Summary of Safety and Clinical Performance

for

MicroPlex™ Coil System (MCS)

HydroCoil™ Embolic System (HES)

SSCP22-0005

MicroVention, Inc.
35 Enterprise
Aliso Viejo, California 92656, USA

DOCUMENT CHANGE HISTORY

SSCP Revision	Change Description	NB approved/verified
A	Initial Release using the latest template	☒Yes ☐ No* Validation language: English

*Annual entries must be included. An entry stating such must be added if a revision is not required.

TABLE OF CONTENTS

1 SUMMARY OF SAFETY AND CLINICAL PERFORMANCE 4
1.1 Device Identification and General Information 4
1.2 Intended Purpose of the Device 5
1.3 Device Description 5
1.4 Risks and Warnings 6
1.4.1 Residual Risks and Undesirable Effects 6
1.4.2 Warnings and Precautions 7
1.4.3 Potential Complications / Adverse Effects 9
1.4.4 Other Aspects of Safety 9
1.5 Summary of the Clinical Evaluation and PMCF 10
1.5.1 Equivalent Device Clinical Data 10
1.5.2 Pre-CE-Mark Clinical Data 10
1.5.3 Clinical Data 10
1.5.4 Clinical Performance and Safety 11
1.5.5 Post-Market Clinical Follow-up 13
1.6 Possible Diagnostic or Therapeutic Alternatives 15
1.6.1 Treatment Options and Interventions 15
1.6.2 Available Technologies 16
1.7 Suggested Profile and Training for Users 17
1.8 Reference to any Harmonized Standards and CS 17
1.9 References 20

LIST OF TABLES

Table 1.1 Device Identification and General Information 4
Table 1.2 Intended Use 5
Table 1.3 Device Description 5
Table 1.7 Treatment Options Benefits/Risks 15
Table 1.8 Similar Devices 16
Table 1.9 Harmonized Standards 17

1 SUMMARY OF SAFETY AND CLINICAL PERFORMANCE

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 device.

The SSCP is not intended to replace the Instructions For Use (IFU) 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.

The following information is intended for users/healthcare professionals.

1.1 Device Identification and General Information

Table 1.1 Device Identification and General Information

Device Names	
Device Trade Name	MicroPlex Coil System (MCS) HydroCoil Embolic System (HES)
EMDN Code	MCS and HES: C010402020301
Medical Device Nomenclature (EMDN)	EMBOLIZATION COILS
Device Class	MCS and HES: III (Implantable)
Basic UDI-DI	MCS: 08402732MCSSW HES: 08402732HESSB
Year when the first certificate (CE) was issued for the device (by DQS)	2008
Legal Manufacturer	
Name & Address	**MicroVention, Inc. (referred to as MVI)** 35 Enterprise Aliso Viejo, California 92656, USA
Manufacturer SRN	US-MF-000016658
Authorized Representative	
Name & Address	**MicroVention Europe SARL (referred to as MVE)** 30 bis, rue du Vieil Abreuvoir 78100 Saint-Germain-en-Laye, France
Authorized Representative SRN	FR-AR-000004448
Notified Body	
Name & Address	DQS Medizinprodukte GmbH August-Schanz-Straße 21 D-60433 Frankfurt am Main Germany
Notified Body Identification Number	0297

1.2 Intended Purpose of the Device

Table 1.2 Intended Use

Intended Purpose	
Intended Purpose	The MicroPlex Coil System (MCS) is intended for the endovascular embolization of intracranial aneurysms and other neurovascular abnormalities such as arteriovenous malformations and arteriovenous fistulae. The MCS is also intended for vascular occlusion of blood vessels within the neurovascular system to permanently obstruct blood flow to an aneurysm or other vascular malformation and for arterial and venous embolizations in the peripheral vasculature. The HydroCoil Embolic System (HES) is intended for the endovascular embolization of intracranial aneurysms and other neurovascular abnormalities such as arteriovenous malformations and arteriovenous fistulae. The HES is also intended for vascular occlusion of blood vessels within the neurovascular system to permanently obstruct blood flow to an aneurysm or other vascular malformation and for arterial and venous embolizations in the peripheral vasculature.
Indications for Use	The MicroPlex Coil System (MCS) is intended for the endovascular embolization of intracranial aneurysms and other neurovascular abnormalities such as arteriovenous malformations and arteriovenous fistulae. The MCS is also intended for vascular occlusion of blood vessels within the neurovascular system to permanently obstruct blood flow to an aneurysm or other vascular malformation and for arterial and venous embolizations in the peripheral vasculature. The HydroCoil Embolic System (HES) is intended for the endovascular embolization of intracranial aneurysms and other neurovascular abnormalities such as arteriovenous malformations and arteriovenous fistulae. The HES is also intended for vascular occlusion of blood vessels within the neurovascular system to permanently obstruct blood flow to an aneurysm or other vascular malformation and for arterial and venous embolizations in the peripheral vasculature.
Target Population	The MCS and HES are intended for patients requiring permanent occlusion of the blood flow to an aneurysm or other neurovascular malformations/lesions such as arteriovenous malformation (AVM) or arteriovenous fistula (AVF) in the neurovascular structure.
Contraindications and/or Limitations	None

