FRED™
FRED™ X™

Flow Re-direction Endoluminal Device

INSTRUCTIONS FOR USE

Rx Only: Federal (USA) law restricts this device
to sale by or on the order of a physician.

IFU100170 Rev. A
Revised 2021-09

A. DEVICE DESCRIPTION

The Flow Re-Direction Endoluminal Device (FRED™ System [see Figures 1, 2]) consists of a self-expanding, nickel titanium implant and a delivery system. The implant is designed to expand to a pre-determined diameter when released from the delivery system. The implant features integrated dual layer coverage designed to focus mainly at the neck of an intracranial aneurysm. The implant has distal and proximal markers on its ends and interweaved helical marker strands delineating the inner working length of the implant to provide fluoroscopic visibility. The FRED System is packaged sterile as a single unit with the implant, introducer sheath and a detachable delivery pusher. The surface of the FRED X device is treated with X Technology, a polymer surface modification. It is available in 7 different implant diameters ranging from 2.5 mm to 5.5 mm and in different implant lengths ranging from 13 mm to 45 mm. The FRED System 2.5 mm and 3.0 mm implants are compatible with the Headway™ 21 Microcatheter (FRED-21 System). The FRED System 3.5 mm to 5.5 mm implants are compatible with the Headway 27 Microcatheter (FRED-27 System).

Figure 1: System Setup

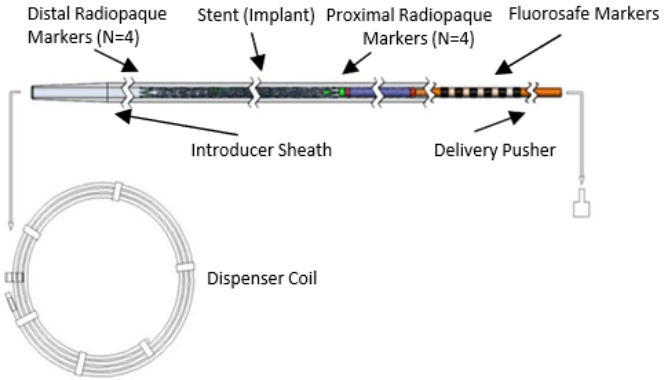


Figure 2: Implant Nomenclature

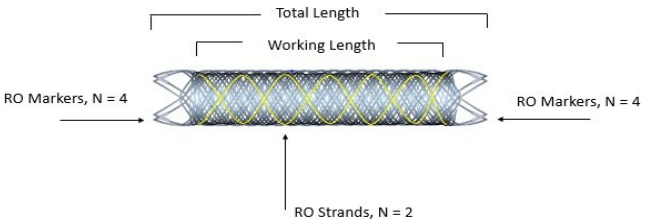


Table 1: Models and Dimensions

Outer Diameter (mm)	Total Lengths (mm)	Working Lengths (mm)
2.5	13 to 30	8 to 26
3.0	13 to 32	9 to 27
3.5	13, 15, 17, 19, 22, 31, 40	7, 9, 11, 13, 16, 24, 36
4.0	13, 15, 18, 20, 23, 32, 44	7, 9, 12, 14, 17, 26, 38
4.5	15, 17, 20, 25, 31, 34, 45	8, 11, 13, 18, 24, 28, 39
5.0	15, 18, 21, 26, 32, 36	9, 11, 14, 19, 26, 29
5.5	22, 28, 32	14, 19, 26

B. INDICATIONS FOR USE

The Flow Re-Direction Endoluminal Device (FRED) System is indicated for use in the internal carotid artery from the petrous segment to the terminus for the endovascular treatment of adult patients (22 years of age or older) with wide-necked (neck width ≥ 4 mm or dome-to-neck ratio < 2) saccular or fusiform intracranial aneurysms arising from a parent vessel with a diameter ≥ 2.0 mm and ≤ 5.0 mm.

C. CONTRAINDICATIONS

Use of the FRED system is contraindicated under these circumstances:

- Patients in whom anticoagulant, anti-platelet therapy, or thrombolytic drugs are contraindicated.
- Patients with known hypersensitivity to metal such as nickel-titanium and metal jewelry.
- Patients with anatomy that does not permit passage or deployment of the FRED System.
- Patients with an active bacterial infection.
- Patients with a pre-existing stent in place at the target aneurysm.
- Patients in whom the parent vessel size does not fall within the indicated range.
- Patients who have not received dual anti-platelet agents prior to the procedure.

D. WARNINGS

The FRED System should only be used by physicians trained in endovascular interventional neuroradiology, radiology, neurosurgery or interventional neurology for the treatment of intracranial aneurysms or other vascular lesions.

The FRED-27 System should only be delivered through a Headway 27 microcatheter and the FRED-21 System should only be delivered through a Headway 21 microcatheter. If repeated friction is encountered during FRED System delivery, verify microcatheter is not kinked or in extremely tortuous anatomy. Confirm that the microcatheter does not ovalize. Confirm that there is adequate sterile heparinized flush solution.

Do not reposition the FRED System in the parent vessel without fully retrieving the device.The FRED system MUST be retrieved/re-sheathed into the microcatheter and re-deployed at the desired target location or removed completely from the patient. The FRED System must not be re-deployed more than three times.

Do not attempt to re-position the FRED implant after deployment/detachment.

Should unusual resistance be felt at any time during access or removal, the introducer/guide catheter/microcatheter and FRED System should be removed as a single unit. Applying excessive force during delivery or retrieval of the FRED System can potentially result in loss or damage to the device and delivery components.

