Compliance/Rev	Description
		cleanroom performance related to air cleanliness by particle concentration
EN ISO 14644-2	2015	Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration
ISO 14644-3	2005	Cleanrooms and associated controlled environments — Part 3: Test methods
EN ISO 14644-3	2005	Cleanrooms and associated controlled environments — Part 3: Test methods
ISO 14644-5	2004	Cleanrooms and associated controlled environments — Part 5: Operations
ISO 14644-5	2004	Cleanrooms and associated controlled environments — Part 5: Operations
ISO 14698-1	2003	Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods
EN ISO 14698-1	2003	Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods
ISO 14698-2	2003/TC1:2004	Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data
EN ISO 14698-2	2003/TC 1:2004	Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data
USP <788>	N/A	PARTICULATE MATTER IN INJECTIONS USP is continuously updated, there are no technical differences between versions
IEC 62366-1	2015	Medical devices — Part 1: Application of usability engineering to medical devices

Standard Reference	Current Year of Compliance/Rev	Description
EN 62366-1	2015	Medical devices — Part 1: Application of usability engineering to medical devices
IEC TR 62366-2	2016	Medical devices — Part 2: Application of usability engineering to medical devices
EN IEC TR 62366-2	2016	Medical devices — Part 2: Application of usability engineering to medical devices
EN ISO 14971	2019	Medical devices — Application of risk management to Medical devices
ISO 14971	2019	Medical devices — Application of risk management to Medical devices
ASTM F1980	2016	Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices
EN ISO 10993-1	2020	Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process
ISO 10993-1	2018	Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process
EN ISO 10993-2	2006	Biological evaluation of medical devices — Part 2: Animal welfare requirements
ISO 10993-2	2006	Biological evaluation of medical devices — Part 2: Animal welfare requirements
EN ISO 10993-3	2014	Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity
ISO 10993-3	2014	Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity
EN ISO 10993-4	2017	Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood
ISO 10993-4	2017	Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood
EN ISO 10993-5	2009	Biological evaluation of medical devices –

Standard Reference	Current Year of Compliance/Rev	Description
		Part 5: Tests for in vitro cytotoxicity
ISO 10993-5	2009	Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity
EN ISO 10993-6	2016	Biological evaluation of medical devices - Part 6: Tests for local effects after implantation
ISO 10993-6	2016	Biological evaluation of medical devices - Part 6: Tests for local effects after implantation
EN ISO 10993-10	2013	Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization
ISO 10993-10	2010	Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization
EN ISO 10993-11	2018	Biological evaluation of medical devices — Part 11: Tests for systemic toxicity
ISO 10993-11	2017	Biological evaluation of medical devices — Part 11: Tests for systemic toxicity
EN ISO 10993-12	2021	Biological evaluation of medical devices — Part 12: Sample preparation and reference materials
ISO 10993-12	2021	Biological evaluation of medical devices — Part 12: Sample preparation and reference materials
EN ISO 10993-17	2009	Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances
ISO 10993-17	2002	Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances
ISO 10993-18	2020/A1:2022	Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process
EN ISO 10993-18	2020/A1:2022	Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process

Standard Reference	Current Year of Compliance/Rev	Description
ASTM F2382	2018	Standard Test Method for Assessment of Circulating Blood-Contacting Medical Device Materials on Partial Thromboplastin Time (PTT)
ASTM F756	2017	Standard Practice for Assessment of Hemolytic Properties of Materials
USP <85>	2019	[Bacterial Endotoxins Test. (Sterility) *USP is continuously updated, there are no technical differences between version 37 (2014) and 38 (2015) and 39 (2016)] USP is continuously updated, there are no technical differences between version
ANSI/AAMI ST72	2019	Bacterial endotoxins - Test methods, routine monitoring, and alternatives to batch testing
EN ISO 11135	2014/A1:2019	Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices
ISO 11135	2014/Amd1:2018	Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices
EN ISO 10993-7	2008/AC:2009	Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals
ISO 10993-7	2008/Cor 1:2009	Biological evaluation of medical devices — Part 7: Ethylene oxide
EN 556-1	AC:2006	Sterilization of medical devices - Requirements for medical devices to be designated "STERILE" - Part 1: Requirements for terminally sterilized medical devices
EN ISO 11737-1	2018	Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products