1.3 Device Description

Table 1.3 Device Description

Device Description	
Description of the Device	The MCS and HES devices consist of an implantable coil attached to a V-Trak™ delivery pusher via a polyolefin elastomer material. The MCS implantable coil is made of bare platinum alloy (Platinum/Tungsten) and the HES implantable coil is made of the same platinum alloy with a hydrogel inner core. The MCS and HES products are available with implantable coils of various coil shapes (helical or complex) and sizes. The V-Grip Detachment Controllers are designed to detach compatible endovascular embolization coils into the peripheral vasculature and/or neurovasculature. The Detachment Controllers are powered by 9V batteries. The device design of the subject devices in each power source category is identical except for the color and logo on the external plastic housings.
Design Characteristics of the Device	The endovascular coiling of neurovascular aneurysms using the MCS or HES products is performed under angiography. The MCS-HES implantable coil is delivered to the aneurysm treatment site via on the Delivery Pusher through standard neuro-interventional micro-catheters. Since the coils are attached to the delivery

	pusher and only detached when the V-Grip Detachment Controller is activated, the coil can be repositioned by the treating physician similar to those made by the Target Therapeutics division of Boston Scientific Corporation and the Cordis division of Johnson and Johnson. Detachment of the MCS and HES from the delivery pusher is performed by means of positive displacement. Manual pressure is applied at the proximal luer port of the delivery pusher using a 1cc or smaller syringe containing radiographic contrast media. This pressure is transmitted through the lumen of the delivery pusher to its distal tip. The high viscosity of the contrast media slows the flow of fluid out of the vent hole and allows pressure to build within the delivery pusher. This pressure detaches the coil from the delivery pusher. Following deployment, the hydrophilic nature of the polymer layer results in an expansion of the primary coil diameter, thereby increasing the physical occlusion potential of the coil. Multiple coils are delivered to the treatment site until the flow of blood into the aneurysm, AVM, or AVF is blocked. Over time, new tissue will cover the opening of the aneurysm, preventing the aneurysm from growing or rupturing. The MCS and HES do not incorporate a medicinal substance, animal tissues, or blood products.
Previous Generations or Variants, if applicable	With the exception of the extension of available coil sizes, all currently available MCS and HES products are identical in design, intended use, principle of operation, packaging, and sterilization method and have not changed during the commercialization of the devices in the EU.
Single use – sterilization method	The MCS and HES coils are packaged and sold sterile, for single use and single patient only. Sterilization method: Electron Beam Radiation
Description of Accessories	The V-Grip Detachment Controller is an integral accessory for use with the MCS and HES products. The Detachment Controller is a self-contained, disposable, hand-held, battery-powered unit that provides the controlled electrical energy for the detachment of the coil from the Delivery Pusher. The detachment controller is packaged and sold separately as a sterile device for a single patient only.
Description of other Devices or Products intended to be used in combination	There is no other device or product intended to be used in combination other than V-Grip Detachment Controller, which is an accessory device to the MCS and HES.

1.4 Risks and Warnings

1.4.1 Residual Risks and Undesirable Effects

Hazards associated with the use of the MCS and HES are assessed, and risks of the resulting harm are minimized through the use of risk mitigation/control measures. All known foreseeable risks have been evaluated and mitigated.

Risks associated with the subject device include the following:

- Accessory product is damaged, and a portion remains in the body
- Aneurysm Rupture during and following deployment
- Biological hazard
- Coil and delivery pusher will not load into the microcatheter
- Coil and delivery pusher will not track to the lesion
- Coil damage during removal
- Coil deploys incorrectly
- Coils pulled into the parent vessel
- Coil will not deploy
- Emboli generated during coil deployment
- Energy hazard

- Environmental hazard
- Excessive microcatheter movement
- Foreign body embolism
- Implant migrates outside of aneurysm into the parent vessel
- Implant migrates outside of aneurysm into the parent vessel Implant
- Improper Use
- Inability to detach product
- Inability to introduce the product into microcatheter
- Inadequate visibility under fluoroscopy
- Inappropriate Therapy selected (Inadvertent)
- Inappropriate Therapy selected (Off Label)
- Incompatibility with accessories
- Loss of microcatheter access to aneurysm
- Partial detachment of implant from pusher
- Premature implant detachment after introduction
- Premature implant detachment during preparation
- Product becomes contaminated due to the manufacturing environment
- Product becomes contaminated during shipping, distribution, or storage
- Product becomes contaminated during use
- Product separates and a portion remains in the body
- Product is re-used
- Stretch-resistant member breaks
- Subsequent coils unable or difficult to place
- Thromboembolic embolism
- Traumatic tip, etc.
- Vasospasm due to vessel wall irritation

1.4.2 Warnings and Precautions

The warnings/precautions for the MCS and HES are:

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

- The MCS/HES is sterile and non-pyrogenic unless the unit package is opened or damaged.
- The MCS/HES is intended for single use only. Do not resterilize and/or reuse the device. After use, dispose in accordance with hospital, administrative, and/or local government policy. Do not use it if the packaging is breached or damaged.
- The MCS/HES must be delivered only through a wire-reinforced microcatheter with a PTFE inner surface coating. Damage to the device may occur and necessitate removal of both the MCS/HES and microcatheter from the patient.