The FRED System is provided sterile for single use only. Do not reuse, reprocess or resterilize. Reuse, reprocessing or resterilization may compromise the structural integrityof the device and/or lead to device failure which, in turn, may result in patient injury, illness, or death. Reuse, reprocessing, or resterilization may also create a risk of contamination of the device and/or cause patient infection or cross-infection, including, but not limited to, the transmission of infectious disease(s) from one patient to another. Contamination of the device may lead to injury, illness or death of the patient.

The FRED System delivery wire should not be utilized as a guidewire. Do not torque the FRED System. A torque device should not be used.

Placement of multiple implants may increase the risk of ischemic complications. Delayed rupture may occur with large and giant intracranial aneurysms.

The safety and effectiveness of the device has not been established in the treatment of ruptured intracranial aneurysms.

The benefits may not outweigh the risks of treatment of small and medium stable asymptomatic extradural intracranial aneurysms in patients without additional risk factors,including those located in the cavernous internal carotid artery. The risk of rupture for small and medium stable asymptomatic extradural intracranial aneurysms is very low if not negligible.

A slight decrease in the proportion of patients who achieve complete aneurysm occlusion without significant parent artery stenosis has been observed with the use of the device in the communicating segment (C7) of the internal carotid artery (ICA) [52.6% (10/19)] subjects in the FRED IDE study at 1 year)), including those intracranial aneuryms (IAs) fed by the posterior circulation or have retrograde filling. Ensure appropriate patient selection and weigh the benefits and risks of alternative treatments prior to the treatment of intracranial aneurysms located in this region of the ICA. The following anatomical characteristics, associated with retrograde filling, should be carefully considered during procedural planning of C7 intracranial aneurysms:

1. Observed posterior communicating artery (PComm) of fetal origin (A posterior cerebralartery (PCA) of fetal origin is defined as a small, hypoplastic, or absent P1 segment of the PCA with the PComm artery supplying a majority of blood flow to the ICA);
2. PComm branch arising from the aneurysm neck; and/or
3. PComm branch arising from the dome of the aneurysm.

E. PRECAUTIONS

The FRED System does not contain latex or polyvinyl chloride (PVC) materials.

Carefully inspect the sterile package and the FRED System prior to use to verify that neither has been damaged during shipment. Do not use kinked or damaged components, or if the package is opened or damaged.

See the product label for shelf life. Do not use the FRED System beyond the labeled use by date. Exercise caution when crossing the deployed/detached FRED System with adjunctive devices such as guidewires, catheters, microcatheters or balloon catheters to avoid disrupting the device geometry and device placement.

Carefully weigh the benefits of treatment vs. the risks associated with treatment using the device for each individual patient based on their medical health status and risks factors for intracranial aneurysm rupture during their expected life time such as age, medical comorbidities, history of smoking, intracranial aneurysm size, location, and morphology, family history, history of prior asymptomatic subarachnoid hemorrhage (aSAH), documented growth of intracranial aneurysm on serial imaging, presence of multiple intracranial aneurysms, and presence of concurrent pathology. The benefits of device use may not outweigh the risks associated with the device in certain patients; therefore,judicious patient selection is recommended.

The FRED implant may create local field inhomogeneity and susceptibility artifacts during magnetic resonance angiography (MRA), which may degrade the diagnostic quality to assess effective intracranial aneurysm treatment.

Operators should take all necessary precautions to limit X-radiation doses to patients and themselves by using sufficient shielding, reducing fluoroscopy times, and modifying X-ray technical factors were possible.

The safety and effectiveness of the device has not been established for treatment of fusiform IAs.

F. POTENTIAL COMPLICATIONS

Below is a list of the probable adverse effects (e.g., complications) associated with the useof neurovascular flow diverting stents.

- Allergic reaction, including but not limited to: contrast dye, nitinol metal, and any other medications used during the procedure
- Amaurosis fugax or transient blindness
- Aphasia
- Blindness
- Cardiac arrhythmia
- Complications of arterial puncture including pain, local bleeding, or injury to the artery,or adjacent nerves
- Cranial neuropathy
- Death
- Device fracture, migration or misplacement
- Diplopia
- Dissection or perforation of the parent artery
- Headache
- Hemiplegia
- Hemorrhage, including intracranial hemorrhage (ICH), subarachnoid hemorrhage (SAH), and retroperitoneal
- Hydrocephalus
- Infection
- Mass effect
- Myocardial infarction
- Neurological deficits
- Pseudoaneurysm formation
- Reactions to anti-platelet or anti-coagulant agents
- Reactions due to radiation exposure, including alopecia, burns ranging in severity from skin reddening to ulcers, cataracts, and delayed neoplasia.
- Reactions to anesthesia and related procedures
- Reactions to contrast agents including allergic reactions and kidney failure

- Reduced visual acuity or visual field
- Retinal artery occlusion or infarction
- Retinal ischemia
- Rupture or perforation of the aneurysm
- Stenosis of stented segment
- Seizure
- Stent thrombosis
- Stroke or TIA (transient ischemic attack)
- Thromboembolic event
- Vasospasm
- Visual impairment

G. MR ENVIRONMENT

Non-clinical testing has demonstrated that the FRED System is MR Conditional. A patient with this device can be safely scanned in an MR system under the following conditions:

- Static magnetic field of 1.5-Tesla and 3-Tesla, only
- Maximum spatial gradient magnetic field of 2,500-gauss/cm (25-T/m)
- Maximum MR system reported, whole body averaged specific absorption rate (SAR) of2-W/kg for 15 minutes of scanning (i.e., per pulse sequence) in the Normal Operating Mode

Under the scan conditions defined, the FRED System is expected to produce a maximum temperature rise of 2.8 ºC at 1.5-Tesla or 3.6 ºC at 3-Tesla after 15-minutes of continuous scanning (i.e., per pulse sequence).

