DE NOVO CLASSIFICATION REQUEST FOR SURFACER INSIDE-OUT ACCESS CATHETER SYSTEM

REGULATORY INFORMATION

FDA identifies this generic type of device as:

Reverse central venous recanalization system. A reverse central venous recanalization system is a prescription device for obtaining central venous access to facilitate catheter insertion into the central venous system. Reverse recanalization involves the initiation of an access path from within the vein and then progressing to the skin for patients with upper body venous occlusions or other conditions that preclude central venous access by other methods.

NEW REGULATION NUMBER: 21 CFR 870.1342

CLASSIFICATION: Class II

PRODUCT CODE: QJH

BACKGROUND

DEVICE NAME: Surfacer Inside-Out Access Catheter System

SUBMISSION NUMBER: DEN190038

DATE DE NOVO RECEIVED: August 15, 2019

SPONSOR INFORMATION:

Bluegrass Vascular Technologies, Inc.
12500 Network Boulevard, Suite 308
San Antonio, Texas 78249

INDICATIONS FOR USE

The Surfacer Inside-Out Access Catheter System is intended to obtain central venous access to facilitate catheter insertion into the central venous system for patients with upper body venous occlusions or other conditions that preclude central venous access by conventional methods.

LIMITATIONS

The sale, distribution, and use of the Surfacer Inside-Out Access Catheter System are restricted to prescription use in accordance with 21 CFR 801.109.

Only physicians who have received appropriate training and are familiar with the principles, clinical applications, complications, side effects and hazards commonly associated with interventional procedures should use this device.

This device should be used only in institutions where emergency surgery can be performed and where blood transfusions can be performed.

The Surfacer Inside-Out Access Catheter System is contraindicated for patients with an occlusion of the right femoral vein, right iliac vein or inferior vena cava, or acute thrombosis within any vessel to be crossed by the Surfacer Inside-Out Access Catheter System. Special precautions may be required for patients with coagulation disorders or on anti-coagulation therapy.

The Surfacer Inside-Out Access Catheter System System is not intended for use in the coronary or cerebral vasculature. This device is not to be used in the arterial system.

PLEASE REFER TO THE LABELING FOR A COMPLETE LIST OF WARNINGS, PRECAUTIONS AND CONTRAINDICATIONS.

DEVICE DESCRIPTION

The Surfacer Inside-Out Access Catheter System (Figure 1) is used to gain central venous access by directing a needle from inside the vein to skin, as opposed to the traditional approach of inserting a needle inwards. The Surfacer Device is percutaneously introduced into the right femoral vein. It is advanced up the inferior vena cava, via the superior vena cava (SVC), to the location of the occlusion. When the occlusion has been visualized under fluoroscopy, a needle wire is oriented to advance through or to cross the occlusion and to exit to a pre-determined external target. A new central venous catheter is then back-loaded into a peel-able introducer sheath and positioned below the occlusion for central venous access.

The Surfacer Inside-Out Access Catheter System is comprised of four components: A Workstation Sheath for percutaneous access via the femoral vein; a Surfacer Device, comprising a (b)(4) Needle Wire and Needle Guide, which is advanced to the supraclavicular space; an Exit Target, which provides fluoroscopic guidance to mark the exit point; and a (b)(4) (b)(4) Peel-able Introducer Sheath, which is introduced over the Needle Wire to access the central venous system. Once the access is obtained and a catheter is in place, the Surfacer System is removed. Please refer to the Instructions for Use for additional details.