- High quality, digital subtraction fluoroscopic road mapping is mandatory to achieve correct placement of the MCS/HES.
- Do not advance the V-Trak delivery pusher with excessive force. Determine the cause of any unusual resistance, remove the MCS/HES, and check for damage.
- Advance and retract the MCS/HES device slowly and smoothly. Remove the entire MCS/HES if excessive friction is noted. If excessive friction is noted with a second MCS/HES, check the microcatheter for damage or kinking.
- If repositioning is necessary, take special care to retract the coil under fluoroscopy in a one-to-one motion with the V-Trak delivery pusher. If the coil does not move in a one-to-one motion with the V-Trak delivery pusher, or if repositioning is difficult, the coil may have become stretched and could possibly break. Gently remove and discard the entire device.
- Due to the delicate nature of the MCS/HES coils, the tortuous vascular pathways that lead to certain aneurysms and vessels, and the varying morphologies of intracranial aneurysms, a coil may occasionally stretch while being maneuvered. Stretching is a precursor to potential coil breaking and migration.
- If a coil must be retrieved from the vasculature after detachment, do not attempt to withdraw the coil with a retrieval device, such as a snare, into the delivery catheter. This could damage the coil and result in device separation. Remove the coil, microcatheter, and any retrieval device from the vasculature simultaneously.
- If resistance is encountered while withdrawing a coil that is at an acute angle relative to the microcatheter tip, it is possible to avoid coil stretching or breaking by carefully repositioning the distal tip of the catheter at, or slightly inside, the ostium of the aneurysm. By doing so, the aneurysm and artery act to funnel the coil back into the microcatheter.
- Delivery of multiple MCS/HES coils is usually required to achieve the desired occlusion of some aneurysms or lesions. The desired procedural endpoint is angiographic occlusion.
- The long-term effect of this product on extravascular tissues has not been established so care should be taken to retain this device in the intravascular space.
- Always ensure that at least two MicroVention V-Grip detachment controllers are available before starting an MCS/HES procedure.
- The MCS/HES cannot be detached with any power source other than a MicroVention V-Grip detachment controller.
- Always advance an appropriately sized guidewire through the microcatheter after detaching the coil and removing the pusher to ensure that no part of the coil remains within the microcatheter.

- Do NOT place the V-Trak delivery pusher on a bare metallic surface.
- Always handle the V-Trak delivery pusher with surgical gloves.
- Do NOT use in conjunction with radio frequency (RF) devices.
- No modification of this equipment is allowed.

1.4.3 Potential Complications / Adverse Effects

The potential complications / adverse effects for the MCS and HES are:

- Hematoma at the site of entry
- Vessel perforation
- Aneurysm rupture
- Parent artery occlusion
- Incomplete aneurysm filling
- Emboli
- Hemorrhage
- Ischemia
- Vasospasm
- Coil migration or misplacement
- Premature or difficult coil detachment
- Clot formation
- Revascularization
- Post-embolization syndrome
- Neurological deficits including stroke and possibly death

Cases of chemical aseptic meningitis, edema, hydrocephalus, and/or headaches have been associated with the use of embolization coils in the treatment of large and giant aneurysms. The physician should be aware of these complications and instruct patients when indicated. Appropriate patient management should be considered.

1.4.4 Other Aspects of Safety

Of the 1,545 complaints received by MicroVention for the evaluation period of 01 October 2021 to 30 September 2022 regarding the MCS and HES, 97 complaints were deemed reportable to EU authorities resulting in a reportable complaint rate of 0.056%. There was one death reported during the PMS review period. It was reported that during treatment of a ruptured right distal vertebral artery aneurysm, the aneurysm re-ruptured during placement of an embolization coil implant.

No field actions or recalls were initiated by MicroVention for the MCS and HES from 01 October 2021 to 30 September 2022.

1.5 Summary of the Clinical Evaluation and PMCF

1.5.1 Equivalent Device Clinical Data

Equivalency is not claimed in the clinical evaluation for the MCS and HES.

1.5.2 Pre-CE-Mark Clinical Data

There is no Clinical Development Plan for the HES/MCS Coils because they were approved for CE Mark under the MDD and no premarket clinical studies were required for market approval. HES and MCS are considered equivalent devices to one another and there is sufficient clinical data to support safety and performance for their intended.