In non-clinical testing, the image artifact caused by the device extends approximately 4- mm from the FRED System when imaged with a gradient echo pulse sequence and a 3- Tesla MR system.

MicroVention, Inc. recommends that the patient register the MR conditions disclosed in this IFU with the MedicAlert Foundation or equivalent organization. A FRED System patient implant card is included in the package, which should be completed and provided to the patient.

H. CLINICIAN USE INFORMATION

1. MATERIALS

The following parts are required to use the FRED System:

Note: Other accessories for performing a procedure are NOT supplied; should be selected based on the physician's experience and preferences

- Appropriate-sized guiding or intermediate catheter for use with selected microcatheter
- Headway 27 microcatheter (FRED-27 System)
- Headway 21 microcatheter (FRED-21 System)
- Microcatheter-compatible guidewires
- Saline solution/heparin-saline solution continuous flush set
- Contrast solution
- Rotating Hemostatic Valve (RHV)
- Pressurized sterile Infusion solutions – IV stand
- Femoral arterial sheath, compatible with delivery guide catheter
- Femoral artery access device, sterile needle, guidewire

2. PACKAGING AND STORAGE

The FRED System is placed inside a protective, plastic dispenser coil and packaged in a pouch and unit carton. The FRED System and dispenser coil will remain sterile unless the package is opened, damaged, or the expiration date has passed. Store at a controlled room temperature in a dry place.

3. SHELF LIFE

See the product label for the device shelf life. Do not use the device beyond the labeled use by date.

4. PREPARATION FOR USE

Device and Delivery System Selection

Appropriate selection of the FRED System is important for patient safety. In order to choose the optimal FRED System model size for any given lesion, examine pre-treatment angiograms for correct and accurate vessel measurements.

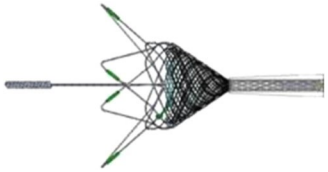
I. DIRECTIONS FOR USE

1. Gain vascular access according to standard angiographic practice and perform diagnostic angiogram to document target intracranial aneurysm and parent vessel to confirm vessel diameter.
2. Place appropriate size guide or intermediate catheter according to standard practice.
3. Coaxially navigate the appropriately sized microcatheter, Headway 27 microcatheter(FRED-27 System) or Headway 21 microcatheter (FRED-21 System), over a guidewire distal to the aneurysm neck or target location. Remove the guidewire.
4. Maintain flush through the microcatheter(s) per standard endovascular practice.
5. Select an appropriate-sized FRED System (refer to the FRED System in-service guide)according to the size of the parent vessel/intracranial aneurysm neck.
6. Note: The FRED System implant foreshortens (up to 60%) as it expands to the diameter of the parent vessel. Take implant foreshortening into account when sizing and deploying the FRED System.
7. Carefully inspect the package for damage to the sterile barrier. Peel open the pouch using aseptic technique and place the dispenser coil into the sterile field.

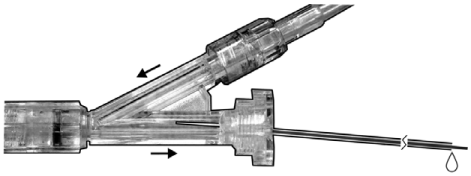
   a. Unclip the molded cap attached to the delivery wire from the dispenser coil. Pull on the proximal end of the delivery wire until the introducer exits the dispenser coil. Hold the delivery wire and introducer together while continuing to remove the entire device.

b. After removal from the dispenser coil, carefully push on the delivery wire in a bowl of saline, only partially deploy the FRED implant up to 5 mm or 50% (whatever occurs first, being careful not to detach the implant) from the distal introducer tip.

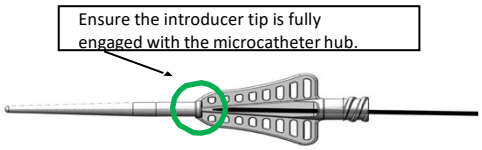
8. Check for the following:
   - Implant distal marker uniformity
   - Implant distal end shows even displacement with no entanglement
   - Implant tracks smoothly through introducer



9. Warning: Do Not Fully Deploy FRED System.
10. With the FRED implant and introducer sheath positioned and hydrated within the bowl of saline, gently manipulate the FRED implant within the saline to hydrate the implant. Carefully pull back on the delivery wire to fully retrieve the FRED implant and delivery wire tip within the introducer.
11. Warning: DO NOT CONTINUE if any defect is observed; return the unit to MicroVention, Inc.
12. Confirm that the device is entirely within the introducer, the tip of the delivery wire is not kinked, and the introducer tip is not damaged. DO NOT CONTINUE if either defect is observed; return the unit to MicroVention, Inc.
13. Partially insert the distal end of the introducer into the RHV connected to the compatible Headway microcatheter. Tighten the RHV locking ring. Flush the RHV with sterile saline and verify that fluid exits the proximal end of the introducer, hydrating the introducer.
14. Warning: Purge the FRED System carefully to avoid the accidental introduction of air into the system.



15. Untighten the RHV locking ring and advance the introducer until it is fully engaged withthe Headway microcatheter hub, then tighten the RHV locking ring.
16. Caution: The introducer must be properly engaged with the microcatheter hub to enable FRED X System to be introduced into the microcatheter.