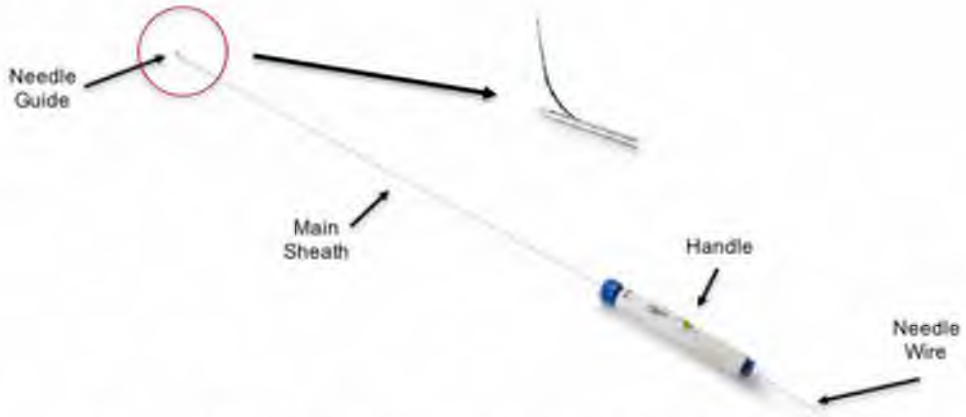

Figure 1: The Surfacer Inside-Out Access Catheter System

SUMMARY OF NONCLINICAL/BENCH STUDIES

BIOCOMPATIBILITY/MATERIALS

The Surfacer Inside-Out Access Catheter System is an externally communicating device in contact with circulating blood with limited contact duration (< 24 hours). The biocompatibility testing summarized below was performed in accordance with FDA's Guidance Document titled *Use of International Standard ISO 10993-1, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process"* to demonstrate that the device is biocompatible for its intended use.

Table 1: Biocompatibility Testing Summary

Test	Description (Method)
Cytotoxicity	MEM Elution Assay with L-929 Mouse Fibroblast Cells (ISO 10993-5)
Sensitization	Guinea Pig Maximization (ISO 10993-10)
Irritation	Intracutaneous Reactivity (ISO 10993-10)
Acute System Toxicity	Acute System Injection (ISO 10993-11)
Hemocompatibility	ASTM Hemolysis Assay – Direct & Indirect Contact Methods (ASTM Method F756-08)
	Complement Activation C3a and SC5b-9 Determination of SC5b-9 Terminal Chain Complex

	(TCC) and C3a-desArg Present in Normal Human Serum Through Enzyme Immunoassay (ISO 10993-4)
	In-vivo Thromboresistance (GLP non-anticoagulated venous implant (NAVI) sheep thromboresistance study)
Pyrogenicity	Material-mediated Rabbit Pyrogen (USP Rabbit Pyrogen Test Procedure, Section 151)
	Endotoxin-mediated (LAL) (USP Rabbit Pyrogen Test Procedure, Section 85)

SHELF LIFE/STERILITY

The shelf-life of the Surfacer Inside-Out Access Catheter System has been established at (b)(4) based on a combination of real-time and accelerated aging testing equivalent to (b)(4) in accordance with ASTM F1980 - 07 Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices. Following aging, the devices were bubble leak tested per ASTM F2096, and package seals were tested per ASTM F88. Aged devices also underwent repeat engineering bench testing to confirm acceptable performance.

The Surfacer Inside-Out Access Catheter System is labeled as sterile and has a validated sterility assurance level (SAL) of 10^{-6}. The Surfacer Inside-Out Access Catheter System has been validated to be sterilized via ethylene oxide per ISO 11135:2014 and AAMI TIR 28:2016.

MAGNETIC RESONANCE (MR) COMPATIBILITY

The Surfacer Inside-Out Access Catheter System is intended as a temporary use device and has not been tested for MR compatibility.

PERFORMANCE TESTING - BENCH

Table 2: Performance Testing Summary

Test	Description/Acceptance Criteria
Compatibility of system components	Sheath inner diameter passes a 0.035" GW. Sheath inner diameter passes the delivery instrument. Dilator outer diameter passes through sheath and Tuohy-Borst valve.
Visual and dimensional inspection of all components	Verification of the following dimensions to specifications: Sheath outer diameter Sheath distal/proximal inner diameter Sheath total and effective length

	Dilator outer diameter Dilator effective and taper length Dilator tip inner diameter Vent hole inner diameter Markerband length Needle guide bend angle Rotational alignment of needle guide vs sheath Rotational alignment of needle guide vs handle Tip slot width, for radiopacity, and for needle guide Shaft length Shaft OD Needle guide OD Needle guide bend angle accuracy Max length of needle guide extending from shaft Total length of delivery instrument with plunger Needle wire travel relative to the main sheath Visual verification of: The presence of two vents holes. Sheath and Dilator free of extraneous matter at (b)(4) magnification. Sheath free from surface defects at (b)(4) magnification. Verified the material of: The radiopaque marker bands. Dilator shaft radiopaque constituents.
Corrosion resistance	Boil test per ISO 11070, sec. (b)(4) Visual inspection for corrosion.
Simulated use	Assessment of the following: • Ease of insertion • Sufficient control • Catheter effective to position device relative to mock occlusion • Workstation, delivery instrument, guidewire and tip visible in fluoroscopy • Ability to place and position in peripheral vasculature • Insertion into vessel • Pushability • Kink resistance • Tortuosity/occlusion access • Ability to cross occlusion
Mechanical strength, including joint strength, buckle, activation force, kink resistance and peeling	Joint strengths all (b)(4) • Dilator-Hub • Sheath-Hub • Markerband-Sheath • Valve to tubing • Tubing to luer Kink resistant at (b)(4) in (b)(4) water bath. Needle wire cycles (b)(4) without any failures or excessive curvature changes which would affect safety or efficacy