1.5.3 Clinical Data

Clinical evidence was identified, collected, and appraised from a variety of trusted sources including post-market studies and registries (both manufacturer-sponsored, and investigator-sponsored studies), published peer-reviewed literature, and the company's post-market surveillance data.

There are 15 completed post-market clinical studies and registries identified that are directly sponsored or funded by research grants from MicroVention, including a total of 2,817 patients using the HES for endovascular embolization of intracranial aneurysms; of these studies, the clinical data for 13 studies are available for analysis including 2,087 patients. While the HYBRID study and the COAST study are completed, the data from both studies are pending, and they will be provided once the studies are published. There is also one ongoing post-market observational study, which is the RAGE study, including 1000 enrollments; this is a MicroVention-sponsored study, which is in the 18-month follow-up phase. Any update is anticipated after September 2024. Of the 2,087 patients identified from the available completed post-market clinical studies data, some of these patients were also identified from the peer-reviewed published literature by systematic literature search and review.

The literature search detailed in this report presents relevant clinical data from the scientific literature for the MCS and HES. There were 3 additional references added for the 2023 Update in addition to 18 references included from the previous CER (CER20-0003E). A total of 21 published literature including 4 randomized controlled trials, 5 case series, 8 cohort studies, and 4 case-control studies for the MCS and HES were included; the included published literature identified 3,833 patients with the use of subject devices. The literature search results demonstrate clinical use of the MCS and HES for endovascular embolization of intracranial aneurysms, arteriovenous fistulae (AVF) as well as for occlusion of the gastroduodenal artery using radioembolization procedure in all studies with 3,833 patients.

Post-market surveillance data show the use of MCS and HES in 170,466 cases from 01 October 2021 through 31 September 2022 with 1 report of complaint that resulted in patient death due to complications from hemorrhage; MicroVention received 114 product complaints concerning the MCS and HES, resulting in a complaint rate of 0.07%. Of these complaints, 97 were considered

reportable to EU authorities for a reportable complaint rate of 0.056%. Clinical risks of the use of the MCS and HES are consistent with the SOTA for embolization coils, showing low rates of adverse events and low rates of complaints failure across several published studies with a large cumulative patient population and substantial post-market surveillance data.

1.5.4 Clinical Performance and Safety

Clinical Benefits (Performance)

Coil Embolization using the MicroVention MCS or HES systems is a highly effective interventional modality used in both neuro or peripheral vasculature for patients with various intracranial and peripheral aneurysm, vascular lesions or abnormalities to prevent aneurysm rupture, control bleeding, or use in conjunction with radioembolization. Coil embolization with the MCS or HES in general is much less invasive than open surgery, and it is part of the standard of care in managing various neuro and peripheral complex diseases (e.g.: intracranial aneurysm, cerebral AVM, dAVF, or various peripheral visceral artery aneurysm).

Placing the MCS or HES system in neuro or peripheral vasculature into an aneurysm or a blood vessel can block blood flow to an area of the body or prevent rupture or hemorrhage. It may be used in patients with various neuro or peripheral aneurysms or vascular lesions or abnormalities, to control or prevent abnormal bleeding, close off vessels supplying blood to a tumor, eliminate abnormal connections between arteries and veins, or treat aneurysms.

Clinical data on clinical benefits for the MCS and/or HES reported in the published literature include:

*The data also includes published data from the post-market clinical studies

- 93.3%-98.6% technical success (success of the procedure or coil detachment)[2, 5, 9, 25]
- 100%% successful rate of cure within 6 months[14]
- 16%-84% immediate complete occlusion[2, 4, 6-10, 12, 17, 20, 22, 24]
- 42.6%-100% immediate complete or near complete occlusion[4, 6, 7, 12, 17, 20, 22, 24]
- 91.3% complete occlusion during first 30 minutes of gastroduodenal artery (GDA)[15]
- 53%-90.9% complete occlusion at follow-up (6 months-60 months)[3, 5, 7, 8, 10-13, 17, 24]
- 61.1%-100% complete or near complete occlusion at follow-up (6 months-60 months)[5, 7, 11-13, 17, 24]
- 76.8%-96.7% good clinical outcome (mRS 0-2) at follow-up (6 months-47.9 months)[7, 11, 24]

Clinical data on clinical benefits for the MCS and/or HES reported in the post-market clinical studies include (unpublished data):

- 75% immediate complete occlusion
- 92.5% immediate complete or near complete occlusion
- 90.5% good clinical outcome (mRS 0-2) at follow-up (18 months)

Clinical Risks (Safety)

The harms identified through risk management were compared with the adverse events identified in the clinical evaluation in the published literature as well as post-market clinical studies and the manufacturer's post-market surveillance data. No new harms were identified in this clinical evaluation and all identified harms are included in the risk documentation. Harms are appropriately described within the MCS and HES IFUs. In comparison, the safety outcomes reported in the literature of the MCS and HES were consistent with similar devices in most parameters.