Standard Reference	Current Year of Compliance/Rev	Description
ISO 11737-1	2018	Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products
EN ISO 11138-2	2017	Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes
ISO 11138-2	2017	Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes
EN ISO 15223-1	2016	Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements
ISO 15223-1	2016	Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements
EN 1041	2008	Information supplied by the manufacturer of medical devices
EN ISO 11607-1	2009/A1:2014	Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems
ISO 11607-1	2006/A1:2014	Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems
EN ISO 11607-2	2006	Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes
ISO 11607-2	2006	Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes
ASTM D4169	2016	Standard Practice for Performance Testing of Shipping Containers and Systems

Standard Reference	Current Year of Compliance/Rev	Description
ASTM F1886/F1886M	2016	Standard Test Method for Determining Integrity of Seals for Flexible Packaging by Visual Inspection
ASTM F2825	2018	Standard Practice for Climatic Stressing of Packaging Systems for Single Parcel Delivery
ASTM F2096	2011	Standard Test Method for Detecting Gross Leaks in Medical Packaging by Internal Pressurization (Bubble Test)
ASTM F88/F88M	2015	Standard Test Method for Seal Strength of Flexible Barrier Materials
MDCG 2021-24		Guidance on classification of medical devices
MDCG 2020-3		Guidance on significant changes regarding the transitional provision under Article 120 of the MDR with regard to devices covered by certificates according to MDD or AIMDD
MDCG 2020-8		Post-market clinical follow-up (PMCF) Evaluation Report Template A guide for manufacturers and notified bodies
MDCG 2020-7		Post-market clinical follow-up (PMCF) Plan Template A guide for manufacturers and notified bodies
MDCG 2020-6		Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC
MDCG 2019-9 - Rev.1		Summary of safety and clinical performance A guide for manufacturers and notified bodies
MDCG 2019-8 v2		Guidance document Implant Card relating to the application of Article 18 Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices
MDCG 2020-15		MDCG Position Paper on the use of the EUDAMED actor registration module and of the Single Registration Number (SRN) in the Member States

Standard Reference	Current Year of Compliance/Rev	Description
MDCG 2021-11		Guidance on Implant Card – 'Device types'
MDCG 2021-19		Guidance note integration of the UDI within an organisation's quality management system
MDCG 2018-1 Rev. 4		Guidance on BASIC UDI-DI and changes to UDI-DI
MDCG 2019-2		Guidance on application of UDI rules to device-part of products referred to in Article 1(8), 1(9) and 1(10) of Regulation 745/2017
MDCG 2019-1		MDCG guiding principles for issuing entities rules on Basic UDI-DI
MDCG 2018-7		Provisional considerations regarding language issues associated with the UDI database (Annex VI, Part A Section 2 and Part B of the Medical Device Regulation (EU) 2017/745 (MDR) and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746 (IVDR))
MDCG 2018-6		Clarifications of UDI related responsibilities in relation to Article 16 of the Medical Device Regulation (EU) 2017/745 and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746
MDCG 2018-4		MDCG 2018-4 Annex: UDI database Definitions/Descriptions and formats of the UDI core elements for systems or procedure packs
MDCG 2018-3 Rev.1		Guidance on UDI for systems and procedure packs
MDCG 2021-25		Regulation (EU) 2017/745 - application of MDR requirements to 'legacy devices' and to devices placed on the market prior to 26 May 2021 in accordance with Directives 90/385/EEC or 93/42/EEC
Meddev 2.12-2 Rev 2		Guidance document Medical devices - Market surveillance - Post Market Clinical Follow-up studies - MEDDEV 2.12/2 rev.2

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3.0 REVISION HISTORY

SSCP revision number	Date issued	Change description	Revision validated by the Notified Body
SSCP-FS-2022	January 20, 2023	Initial Issue, upon MDR CE certification	**X** Yes Validation language: English ☐ No (only applicable for class IIa or some IIb implantable devices (MDR, Article 52 (4) 2nd paragraph) for which the SSCP is not yet validated by the NB) ☐ Other (explain):
SSCP-FS-2023 – Revision 1	March 15, 2024	Updated for the period between January 1, 2019 through December 31, 2023.	X Yes Validation language: English ☐ No (only applicable for class IIa or some IIb implantable devices (MDR, Article 52 (4) 2nd paragraph) for which the SSCP is not yet validated by the NB) ☐ Other (explain):