Fluid flow, including Leakage, aspiration and flush	Liquid leakage through Tuohy-Borst valve for (b)(4) at (b)(4) drops permitted. Air leakage through Tuohy-Borst valve with negative pressure. No leakage (bubbles) permitted in open, half-open or closed positions. Flushing test: must be able to flush the Workstation sheath.

PERFORMANCE TESTING - ANIMAL AND/OR CADAVER

No suitable animal model was identified to evaluate the performance of the Surfacer Inside-Out Access Catheter System in human anatomy. In the absence of a suitable animal model, cadaver testing was performed which include five assessments on a single cadaver. These are summarized in the following table:

Table 3: Cadaver Testing Summary

Description	Acceptance criteria
Force to tunnel through the occluded vein	Physician evaluation (acceptable/unacceptable)
Distance of wire exit from target location	No more than (b)(4) in any direction from the center of the target
Force to pull the introducer into the vena cava	Physician evaluation (acceptable/unacceptable)
Critical device failures	None

SUMMARY OF CLINICAL INFORMATION

The primary clinical data provided to support the De Novo request was the United States SAVE-US IDE Study. Additional clinical data was provided from the International Post Market SAVE Registry. Details of the design of these studies and selected clinical results are provided below.

United States SAVE-US IDE Study

Purpose: To assess the safety and effectiveness of the Surfacer Inside-Out Access Catheter System used to facilitate upper body central venous access.

Design: The SAVE-US Study was a prospective, single-arm, multi-center study using the Surfacer Inside-Out Access Catheter System in subjects who require central venous access. A total of thirty (30) subjects at seven (7) centers in the United States were treated. Subjects who required central venous access and met the study inclusion/exclusion criteria were enrolled and treated with the Surfacer Inside-Out Access Catheter System.

An Independent Data Safety and Monitoring Board (DSMB) was created to monitor the study. Proctors representing Bluegrass Vascular Technologies, Inc. were present for 29/30 cases.

Primary Endpoints:

1) Safety: The primary safety endpoint was acute device safety, defined as the absence of procedural complications (hemopericardium, hemothorax, pneumothorax, blood transfusion,

resuscitation, emergency post-procedural intervention, transfer to an intensive care unit, and death) at discharge and 7 days post-procedure. Overall device and procedure related anticipated adverse events were compared to historical safety data from central vein placement procedures.

2) Effectiveness: The primary effectiveness endpoint was the rate of safe insertion and patency of central venous catheters (CVCs) created across venous occlusions.

Secondary Endpoints: Secondary endpoints consisted of the following:

1) Safety: The rate of conversion to alternative central vein placement techniques.
2) Effectiveness: Surfacer System clinical utility assessed by the ability of the Surfacer System to facilitate central venous access placement.

Eligibility Criteria Summary: The study population consisted of male and female subjects, between 18 - 80 years of age.

Key inclusion criteria included the following:

- Subjects have been referred for placement of central venous access catheter.
- Subjects have limited or diminishing upper body venous access or pathology impeding standard access methods.

Key exclusion criteria included the following:

- Subjects were contraindicated for Surfacer System use if one of the following are found (per the IFU):
    - Occlusion of the right femoral vein;
    - Occlusion of the iliac vein;
    - Occlusion of the inferior vena cava.
- Subject with acute thrombosis within any vessel (superior vena cava (SVC), jugular, inferior vena cava (IVC), brachiocephalic and subclavian) planned to be crossed by Surfacer System.
- Subjects with tortuous anatomy which precludes a straight line from femoral venous entry to subclavian exit.

Accountability: Subjects were exited from the study upon completing the final protocol required 7-day follow-up visit. In three cases, subjects prematurely exited or withdrew from the study because the subject was determined to be ineligible during procedural imaging, which showed anatomical tortuosity that precluded safe advancement of the Surfacer System.