Clinical data on adverse events for the MCS and/or HES reported in the published literature include:

*The data also includes published data from the post-market clinical studies

- Recurrence in 4.4%-21.5% of patients[3, 8, 10, 16, 23]
- Recanalization in 4.1%-23.6% of patients[4, 5, 12, 13, 22]
- Retreatment in 0.8%-13.7% of patients[3, 5, 10-12, 16, 18, 23, 24]
- Aneurysm rupture in 0.2%-4.0% of patients[5, 24]
- Hydrocephalus in 1.6%-17.1% of patients[4, 10, 13]
- Perforation in 1.0%-4.0% of patients[4-6, 10]
- Parent artery occlusion in 0.9%-1.6% of patients[4, 5, 25]
- Hematoma in 1.0%-3.6% of patients[4, 10, 25]
- Dissection in 0.7%-1.6% of patients[5, 11]
- Vasospasm in 5.0%-9.7% of patients[5, 11]
- Neurologic complications in 2.1%-14.9% of patients[6, 8, 10, 25]
- Subarachnoid hemorrhage (SAH) in 2.2%-10.0% of patients[2, 3, 5, 7, 8, 10]
- Stroke in 1.6%-3.7% of patients[12, 23]
- Transient ischemic attack (TIA) in 1.6% of patients[8]
- Thromboembolic complications in 1.6%-8.7% of patients[4-6, 8-11, 20, 24, 25]
- Procedure-related complications in 3.8%-17.1% of patients[3, 7-9, 11, 13, 23]
- Device-related complications in 1.0%-6.0% of patients[2, 4, 9, 10, 25]
    - Device-related aneurysm sac rupture in 4% of patients[9]
    - Device-related thromboembolic events in 5% of patients[9]
    - Device-related detachment problems in 2% of patients[9]
    - Device-related in irretrievable coil catheter unit in 1% of patients[9]
    - Vision Change in 1.6% of patients[10]
    - Coil protrusion in 1.0%-3.3% of patients[2, 4]
    - Coil migration in 6.0% of patients[25]
- Morbidity in 0.5%-6.4% of patients[4, 5, 9, 10, 23]
- Death in 0.7%-10.0% of patients[2, 3, 5, 7-11, 18, 23-25]

Clinical data on adverse events for the MCS and/or HES reported in the post-market clinical studies include (unpublished data):

- Recanalization in 9% of patients
- Recurrence in 27.9% of patients
- Retreatment in 11.6% of patients
- Hydrocephalus in 17.1% of patients
- Hematoma in 0.5% of patients
- Thromboembolism in 2.6% of patients
- Device-related complications in 2.3% of patients
    - Initial treatment failure in 2.3% of patients
- Retreatment-related complications in 2.3% of patients
- SAH in 0.9% of patients
- Stroke in 0.9% of patients
- TIA in 0.5% of patients
- Serious adverse events (SAE) in 6.3% of patients
- Morbidity in 17.1% of patients
- Mortality in 5.9% of patients

The manufacturer's post-market surveillance (PMS) data show the use of the MCS and HES in 170,466 cases from 01 October 2021 through 30 September 2022 with 1 report of complaint that resulted in patient death; MicroVention received 1,545 product complaints concerning the MCS and HES, resulting in a complaint rate of 0.0091%. Of these complaints, 97 were considered reportable to EU authorities for a reportable complaint rate of 0.056%. Clinical risks of the use of the MCS and HES are consistent with the SOTA for embolization coils, showing low rates of adverse events and low rates of complaints failure across several published studies with a large cumulative patient population and substantial PMS data.

1.5.5 Post-Market Clinical Follow-up

Post-Market Clinical Follow-up (PMCF) activities outlined in the latest PMCFP:

1. RAGE (Ruptured Aneurysms Treated with Hydrogel Coils)
    - Description of the activity
        - RAGE is an ongoing prospective, non-randomized, multicenter, post-market study sponsored by MicroVention. The RAGE study is designed to determine the safety and occlusion rates of hydrogel coils in the ruptured aneurysm study population. Secondary objectives include determining clinical outcomes, packing density, occlusion stability, rates of recurrence, rebleed, retreatment, and adverse events.
    - Timeline of the activity
        - Study Start: 11/27/2017 (Actual)
        - Primary Completion Date: 2025-06 (Estimated)

- Completion Date: 2025-12 (Estimated)
- As of November 2023, the recruitment is completed, and the study is in an ongoing 18-month follow-up phase