17. Advance the delivery wire to transfer the FRED System from within the introducer into the microcatheter.
18. Warning: Do not torque the delivery wire while advancing or retracting the FREDSystem.
19. Continue advancing the delivery wire into the microcatheter until the proximal tip of the delivery wire enters the introducer. Loosen the RHV locking ring, remove the introducer, and set it aside.
20. Note: Fluoroscopy may be used up to this point at the physician's discretion.
21. Warning: Do not apply undue force. If resistance is encountered at any point during delivery or manipulation, withdraw the unit and select a new FRED System.
22. Carefully advance until the device exit marker on the proximal end of the delivery wire approaches the RHV. At this time, fluoroscopic guidance must be initiated.
23. Position the FRED System for deployment by aligning the FRED System implant distal radiopaque end markers past the aneurysm neck, allowing for adequate distal and proximal device landing zones as shown in the following figures for FRED-27 System andFRED-21 System.
24. FRED-27 Positioning

25. FRED X-21 Positioning

26. Note: A slow, proper push/pull technique, encompassing sufficient delivery wire push force, in addition to an opposing microcatheter withdrawal force, to remove excess microcatheter slack while maintaining the microcatheter tip within the center of the parent vessel, will facilitate properly deploying the FRED System at the proper location,to achieve full expansion and good vessel apposition.
27. Caution: Using a rapid microcatheter withdrawal technique to deploy the FRED System is not recommended and may result in device elongation or improper deployment. Be aware of delivery wire tip position during deployment.
28. If the FRED System positioning is not satisfactory, the implant may be recaptured and repositioned if it is not fully deployed. The implant may be recaptured up to 75% of its deployed length.
29. Caution: If resistance is felt while recapturing the device, do not continue to recapture.Withdraw the microcatheter slightly to unsheath the device (without exceeding the recapture

limit), and then attempt to recapture again.

30. *Caution: The* FRED System *must not be re-deployed more than three times.*

31. If FRED System positioning is satisfactory, carefully advance the delivery wire while retracting the microcatheter as needed to minimize slack, maintaining the microcatheter around the center of the parent vessel, to allow the implant to deploy across the neck of the aneurysm. Ensure the implant proximal radiopaque end markers are in the advised position (see step 23) proximal to the aneurysm neck for adequate coverage.

32. Note: The FRED System will expand and may foreshorten up to 60% from its undeployed length. Visually verify opening of the proximal end, ensuring that the microcatheter distal tip marker is pulled back, adequately away from the implant proximal end, to allow the proximal end to freely open. Push forward on the delivery wire to assist in maintaining access within the implant as needed.

33. Note: Visualize and refer to implant radiopaque end markers to maintain adequate implant length on each side of the aneurysm neck/target location to ensure appropriate coverage.

34. Warning: Do not fully deploy the FRED System if positioning in the parent vessel is not satisfactory.

35. If necessary, to maintain access through the implanted device, advance the microcatheter distal to the implanted device. Remove and discard the delivery wire.

36. Caution: The FRED System delivery wire should not be utilized as a guidewire. Do not torque the FRED System. A torque device should not be used.

37. Carefully inspect the deployed FRED implant under fluoroscopy to confirm that it is completely open and opposed to the vessel wall and not kinked. If the implant is not fully open and apposed or is kinked, consider utilizing a suitable micro guidewire and/or occlusion balloon catheter to fully open the implant.

38. After completing the procedure, withdraw and discard all applicable accessory devices. *Caution: Carefully watch the FRED implant distal and proximal markers when passing through the implanted device with other devices to avoid displacing the implant.*

J. OVERVIEW OF CLINICAL STUDIES

1. Design

The study, titled *"Pivotal Study of the MicroVention, Inc. Flow Re-Direction Endoluminal Device System in the Treatment of Intracranial Aneurysms,"* was an open-label, multi-center, prospective, single-arm study with follow-up at hospital discharge, 30 days, 180 days and 12 months post procedure. There were 23 investigational sites, 22 in the US and 1 in Japan.

2. Inclusion and Exclusion Criteria

Enrollment in the FRED pivotal clinical study was limited to patients who met the following inclusion criteria.

- Subject whose age is ≥ 22 and ≤ 75 years.
- Subject had a single target aneurysm located in the:
  - Petrous through superior hypophyseal segments of the ICA
  - Communicating segment of the ICA through A1 or M1 segment
  - Posterior Circulation
    - Basilar artery (not including the basilar bifurcation)
    - Vertebral artery (distal to the posterior inferior cerebellar artery (PICA))
    - Vertebral artery (proximal to the PICA)

As well as any of the following criteria:

- Subject for whom existing endovascular options (coiling, stent-assisted coiling) would had been ineffective because the aneurysm was predisposed to recurrence due to having any of the following characteristics:
  - A. Aneurysm had a maximum fundus diameter less than 10 mm but ≥ 2mm.
    - a. To mitigate the risk for the treatment of subjects with small stable aneurysms that may not require treatment with respect to the possible risks and benefits associated with treatment, the treating clinician had to record a treatment justification (such as increased risk of rupture) for the aneurysms < 7 mm that were selected for treatment.
  - B. Aneurysm had any of the following morphologies:
    - a. No discernible neck
    - b. Segmental parent artery dysplasia
    - c. Aneurysm neck involving > 180 degrees of parent artery circumference
    - d. Complex lobulations limiting stent/coiling as a treatment option
    - e. Neck ≥ 4 mm or dome-to-neck ratio < 2

OR

Subject had a fusiform aneurysm of any size requiring treatment.

OR

Subject was a poor candidate for open surgical treatment because of prior surgical procedures, comorbidities or location limiting conventional surgical options.