Patients were followed per the following scheduled assessments:

Table 4: Scheduled Assessments

Assessments/Interval	Screening	Baseline	Intra-Procedural	Hospital Discharge	7 Days (+7) Post Procedure
Informed Consent	X				
Study Eligibility	X				
Medical History/Demographics	X				
Physical Exam including Vital Signs		X		X	X
TCVO Lesion Type Classification		X			
Procedural Complication Assessment			X	X	X
Study Device Performance			X		
Medications (Antithrombotic & Cardiovascular)		X		X	X
Clinical Laboratory Tests					
Pregnancy Test	X				
Creatinine		X			
Coagulation Profile (APTT/PT/INR)		X		X	
CRP		X		X	
LDH/ASAT/ALAT		X		X	
Fibrinogen/D-dimer		X		X	
Exams and Tests					
AP and LAT Chest X-Ray or cine-fluoroscopy		X	X	X	
Ultrasound or Venous Duplex Venography		X			
ECG 12-lead		X			
TTE			Only If Cardiac Events	Only If Cardiac Events	
Contrast Angiography			X		
Fluoroscopy			X		
Cone Beam CT/cardiac echo/advanced imaging modalities			X		
Adverse Events			X	X	X
Protocol Deviations		X	X	X	X

Demographics: The total population consisted of 30 subjects. Demographic information on the subjects is provided in Table 5 below.

Table 5: Subject Demographics

Characteristic	**Enrolled (ITT) (N=30) n, %**	**Treated (PP) (N=27) n, %**
Respiratory diseases	14, 46.7%	12, 44.4%
Asthma	7, 23.3%	7, 25.9%
Chronic obstructive pulmonary disease (COPD)	6, 20.0%	4, 14.8%
Pulmonary hypertension	2, 6.7%	2, 7.4%
Allergy or intolerance to anticoagulation or antiplatelet therapy that cannot be pre-treated.	0, 0.0%	0, 0.0%
Angina	3, 10.0%	3, 11.1%
Bleeding diatheses or coagulopathy	1, 3.3%	1, 3.7%
Carotid Stenosis	4, 13.3%	4, 14.8%
Coronary Artery Disease	11, 36.7%	10, 37.0%
Previous CAD interventional procedures	6, 20.0%	5, 18.5%
Previous Stroke	6, 20.0%	6, 22.2%
Previous Transient Ischemic Attack (TIA)	5, 16.7%	5, 18.5%
Diabetes	14, 46.7%	12, 44.4%
Type 1 Type 2	2, 6.7% 12, 40.0 %	2, 7.4% 10, 37.0%
Controlled by diet	7, 23.3%	6, 22.2%
Controlled by medication	8, 26.7%	7, 25.9%
Dyslipidemia	6, 20.0%	4, 14.8%
Active Endocarditis	0, 0.0%	0, 0.0%
Hypertension	21, 70.0%	18, 66.7%
Hyperlipidemia	15, 50.0%	12, 44.4%
Previous Myocardial Infarction	5, 16.7%	5, 18.5%
Active Pericarditis	0, 0.0%	0, 0.0%
Peripheral Vascular Disease (PVD)	10, 33.3%	9, 33.3%
Chronic Kidney Disease (CKD)	28, 93.3%	25, 92.6%
Dialysis	28, 93.3%	25, 92.6%
Renal Dysfunction	24, 80.0%	22, 81.5%
Smoking status (current or Ex-)	11, 36.7%	10, 37.0%
Pneumothorax	0, 0.0%	0, 0.0%
Hemothorax	1, 3.3%	1, 3.7%
Prior CVA (central venous access)	19, 63.3%	18, 66.7%
Other Relevant Procedures (hysterectomy, ileostomy, colectomy, heart transplant, bilateral mastectomy, kidney transplant, testicular surgery, sympathectomy, renal transplant Hero graft placement).	11, 36.7%	10, 37.0%
Other Relevant History (chronic AF, CHF, Quadriplegia, Lymphoma, Peripheral Neuropathy, Sickle Cell Anemia, Prostate Cancer)	13, 43.3%	12, 44.4%

Adverse Events: The adverse events presented in Table 6 were observed in SAVE-US. A total of ten (10) adverse events (AEs) were reported in seven (7) subjects at five sites. Five (5) adverse events in four subjects were reported as a serious adverse events (SAE).