2. HYBRID (Hydrogel Coil Versus Bare Platinum Coil in Recanalization Imaging Data Study)
    - Description of the activity
        - The HYBRID is a prospective randomized open label controlled multi-center trial sponsored by an investigator initiator to compare Hydrocoil and bare platinum coil for recanalization after endovascular treatment of intracranial aneurysms.
    - Timeline of the activity
        - Study Start: 2012-06 (Actual)
        - Primary Completion Date: 2018-03 (Actual)
        - Completion Date: 2019-06 (Actual)
        - As of November 2023, the study is completed, with pending clinical data. There is no publication available yet.
3. COAST (Coiling of Aneurysms Smaller Than 5mm With Hypersoft and Hydrogel Coils**)**
    - Description of the activity
        - The COAST is a prospective, single-arm, multi-center post-marketing Study sponsored by an investigator initiator. The Study will commence as a single phase, with an optional second phase to follow at the discretion of the sponsor. Up to 300 eligible Subjects with small (< 4.9 mm) intracranial aneurysms, who consent to Study participation, will be treated in Phase 1 with MicroVention HyperSoft 3D and HyperSoft Helical coils with or without balloon remodeling or stent assistance at the discretion of the treating physician.
    - Timeline of the activity
        - Study Start: 2014-07 (Actual)
        - Primary Completion Date: 2021-01-25 (Actual)
        - Completion Date: 2021-01-25 (Actual)
        - As of November 2023, the study is completed, with pending clinical data. There is no publication available yet.

1.6 Possible Diagnostic or Therapeutic Alternatives

Treatment of an unruptured aneurysm attempts to prevent the aneurysm from rupturing. The treatment of a ruptured intracranial aneurysm aims to prevent further hemorrhage. Small, asymptomatic aneurysms less than 10 mm in diameter may be monitored without any intervention other than treatment for underlying risk factors such as hypertension[1]. The current treatment of unruptured aneurysms involves microsurgical clip ligation or endovascular embolization[19, 21].

Over the past decade, endovascular treatment of intracranial aneurysms (IAs) with stent-assisted coiling (SAC) has been widely accepted as well. The increasing SAC studies reported the good clinical outcomes of the SAC technique; stent deployment serves as a scaffold to prevent coil prolapse, which preserves the parent vessel and promotes thrombosis in the aneurysm. The primarily used intracranial stents include Laser-cut (i.e.: Neuroform from Stryker, Enterprise from Codman, Solitaire from Medtronic) and braided (i.e.: LVIS/LVIS Jr/LVIS EVO from MicroVention, LEO Baby from Balt) stents; a systematic review of SAC of IAs, including a total of 4,373 patients concluded that laser-cut or braided stents mediated SAC was effective and safe. Rates of thromboembolic events, stent stenosis, mortality, and recanalization were comparable between the stent types. Braided stents were associated with lower permanent morbidity while laser-cut stents were associated with more favorable rates of successful deployment and periprocedural intracranial hemorrhage[26].

In addition to MCS and HES, there are similar embolization coils that are well-established medical devices with numerous types and styles available from a variety of manufacturers. A few examples of the embolization coils similar to the subject devices are listed in **Table 1.4** below.

1.6.1 Treatment Options and Interventions

A) For intracranial aneurysms

- Microsurgical clip ligation
- Endovascular embolization
- Stent-assisted coiling (SAC)

B) For peripheral vascular diseases and abnormalities

- Peripheral intervention – open surgery & endovascular therapy

Table 1.4 Treatment Options Benefits/Risks

Treatment Option	Pro/Benefit	Con/Risks
Microsurgical clip ligation	• Clipping is associated with a higher rate of occlusion of the aneurysm and lower rates of residual and recurrent aneurysms.	• For a ruptured intracranial aneurysm with subarachnoid hemorrhage, surgical clipping is not considered the first choice due to the risk. • Open surgical clipping, involving craniotomy and placement of a clip across the neck of the aneurysm, is

		associated with surgical risks and neurological deficits.
Endovascular embolization with coils	• Coil embolization is widely used to treat all aneurysms as the first choice of treatment. • Endovascular coiling is less invasive than surgical clipping, especially in posterior circulation intracranial aneurysms, and is also associated with better clinical outcomes (lower morbidity and mortality). • Endovascular techniques trend toward improved patient outcomes compared to surgical strategies in some studies.	• There are risks associated with this technique such as: o Rerupture of the aneurysm o Recurrence of the aneurysm o Hemorrhagic complications
Stent-assisted coiling (SAC)	• Widely accepted treatment options over the past decade with good clinical outcomes reported with this technique. • Stent deployment prevents coil prolapse, which helps with thrombosis in the aneurysm by preserving the parent vessel.	• Potential complications associated with stent exist such as: o Ischemic complications o Hemorrhagic complications o Intraprocedural rupture
Peripheral intervention	• In peripheral intervention, both open surgery and endovascular therapy are the treatments of choice for many vascular abnormalities and diseases.	• Potential complications associated with stent exist such as: o Dissections o Vessel occlusions o Perforations

1.6.2 Available Technologies

Embolization coils, such as those listed within the MCS and HES, are well-established medical devices with numerous types and styles available from a variety of manufacturers. A few examples of the embolization coils similar to the subject devices are listed in **Table 1.5**.