Additionally, the subjects met the following criteria:

- The parent artery diameter was 2.0 – 5.0 mm distal/proximal to the target intracranial aneurysm;
- Subject fulfilled study requirements, and the subject or his/her Legally Authorized Representative provided a signed informed consent form;
- Negative pregnancy test (serum or urine) in a female subject who has had menses in the last 18 months;
- Subject committed to return to the investigational site for the 30-day, 180-day, and 12-month follow-up evaluations.

Patients were not permitted to enroll in the FRED X pivotal clinical study if they met any of the following exclusion criteria.

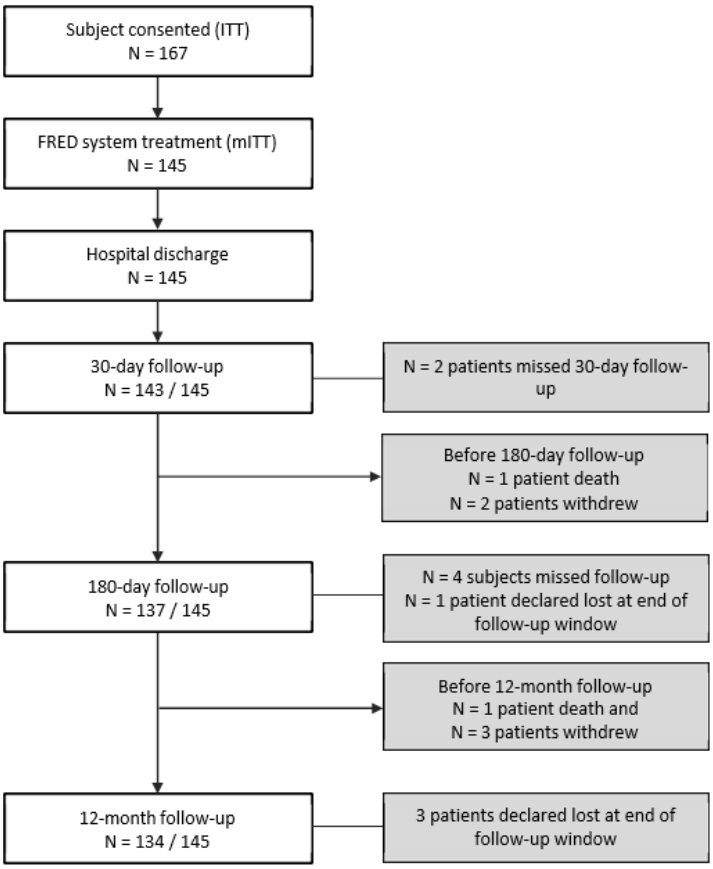
- Subject who suffered from a subarachnoid hemorrhage in the last 60 days;
- Subject who suffered from any intracranial hemorrhage in the last 30 days;
- Subject who presented with an intracranial mass or was currently undergoing radiation therapy for carcinoma or sarcoma of the head or neck region;
- Subject with symptomatic extracranial or intracranial stenosis of the parent artery (> 50%) proximal to the target intracranial aneurysm;
- Subject with an irreversible bleeding disorder, a platelet count of less than 100,000/ml;
- < 100 x10^3 cells/mm^3 or known platelet dysfunction or a contraindication to or inability to tolerate anticoagulants/antiplatelet agents;
- Active peptic ulcer disease, major systemic hemorrhage within 30 days, active bleedingdiathesis, platelet < 100,000 or known platelet dysfunction, INR ≥ 1.5, clotting factor abnormality, current alcohol or substance abuse, uncontrolled severe hypertension (systolic pressure >180 mmHg or diastolic pressure >115 mmHg), creatinine ≥ 3.0 mg/dL (unless on dialysis);

- Subject with contraindications or known allergies to anticoagulants or antiplatelet (aspirin, heparin, ticlopidine, clopidogrel, prasugrel or ticagrelor);
- Subject with known hypersensitivity to metal, such as nickel-titanium and metal jewelry;
- Subject with documented contrast allergy, or other condition, that prohibits imaging;
- Evidence of active infection at the time of treatment;
- Presence of any of the following unequivocal cardiac sources of embolism; chronic or paroxysmal atrial fibrillation, mitral stenosis, mechanical valve, endocarditis, intracardiac clot or vegetation, myocardial infarction within three months, dilated cardiomyopathy, left atrial spontaneous echo contrast, ejection fraction less than 30%;
- Subject who had a previous intracranial stenting procedure associated with the target aneurysm;
- Subject who was unable to complete the required follow-ups;
- Subject with life-threatening diseases;
- Subject who was pregnant or breastfeeding;
- Subject of childbearing potential and unwilling to prevent pregnancy during their participation in the study.

Angiographic Exclusion Criteria

- Subject had a cerebral diagnostic angiogram that demonstrated an aneurysm that was not appropriate for endovascular treatment;
- Subject had an extracranial stenosis greater than 50% in the carotid artery of the target aneurysm;
- Subject had an intracranial stenosis greater than 50% in the treated vessel;
- Subject had a mycotic or dissecting aneurysm;
- Subject had a bifurcation aneurysm for example at the bifurcation of the internal carotid artery, the middle cerebral artery or at the anterior communicating artery such that placement of the device would fail to satisfactorily cover the entire neck of the aneurysm or a major cerebral artery would be put at risk through “jailing”;
- Subject had a posterior circulation aneurysm with the following morphology:
- Placement of the device would include the basilar artery bifurcation
- Large or giant dolichoectatic aneurysm
- Subjects aneurysm had significant branch exiting from dome of aneurysm (for example,ophthalmic artery);
- Subject was harboring more than one aneurysm with both aneurysms requiringtreatment at the same time;
- Subject had an arteriovenous malformation (AVM) in the area of the target aneurysm.