Table 6: Adverse Event Classification, Severity and Device/Procedure Relatedness

AE Term N=30 pts	AE # Subjects (%*) [#Events]	SAE #Subjects[1] (%*) [#Events]	Device Related # Subjects[1] (%*) [#Events]	Procedure Related AEs # Subjects[1] (%*) [#Events]
Experienced at least one AE	7 (23.3%) [10]	4 (13.3%) [5]	0 (0%) [0]	5 (16.7%) [6]
Bleeding	2 (6.7%) [2]	2 (6.7%) [2]	0 (0%) [0]	2 (6.7%) [2]
Adverse tissue reaction[2]	1 (3.3%) [1]	0 (0%) [0]	0 (0%) [0]	1 (3.3%) [1]
Allergic reaction	1 (3.3%) [1]	0 (0%) [0]	0 (0%) [0]	0 (0%) [0]
Unintended embolization	1 (3.3%) [1]	1 (3.3%) [1]	0 (0%) [0]	1 (3.3%) [1]
Other events	3 (10.0%) [5]	2 (6.7%) [2]	0 (0%) [0]	2 (6.7%) [2]

* Calculated as (n/N) 100%, where n = number of subjects experiencing AE, N = total number of enrolled subjects.
[1] One subject experienced more than one AE/SAE from different category.
[2] One subject experienced a skin reaction to the access site dressing.

Results:

Primary Safety Endpoint: The primary safety endpoint was analyzed in all enrolled subjects based on acute device safety, defined as the absence of procedural complications at discharge and 7 days post procedure. Specifically, procedure-related adverse events were observed in 4/30 subjects (13.3%) through the 7-day follow-up period (one patient experienced two events). The four (4) subjects whom the analysis classified as not having met the primary safety endpoint included: unintended embolization; hemodynamic instability; bleeding; and hypotension and bleeding. There was one (1) subject who experienced an adverse tissue reaction which was classified as a procedure-related adverse event but met the primary safety endpoint. No anticipated (ADE) or unanticipated (UADE) device related adverse events were reported. Absence of device-related adverse events in 100% of treated subjects was evaluated and monitored by the DSMB.

Table 7: Primary Safety Outcome ITT

		95% CI[1]	
Characteristic	**%(n/N)**	**Lower Confidence Limit**	**Upper Confidence Limit**
% subjects without serious procedural complications at discharge and 7 days post procedure	86.7% (26/30)	69.3%	96.2%

[1] *Exact Binomial CI*
[2] *where n = number of subjects with serious procedural complication, N = total number of enrolled subjects*

Table 8: Adverse Event Classification for IDE study

Category	Overall Event Rate ITT Population (N= 30) N (%) 95% CI[1]	Overall Event Rate PP Population (N= 27) N (%) 95% CI[1]
Device / Procedure Related		
Hemopericardium	0 (0.0%) 0.0%, 11.6%	0 (0.0%) 0.0%, 12.7%
Blood Transfusion	2 (6.7%) 0.1%, 22.1%	2 (7.4%) 0.1%, 24.3%
Pneumothorax	0 (0.0%) 0.0%, 11.6%	0 (0.0%) 0.0%, 12.7%
Hemothorax	0 (0.0%) 0.0%, 11.6%	0 (0.0%) 0.0%, 12.7%
Resuscitation	0 (0.0%) 0.0%, 11.6%	0 (0.0%) 0.0%, 12.7%
Emergency Post Intervention	0 (0.0%) 0.0%, 11.6%	0 (0.0%) 0.0%, 12.7%
ICU Transfer	0 (0.0%) 0.0%, 11.6%	0 (0.0%) 0.0%, 12.7%
Death	0 (0.0%) 0.0%, 11.6%	0 (0.0%) 0.0%, 12.7%
Bleeding (SAE)	2 (6.7%) 0.1%, 22.1%	2 (7.4%) 0.1%, 24.3%
Unintended embolization or thrombosis (SAE)	1 (3.3%) 0.1%,17.2%	1 (3.7%) 0.1%,19.0%
Other SAE Events: (1) hemodynamic instability requiring prolonged hospitalization and one (1) hypotension	2 (6.7%) 0.1%, 22.1%	2 (7.4%) 0.1%, 24.3%
Composite SAE rate (# Subjects) as described in the study protocol	**4 (13.3%) 3.8%, 30.7%**	**4 (14.8%) 4.2%, 33.7%**

Primary Effectiveness Endpoint: Primary efficacy endpoints were analyzed based on rate of safe insertion and patency created across venous occlusions. In the per protocol (PP) population the analysis of both the primary and secondary efficacy endpoints resulted in a 100% success rate (27/27). In the intent-to-treat (ITT) population, 27/30 subjects (90%) obtained central venous access (CVA) using the Surfacer System with a confidence interval (CI) of 73.5%, 97.9%. Three (3) subjects did not receive access via the Surfacer System due to extreme vessel tortuosity. In these cases, imaging during intra-procedural venography revealed the inability to safely exit due to tortuosity of upper vasculature anterior, posterior, right and left.