Table 1.5 Similar Devices

Device	Manufacturer	Intended Purpose
Axium Detachable Coil	Medtronic	AXIUM™ Detachable Coils are intended for the endovascular embolization of intracranial aneurysms. AXIUM™ Detachable Coils are also intended for the embolization of other neurovascular abnormalities such as arteriovenous malformations and arteriovenous fistulae.
Target Detachable Coil	Stryker	Target Detachable Coils are intended to endovascularly obstruct or occlude blood flow in vascular abnormalities of the neurovascular and peripheral vessels. Target Detachable Coils are indicated for endovascular embolization of: • Intracranial aneurysms • Other neurovascular abnormalities such as arteriovenous malformations and arteriovenous fistulae • Arterial and venous embolization in the peripheral vasculature
MICRUSFRAME, DELTAFILL,	Cerenovus	MICRUSFRAME, DELTAFILL, DELTAXSFT, and GALAXY G3 Microcoil Delivery Systems are intended for endovascular

DELTAXSFT, and GALAXY G3 Microcoil Delivery Systems		embolization of intracranial aneurysms, other neurovascular abnormalities such as arteriovenous malformations and arteriovenous fistulae, and are also intended for arterial and venous embolizations in the peripheral vasculature.

1.7 Suggested Profile and Training for Users

The procedure should be performed by physicians who have undergone training in the use of the MCS and HES devices for neurovascular or peripheral embolization procedures.

1.8 Reference to any Harmonized Standards and CS

The MCS and HES were designed, developed, and tested following the standards and guidance documents listed in **Table 1.6.**

Table 1.6 Harmonized Standards

Common specification(s) to comply with (if applicable): N/A		
Harmonized standard(s) to comply with:		
Standards	**Edition**	**Title**
Quality System		
EN ISO 13485	2016/A11:2021	Medical devices - Quality management systems - Requirements for regulatory purposes (ISO 13485:2016)
Risk Management		
EN ISO 14971	2019/A11:2021	Medical devices - Application of risk management to medical devices (ISO 14971:2019)
EN IEC 60812	2018	Failure modes and effects analysis (FMEA and FMECA) (IEC 60812:2018)
Usability		
EN ISO IEC 62366-1	2015/A1:2020	Medical devices – Part 1: Application of usability engineering to medical devices (IEC 62366- 1:2015/A1:2020)
Clinical - N/A		
Post Market Surveillance		
ISO/TR 20416	2020	Medical Devices-Post Market Surveillance for Manufacturers
Labeling		
EN ISO 15223-1	2021	Medical devices - Symbols to be used with medical device labels, labelling and information to be supplied by the manufacturer - Part 1: General requirements (ISO 15223-1:2021)
EN ISO 20417	2021	Medical devices - Information to be supplied by the manufacturer of medical devices (ISO 20417:2021, Corrected version 2021-12)
Packaging		
EN ISO 11607-1	2020/A11:2022	Packaging for Terminally Sterilized Medical Devices - Part 1: Requirements for Material, Sterile Barrier Systems and Packaging Systems (ISO 11607-1:2019)
EN ISO 11607-2	2020/A11:2022	Packaging for terminally sterilized medical devices - Part 2: Validation requirements for forming, sealing and assembly processes (ISO 11607-2:2019)
ISTA 3A	2018	ISTA (International Safe Transit Association) Procedure 3A – Performance Tests for Packaged-Products for Parcel Delivery System 150 lbs. (70 kg) or Less
ASTM D4169	2023e1	Standard Practice for Performance Testing of Shipping Containers and Systems
ASTM F88	2023	Standard Test Method for Seal Strength of Flexible Barrier Materials