3. Subject Accountability Flowchart



*Intent-to-Treat (ITT): All subjects who signed the informed consent document.

**Modified ITT (mITT): ITT subjects in whom treatment with the FRED System was attempted

4. Demographics

The demographic of the patient population in the FRED pivotal clinical study (see Table 2)reflects epidemiological prevalence of the disease in general population in respect to gender, race and age. The study primary endpoint analyses are based on the modified Intent-to-Treat (mITT) population of 145 patients who signed the informed consent form,met inclusion/exclusion criteria, and in which the device was attempted. Baseline IA characteristics are reported per the site evaluation. A total of 106 IAs (73.1%, 106/145) were considered large or giant with a

maximum dimension of 10 mm. Of the 145 mITTpatients, 8 patients had a previously ruptured IA and 137 patients had unruptured IAs.

Table 2: Demographic Characteristics

Characteristic	Mean ± SD N=145	[Median] (min, max)
Age (years)	59.1 ± 11.5	[60.1] (23.9,82.9)
Gender		
Female	129 (89.0%)	
Male	16 (11.0%)	
Ethnicity		
Hispanic or Latino	19 (13.1%)	
Not Hispanic or Latino	126 (86.9%)	
Race		
American Indian or Alaska Native	1 (0.7%)	
Asian	7 (4.8%)	
Black or African American	24 (16.6%)	
Other	9 (6.2%)	
White	104 (71.7%)	

Characteristic	Mean ± SD N=145	[Median] (min, max)
Systolic blood pressure (mm Hg)	131.5 ± 20.2	[130.0] (92.0,208.0)
Diastolic blood pressure (mm Hg)	75.8 ± 11.7	[76.0] (49.0,107.0)
Body temperature (degrees F)	97.8 ± 0.7 (N=129)	[97.9] (95.9,100.0)
Heart rate (beats per minute (BPM))	75.8 ± 13.7	[74.0] (49.0,123.0)

Table 3: Target Intracranial Aneurysm Location

Location	All N=145	Fusiform N=18 (12.4%)	Saccular N=127 (87.6%)
Anterior Circulation, n (%)	**139 (95.9%)**	**16**	**123**
Internal Carotid Artery (ICA)	135	15	120
Carotid Cavernous	41	10	31
Carotid Ophthalmic	50	2	48
Internal Carotid Artery (Supraclinoid)	10	2	8
Superior Hypophyseal	14	1	13
Communicating segment of the ICA	20	0	20
Anterior cerebral artery	2	1	1
Anterior communicating artery	2	0	2
Posterior Circulation, n (%)	**6 (4.1%)**	**2**	**4**
Basilar artery	2	0	2
Posterior inferior cerebellar	2	1	1
Vertebral artery	2	1	1

Table 4: Baseline Intracranial Aneurysm Characteristics

Characteristic	Mean ± SD (Range)
Dome height (mm)	11.5 ± 4.7 (3.7, 29.0)
Dome width (mm)	10.3 ± 4.9 (3.2, 27.4)
Neck width (mm)	6.4 ± 3.2 (3.5, 32.0)
Dome-to-neck ratio	1.7 ± 0.7 (0.5, 4.4)
Distal parent artery diameter (mm)	3.4 ± 0.6 (2.0, 7.9)
Proximal parent artery diameter (mm)	4.0 ± 0.7 (2.0, 7.5)
Mean parent artery diameter (mm)	3.7 ± 0.7 (2.0, 7.7)

K. SUMMARY OF ADVERSE EVENTS IN CLINICAL STUDY

The CEC reviewed and adjudicated all adverse events in the study. Table 5 present serious adverse events and non-serious adverse events that were observed through 12 months in the FRED pivotal clinical study for the mITT population as adjudicated by the CEC, respectively. No unanticipated adverse device effects (UADE) occurred during this trial. A summary of adverse events is shown below.

Table 5. Adverse Events with > 1% Overall Frequency Through 12 Months Post-Procedure by Medical Dictionary for Regulatory Activities (MedDRA) Codes – mITT Population (N=145)

MedDRA Classification		Serious Adverse Events	Non-Serious Adverse Events	All Adverse Events
System/Organ Class	**Preferred Term**	**% (n) [events]**	**% (n) [events]**	**% (n) [events]**
Blood and lymphatic system disorders	Anemia	0.7% (1) [1]	2.1% (3) [3]	2.8% (4) [4]
	Coagulopathy	0	1.4% (2) [2]	1.4% (2) [2]
Cardiac disorders	Arrhythmia	1.4% (2) [3]	2.1% (3) [3]	2.8% (4) [6]
Eye disorders	Visual impairment	1.4% (2) [2]	7.6% (11) [16]	9.0% (13) [18]
Gastrointestinal disorders	Diverticulum	0	1.4% (2) [2]	1 .4% (2) [2]
	Nausea	0	2.1% (3) [3]	2.1% (3) [3]
	Rectal hemorrhage	0	1.4% (2) [2]	1.4% (2) [2]
	Vomiting	0	1.4% (2) [2]	1.4% (2) [2]
General disorders and administration site conditions	Chest pain	0.7% (1) [1]	2.1% (3) [3]	2.8% (4) [4]
	Device dislocation	0.7% (1) [1]	0.7% (1) [1]	1.4%(2) [2]
	Device failure	4.1% (6) [6]	2.1% (3) [3]	6.2% (9) [9]
	Fatigue	0	2.1% (3) [3]	2.1% (3) [3]
	In-stent cerebral artery stenosis	0.7% (1) [1]	2.1% (3) [3]	2.8% (4) [4]