Table 9: Primary Efficacy Endpoint: Rate of safe insertion and patency of CVCs created across venous occlusions.

Characteristic	**N**		
Total # of insertion attempts	30		
		95% CI[1]	
	% (n/N)	**Lower Confidence Limit**	**Upper Confidence Limit**
% safe insertion and patency of CVCs created across venous occlusions	90.0% (27/30)	73.5%	97.9%

[1] *Exact Binomial CI*
[2] *where n = number of subjects with safe insertion and patency, N = total number of enrolled subjects.*

Secondary Safety Endpoint: Secondary safety outcome was evaluated as technique conversion rate and is presented in Table 10 below. Distorted anatomy was reported as main reason for conversion. In total, three (3) subjects or (10%) failed the primary and secondary efficacy endpoints.

Table 10: Secondary Safety Endpoint: Technique Conversion rate and causes

Characteristic	**%(n/N)[2]**	**95% CI[1]**	
		Lower Confidence Limit	**Upper Confidence Limit**
% subjects with conversion	10.0% (3/30)	2.1%	26.5%
Reason for conversion (N=3)			
Reason: subjects' distorted anatomy presented higher risk for placement	100.0% (3/3)		

[1] *Exact Binomial CI*
[2] *where n = number of subjects with a conversion, N= total number of enrolled subjects.*

Secondary Effectiveness Endpoints: The Surfacer System was advanced from entry in the femoral vein to supraclavicular exit in 27/30 (90%) of ITT and 27/27 (100%) of PP treated subjects.

Conclusions: The SAVE-US trial supports the safety and effectiveness of the Surfacer Inside-Out Access Catheter System to facilitate upper body central venous access. Surfacer System deployment was successfully achieved in 90.0% of subjects in the ITT population and 100% in the PP population. The primary safety endpoint success rate, absence of procedural complications, was 86.7% in the ITT population (26/30) and 85.2% in the PP population (23/27). Four of 30 subjects (13.3%) did not meet the safety endpoint of the study.

International Post Market SAVE Registry

Purpose: The Surfacer System to Facilitate Access in Venous Occlusions (SAVE) Registry (ClinicalTrials.gov Identifier: NCT02875899) was established to assess the standard of care and clinical outcomes of the Surfacer Inside-Out Access Catheter System used in routine clinical practice outside the United States.

Design: The International SAVE Registry was a prospective, single-arm, post market, multicenter, international registry of the Surfacer System for the treatment of subjects with limited or diminishing upper body venous access or pathology impeding standard access methods. A total of thirty (30) subjects at five (5) centers in Germany, Italy, Austria and Paraguay were enrolled. Following ethics committee approvals, subject demographics, medical history and type of occlusion were documented at enrollment.

Primary Endpoints:

1) Safety: The primary safety endpoint was a safety evaluation at end of procedure and at discharge. Acute device safety was also assessed, defined as the absence of device related SAEs.
2) Performance: The primary performance endpoint was an evaluation of the success rate defined as the ability to facilitate placement of CVCs using the Surfacer System to establish a transient passage across venous occlusions.

Secondary Endpoints: Secondary endpoints consisted of the following:

1) Safety: The rate of technique conversion and causes, and the rate of CV Access catheter malposition.
2) Performance: Assessment of the ability of the Surfacer System to be advanced from the femoral vein to subclavicular exit to facilitate CVC placement.

Eligibility Criteria Summary: The study population consisted of male and female subjects, at least 18 years of age.

Key inclusion criteria included the following:

- Subjects have been referred for placement of central venous access catheter.

- Subjects have limited or diminishing upper body venous access or pathology impeding standard access methods.

Key exclusion criteria included the following:

- Subjects were contraindicated for Surfacer System use if one of the following are found (per the IFU):
    - Occlusion of the right femoral vein;
    - Occlusion of the iliac vein;
    - Occlusion of the inferior vena cava.
- Subject with acute thrombosis within any vessel (superior vena cava (SVC), jugular, inferior vena cava (IVC), brachiocephalic and subclavian) planned to be crossed by Surfacer System.

Demographics: The mean age of subjects enrolled in the registry was 60.1 years. This included eighteen (18) males and twelve (12) females in whom the Surfacer System was used to establish central venous access. Of the 30 subjects enrolled 17 had thoracic central vein obstruction (TCVO) Type 3 or Type 4 occlusions and 13 had Type 1 or 2 occlusion.

The TCVO occlusion types were defined as follows:

- Type 1: Bilateral internal jugular or one subclavian vein
- Type 2: Unilateral brachiocephalic vein
- Type 3: Both brachiocephalic veins, partially obstructed superior vena cava
- Type 4: Superior vena cava obstruction preventing flow to right atrium

Table 11: Subject demographics (n=30)

VARIABLE	Mean ± SD	Range
Age (years)	60.1 ±12.8	38-80
Weight (kg)	68.0 ±11.5	48-91
Height (cm)	160.4 ±17.9	96-178

Adverse Events: Safety was defined as the rate of serious device-related adverse events (SADEs) that occurred during the first 48 hours to hospital discharge. No SADEs were reported to date. No Procedure related adverse events reported.

Results:

The results of primary safety and performance endpoint evaluations are summarized in Table 12. Device performance and adverse events were collected during the procedure and upon hospital discharge. Of the thirty (30) enrolled subjects, twenty-nine (29) (96.7%) subjects received placement of a central venous catheter.

Evaluation of the secondary performance endpoint, including visualization of the needle guide and needle wire exit under fluoroscopy, placement of patent central venous catheter (CVC) using the exit introducer, was confirmed in the twenty-nine (29) treated subjects.

The study's secondary safety endpoints confirmed successful central venous access in 29 of 30 subjects. One (1) conversion to alternative access method was observed due to significant vascular anatomical tortuosity.

Table 12: Endpoints Evaluation

Primary Endpoints	Outcome # Subjects (%)
Performance (N=30)	
Procedural success rate: ability to facilitate placement of CVC's using the Surfacer to establish a transient passage across venous occlusions.	29 (96.7%)
Safety (N=29*)	
Safety evaluation at end of procedure and at discharge. Freedom from complications.	29 (100%)
Acute device safety, defined as the absence of device related SAEs.	29 (100%)
SECONDARY Endpoints	
Performance (N=30)	
Surfacer advancement from femoral vein to sub-clavicular exit to facilitate CVC placement assessed by:	29 (96.7%)
Ability of Needle Guide and Needle Wire to exit superior vena cava as visualized fluoroscopically	
Ability of exit introducer to facilitate placement of CVC	29 (96.7%)
Safety (N=30)	
Technique Conversion rate	1 (3.3%)
CV Access catheter malposition	0 (0%)

*Includes subjects with Surfacer System only

Conclusions:

The results obtained for subjects enrolled in the SAVE Registry support the safety and efficacy of the Surfacer Inside-Out procedure when used for restoring a right-sided central venous access in subjects with central venous occlusions.

EU Vigilance Reports

Since receipt of CE Mark, four (4) European vigilance reports were filed with events such as bleeding, blood vessel/vein damage; and arterial damage. Two events resulted in patient death. One subject tolerated access of the central venous system with the Surfacer device, but died of acute bleeding into the pleural space after the tract was dilated with an angioplasty balloon to insert a HeRO catheter. None of the vigilance reports were related to device malfunction. Bleeding is a known and anticipated risk of Surfacer System use. Users should follow the instructions/warnings provided in the labeling.

Pediatric Extrapolation

In this De Novo request, existing clinical data were not leveraged to support the use of the device in a pediatric patient population.

POSTMARKET EVALUATION

A postmarket evaluation will be required to obtain a more comprehensive safety profile of the device by collecting short-term safety data associated with real-world US use of the device in the absence of proctors. Safety and effectiveness data will be collected and compared to the pivotal study data that supported this De Novo application.

LABELING

The Surfacer Inside-Out Access Catheter System labeling consists of Instructions for Use and packaging labels. The Instructions for use include the indications for use; a description of the device, contraindications, warnings, precautions; a description of compatible devices; a detailed summary of the clinical data collected in support of the device; a shelf life; and instructions for the safe use of the device. The labeling satisfies the requirements of 21 CFR 801.109.