MedDRA Classification		Serious Adverse Events	Non-Serious Adverse Events	All Adverse Events
	Puncture site hemorrhage	0.7% (1) [1]	3.4% (5) [5]	4.1% (6) [6]
	Thrombosis in device	6.9% (10) [10]	0	6.9% (10) [10]
Infections and infestations	Cellulitis	0.7% (1) [1]	0.7% (1) [1]	1.4% (2) [2]
	Nasopharyngitis	0	1.4% (2) [3]	1.4% (2) [3]
	Pneumonia	1.4% (2) [2]	0	1.4% (2) [2]
	Tooth abscess	0	1.4% (2) [2]	1.4% (2) [2]
	Urinary tract infection	1.4% (2) [2]	6.2% (9) [9]	7.6% (11) [11]
Injury, poisoning and procedural complications	Contusion	0	2.8% (4) [4]	2.8% (4) [4]
	Endotracheal intubation complication	0	1.4% (2) [2]	1.4% (2) [2]
	Incision site hemorrhage	0	1.4% (2) [2]	1.4% (2) [2]
Musculoskeletal and connective tissue disorders	Arthralgia	0	2.1% (3) [3]	2.1% (3) [3]
	Back pain	0	1.4% (2) [2]	1.4% (2) [2]
	Muscular weakness	1.4% (2/145) [2]	0	1.4% (2/145)
	Neck pain	0	1.4% (2/145)	1.4% (2/145)
Nervous system disorders	Cerebral hemorrhage	2.1% (3) [3]	0	2.1% (3) [3]
	Cerebrovascular accident	4.1% (6) [6]	0	4.1% (6) [6]
	Cognitive disorder	0	1.4% (2) [2]	1.4% (2) [2]
	Diplopia	0	2.8% (4) [4]	2.8% (4) [4]
	Dizziness	0	2.1% (3) [3]	2.1% (3) [3]
	Eyelid ptosis	0.7% (1) [1]	0.7% (1) [1]	1.4% (2) [2]
	Headache	0.7% (1) [1]	29.7% (43) [45]	29.7% (43) [46]
	Ischemic stroke	2.8% (4) [4]	0	2.8% (4) [4]
	Sciatica	0	1.4% (2) [2]	1.4% (2) [2]
	Seizure	1.4% (2) [2]	0	1.4% (2) [2]
	Transient ischemic attack	3.4% (5) [5]	1.4% (2) [3]	4.8% (7) [8]
Psychiatric disorders	Depression	0.7% (1) [1]	1.4% (2) [2]	2.1% (3) [3]
Renal and urinary	Acute kidney injury	0.7% (1) [1]	0.7% (1) [1]	1.4% (2) [2]
Respiratory, thoracic and mediastinal disorders	Epistaxis	0	2.1% (3) [3]	2.1% (3) [3]
	Pulmonary embolism	1.4% (2) [2]	0	1.4% (2) [2]
Surgical and medical	Aneurysm repair	7.6% (11) [11]	0	7.6% (11) [11]
Vascular disorders	Carotid artery dissection	0	2.1% (3) [3]	2.1% (3) [3]
	Hematoma	0.7% (1) [1]	6.2% (9) [9]	6.9% (10) [10]
	Hypertension	0	2.1% (3) [3]	2.1% (3) [3]
	Vasospasm	0	11.0% (16) [17]	11.0% (16) [17]

L. CLINICAL STUDIES – SAFETY AND EFFECTIVENESS

1. Patient Analysis Population

The analysis of safety was based on the mITT cohort of 145 patients available for the 12- month evaluation. An additional post-hoc analysis of the primary safety and effectiveness endpoints was performed for only the subjects within the final indications for use with IAs treated within the ICA ["ICA population"] (N=135). The six (6) subjects treated with IAs in the posterior circulation of the neurovasculature and 4 subjects with IAs in the anterior circulation but not within the ICA were excluded from the mITT population resulting in the 135 subjects in the ICA population.

2. Safety Results

The primary safety endpoint, occurrence of death or major stroke within 30 days or neurologic death or major ipsilateral stroke within 12 months 1-year post-procedure occurred in 6.2% (9/145) and 5.9% (8/135) of subjects in the mITT and ICA populations, respectively. The mean of the posterior distribution of the primary safety endpoint at 12 months was 6.8% and 6.6% in the mITT and ICA populations, respectively, which was below the threshold of 15% safety PG; therefore, the primary safety endpoint of the study was met.

Table 6: Primary Safety Endpoint Events through 12 Months - mITT Population

Event	N=145 n (%)	Posterior Mean (95% CI)	Posterior Probability [3]
Pre-specified Primary Safety Endpoint [1]	9 (6.2%)	6.8% (3.3%, 11.3%)	0.999
Primary safety components [2]			
Major stroke within 30 days	6 (4.1%)	4.8% (1.9%, 8.7%)	
Death within 30 days	0 (0.0%)	0.7% (0.0%, 2.5%)	
Major ipsilateral stroke 31-425 days	3 (2.1%)	2.7% (0.7%, 5.8%)	
Neurological death 31-425 days	1 (0.7%)	1.4% (0.2%, 3.7%)	

[1] Pre-specified Primary Safety Endpoint defined as rate of death or major stroke within 30 days or neurologic death or major ipsilateral stroke within 12 months.

[2] Subject may have more than one failed safety component. One subject with stroke expired from neurological death. Also, one subject with a major stroke within 30 days, died at day 77 from a gastric hemorrhage (non-neurological death). All subjects with primary safety endpoint events were those with unruptured IAs treated with the FRED System. There were no primary safety endpoint events in the 8 subjects in the FRED study with a previously ruptured IA.

[3] Posterior probability that the primary safety endpoint event rate is <15%.