Please see the Limitations section above for important warnings and precautions presented in the device labeling.

RISKS TO HEALTH

The table below identifies the risks to health that may be associated with use of a reverse central venous recanalization system.

Table 13: Identified Risks to Health and Mitigation Measures

Identified Risks to Health	Mitigation Measures
Infection	Sterilization validation Shelf life testing Labeling
Adverse tissue reaction	Biocompatibility evaluation
Embolization caused by component fracture	Clinical performance testing Non-clinical performance testing
Death, bleeding, damage to non-target tissue and organs, blood vessel perforation or rupture, hematoma; or delays to therapy from failure to achieve central venous access	Clinical performance testing Non-clinical performance testing Labeling

SPECIAL CONTROLS

In combination with the general controls of the FD&C Act, the reverse central venous recanalization system is subject to the following special controls:

(1) Clinical performance testing must fulfill the following:
   (i) Demonstrate the ability to safely deliver, deploy, and remove the device; and
   (ii) Evaluate all adverse events including death, bleeding, damage to non-target tissue and organs, blood vessel perforation or rupture, and hematoma.

(2) Non-clinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use. The following performance characteristics must be tested:
   (i) Simulated-use testing in a clinically relevant bench anatomic model to assess the delivery, deployment, and retrieval of the system;
   (ii) Compatibility of system components with other devices labeled for use with the device;
   (iii) Tensile strengths of joints and components,
   (iv) Kink resistance of system components;
   (v) Radiopacity of components used to monitor procedure under fluoroscopy;
   (vi) Characterization and verification of all dimensions; and
   (vii) Leakage of air or fluid.

(3) All patient contacting components of the device must be demonstrated to be biocompatible.

(4) Performance data must demonstrate the sterility of the device components intended to be provided sterile.

(5) Performance data must support the shelf life of the device by demonstrating continued sterility, package integrity, and device functionality over the identified shelf life.

(6) Labeling for the device must include:
   (i) Instructions for use, including a description of compatible devices;
   (ii) A detailed summary of the clinical testing conducted; and
   (iii) The shelf life and storage conditions.

BENEFIT-RISK DETERMINATION

The risks of the Surfacer Inside-Out Access Catheter System are based on nonclinical laboratory studies as well as data collected in the clinical studies described above. Potential serious and life-threating complications include death, severe bleeding, perforation of the right atrium, pericardial tamponade, hemothorax, tears of the superior vena cava, and lacerations of the main subclavian artery and its branches, any of which can rapidly lead to cardiac collapse and/or exsanguination.

The probable benefits of the device are also based on nonclinical laboratory studies as well as data collected in the clinical studies as described above.

The Surfacer Inside-Out Access Catheter System has been shown in the IDE trial and other supporting clinical data to be effective at establishing right neck central venous access in selected patients with central venous occlusions. Selected patients requiring central venous access for hemodialysis and infusion therapy despite presence of central venous occlusions may benefit from this device. The Surfacer System could benefit patients as an alternative to chronic femoral venous catheters, which may have high infection rates and hinder mobility. Some patients may also benefit from avoiding the need for higher-risk placement of catheters via translumbar and transhepatic routes.

The United States SAVE-US IDE Study had only a limited cohort size (30 subjects) and proctors were present in the vast majority (29/30) of procedures. Consequently, limited information is available that represents treatment of US patients or US patients without a proctor present. Therefore, to support a favorable benefit/risk decision, additional Post Market data collection was required to monitor the first patients for Adverse Events and Serious Adverse events that may arise during real-world use of the Surfacer device in a US healthcare setting with both proctored and unproctored cases.

Patient Perspectives

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

BENEFIT/RISK CONCLUSION

In conclusion, given the available information above, for the following indication statement:

> The Surfacer Inside-Out Access Catheter System is intended to obtain central venous access to facilitate catheter insertion into the central venous system for patients with upper body venous occlusions or other conditions that preclude central venous access by conventional methods.

The probable benefits outweigh the probable risks for the Surfacer Inside-Out Access Catheter System. The device provides benefits and the risks can be mitigated by the use of general controls and the identified special controls.

CONCLUSION

The De Novo request for the Surfacer Inside-Out Access Catheter System is granted and the device is classified as follows:

> Product Code: QJH
> Device Type: Reverse central venous recanalization system
> Regulation Number: 21 CFR 870.1342
> Class: II