Table 7: Post-hoc Analysis of the Primary Safety Endpoint Events through 12 Months –ICA population

Event	N=135 n (%)	Posterior Mean (95% CI)	Posterior Probability [3]
Primary Safety Endpoint [1]	8 (5.9%)	6.6% (3.1%, 11.3%)	0.999
Primary safety components [2]			
Major stroke within 30 days	5 (3.7%)	4.4% (1.6%, 8.4%)	
Death within 30 days	0 (0.0%)	0.7% (0.0%, 2.7%)	
Major ipsilateral stroke 31-425 days	3 (2.2%)	2.9% (0.8%, 6.3%)	
Neurological death 31-425 days	1 (0.7%)	1.4% (0.2%, 4.0%)	

[1] Primary safety endpoint defined as rate of death or major stroke within 30 days or neurologic death or major ipsilateral stroke within 12 months.

[2] Subject may have more than one failed safety component. One subject with major ipsilateral stroke expired from neurological death. Also, one subject with a major stroke within 30 days, died at day 77 from a gastric hemorrhage (non-neurological death). All subjects with primary safety endpoint events were those with unruptured IAs treated with the FRED System. There were no primary safety endpoint events in the 8 subjects in the FRED study with a previously ruptured IA.

These analyses of the primary safety endpoint were not performed using the worst-case analysis accounting for all missing subjects as primary safety endpoint failures.

The incidence of all cerebrovascular events for patients with treated intracranial aneurysms located within the petrous segment to the terminus of the internal carotidartery (ICA population) is presented in Tables 8 and 9.

Table 8: Cerebrovascular Events (Death or Major/Minor Ischemic or Hemorrhagic Stroke) – ICA Population

Event	N=135 % (n/N)
Neurological Death	0.7% (1/135)
Major Stroke (ischemic or hemorrhagic)	5.9% (8/135) [1]
Minor Stroke (ischemic or hemorrhagic)	5.9% (8/135) [1]
Any of the above	10.4% (14/135) [2]

[1] Two subjects experienced both major and minor strokes.

[2] One subject experienced stroke and then neurological death. One subject experienced a major stroke within 30 days, died at day 77 from a gastric hemorrhage (non-neurological death).

Table 9: Cerebrovascular Events (Transient Ischemic Attack) – ICA Population

Event	N=135 % (n/N)
TIA (Transient Ischemic Attack)	5.2% (7/135)

3. Effectiveness Results

The primary effectiveness endpoint was analyzed in the ICA population in accordance withthe final indications for use. Key effectiveness outcome is presented in Table 10.

Table 10: Primary Effectiveness Endpoint Analysis through 12 Months – ICA Populationwith Imputed Data (N=135)

Endpoint	% [2]	Posterior Mean (95% CI)	Posterior Probability [1]
Primary effectiveness [3]	56.7%	56.6% (48.2%, 64.7%)	0.993

[1] Posterior probability that the primary effectiveness endpoint success rate is > 46%.

[2] Missing data at 12-months from subjects who died, withdrew from the study, lost-to-follow-up, unevaluable or missing imaging (n=14) were imputed per Firth's method of penalized logistic regression.

[3] Primary effectiveness endpoint was defined as the proportion of subjects with Raymond-Roy I IA occlusion with ≤ 50% parent artery stenosis and no re-treatment of the target IA within 12 months

In the ICA population, the primary effectiveness success rate was 56.7%. Using a worst- case analysis of the primary effectiveness endpoint without imputation for missing data subjects at 12-months follow-up, the primary effectiveness endpoint was 54.8% (74/135). The study met the pre-specified primary effectiveness criterion of ensuring that successful intracranial aneurysm treatment at 12-month follow up in the population of subjects withwide-necked intracranial aneurysms was achieved in > 46% of subjects.

Table 11 below shows the number of FRED stents implanted per subject. The majority of subjects (93.1%, 135/145) had a single device deployed.

Table 11: Number of FRED Stents Placed per Subject in FRED Clinical Study

Characteristic	Value
Devices per subject (total subjects = 145)	
Subjects with one device deployed	135 (93.1%)
Subjects with two devices deployed	9 (6.4%)
Subjects with three devices deployed	1 (0.7%)

M. CONCLUSION

The clinical study results support the reasonable assurance of safety and effectiveness of MicroVention FRED System when used in accordance with the indications for use. The benefits of the device outweigh probable risks when considering the clinically significant results of the pivotal data conducted in the intended population under its proposed condition of use

N. HOW SUPPLIED

Sterile: This device is sterilized with E-Beam irradiation.

Non-pyrogenic Contents: One (1) FRED system

Storage: Store product in a dry, cool place.

WARRANTY DISCLAIMER

MicroVention warrants that reasonable care has been used in the design and manufacture of this device. This warranty is in lieu of and excludes all other warranties not expressly set forth herein, whether expressed or implied by operation of law or otherwise, including, but not limited to, any implied warranties of merchantability or fitness for particular purpose. Handling, storage, cleaning, and sterilization of the device as well as factors relating to the patient, diagnosis, treatment, surgical procedure, and other matters beyond MicroVention's control directly affect the device and the results obtained from its use. MicroVention's obligation under this warranty is limited to the repair or replacement of this device through its expiration date. MicroVention shall not be liable for any incidental or consequential loss, damage or expense directly or indirectly arising from the use of thisdevice. MicroVention neither assumes, nor authorizes any other person to assume for it, any other or additional liability or responsibility in connection with this device. MicroVention assumes no liability with respect to devices reused, reprocessed or resterilized and makes no warranties, expressed or implied, including, but not limited to,merchantability or fitness for intended use, with respect to such device.

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SYMBOLS

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