Common specification(s) to comply with (if applicable): N/A		
Harmonized standard(s) to comply with:		
Standards	**Edition**	**Title**
ASTM F1886	2016	Standard Test Method for Determining Integrity of Seals for Flexible Packaging by Visual Inspection
ASTM F1929	2023	Standard Test Method for Detecting Seal Leaks in Porous Medical Packaging by Dye Penetration
ASTM F2096	2011R2019	Standard Test Method for Detecting Gross Leaks in Packaging by Internal Pressurization (Bubble Test)
Shelf Life & /Stability		
ASTM F1980	2016	Standard Guide for Accelerated Aging of Sterile Barrier Systems and for Medical Devices
Biocompatibility		
EN ISO 10993-1	2020	Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process (ISO 10993-1:2018, including corrected version 2018-10)
EN ISO 10993-3	2014	Biological evaluation of medical devices - Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity (ISO 10993-3:2014)
EN ISO 10993-4	2017	Biological evaluation of medical devices - Part 4: Selection of tests for interactions with blood (ISO 10993-4:2017)
EN ISO 10993-5	2009	Biological evaluation of medical devices - Part 5: Tests for in vitro cytotoxicity (ISO 10993-5:2009)
EN ISO 10993-6	2016	Biological evaluation of medical devices - Part 6: Tests for local effects after implantation (ISO 10993-6:2016)
EN ISO 10993-10	2023	Biological evaluation of medical devices - Part 10: Tests for irritation and skin sensitization (ISO 10993- 10:2021)
EN ISO 10993-11	2018	Biological evaluation of medical devices - Part 11: Tests for systemic toxicity (ISO 10993- 11:2017)
EN ISO 10993-12	2021	Biological evaluation of medical devices - Part 12: Sample preparation and reference materials (ISO 10993-12:2021
EN ISO 10993-23	2021	Biological evaluation of medical devices - Part 23: Tests for irritation (ISO 10993-23:2021)
Manufacturing (Environmental Controls)		
EN ISO 14644-1	2015	Cleanrooms and associated controlled environments - Part 1: Classification of air cleanliness by particle concentration (ISO 14644-1:2015)
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 14644-2:2015)
ANSI/AAMI ST72	2019	Bacterial endotoxins – Test methods, routine monitoring, and alternatives to batch testing
Sterilization (Radiation - E-Beam)		
EN 556-1	2001/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/A1:2021	Sterilization of health care products - Microbiological methods - Part 1: Determination of a population of microorganisms on products (ISO 11737-1:2018/Amd 1:2021)
EN ISO 11737-2	2020	Sterilization of health care products - Microbiological methods - Part 2: Tests of sterility performed in the definition, validation and maintenance of a sterilization process (ISO 11737-2:2019)
Gamma or E-Beam Radiation		
EN ISO 11137-1	2015/A2:2019	Sterilization of health care products — Radiation — Part 1: Requirements for development, validation and routine control of a

Common specification(s) to comply with (if applicable): N/A		
Harmonized standard(s) to comply with:		
Standards	**Edition**	**Title**
		sterilization process for medical devices (ISO 11137-1:2006/Amd 2:2018)
EN ISO 11137-2	2015	Sterilization of health care products — Radiation — Part 2: Establishing the sterilization dose (ISO 11137-2:2015)
Device Specific		
Implants		
EN ISO 14630	2012	Non-active surgical implants -General requirements (ISO 14630:2012)
EN ISO 25539-1	2017	Cardiovascular implants - Endovascular devices - Part 1: Endovascular prostheses (ISO 25539-1:2017)
EN ISO 25539-2	2020	Cardiovascular implants - Endovascular devices - Part 2: Vascular stents (ISO 25539-2:2020)
ISO 16428	2005	Implants for surgery – Test solutions and environmental conditions for static and dynamic corrosion tests on implantable materials and medical devices
ASTM F2129	2019a	Standard Test Method for Conducting Cyclic Potentiodynamic Polarization Measurements to Determine the Corrosion Susceptibility of Small Implant Devices
ASTM G16	2013	Standard Guide for Applying Statistics to Analysis of Corrosion Data
Radiopacity		
ASTM F640	2023	Standard test methods for determining radiopacity for medical use
MRI		
ASTM F2052	2021	Standard Test Method for Measurement of Magnetically Induced Displacement Force on Medical Devices in the Magnetic Resonance Environment
ASTM F2119	2007R2013	Standard Test Method for Evaluation of MR Image Artifacts from Passive Implants
ASTM F2182	2019e2	Standard Test Method for Measurement of Radio Frequency Induced Heating on or Near Passive Implants During Magnetic Resonance Imaging
ASTM F2213	2017	Standard test method for measurement of magnetically induced torque on passive implants in the magnetic resonance
ASTM F2503	2023e1	Standard practice for marketing medical devices and other items for safety in the magnetic resonance environment

1.9 References

1. (2006). "Coil embolization for intracranial aneurysms: an evidence-based analysis." Ont Health Technol Assess Ser **6**(1): 1-114.

2. A. S. Arthur (2005). "<8 - Arthur 2005.pdf>."

3. B. R. Bendok, K. R. Abi-Aad, J. D. Ward, J. F. Kniss, M. J. Kwasny, R. J. Rahme, S. G. Aoun, T. Y. El Ahmadieh, N. E. El Tecle, S. G. Zammar, R. J. N. Aoun, D. P. Patra, S. A. Ansari, J. Raymond, H. H. Woo, D. Fiorella, G. Dabus, G. Milot, J. E. Delgado Almandoz, J. A. Scott, A. J. DeNardo, S. R. Dashti and H. S. Investigators (2020). "The Hydrogel Endovascular Aneurysm Treatment Trial (HEAT): A Randomized Controlled Trial of the Second-Generation Hydrogel Coil." Neurosurgery **86**(5): 615-624.

4. Berenstein (2006). "<Berenstein-2006-Treatment of cerebral aneurysm.pdf>."

5. W. Brinjikji, A. P. Amar, J. E. Delgado Almandoz, O. Diaz, P. Jabbour, R. Hanel, F. Hui, M. Kelly, K. D. Layton, J. W. Miller, E. Levy, C. Moran, D. C. Suh, H. Woo, R. Sellar, B. Ho, A. Evans and D. F. Kallmes (2018). "GEL THE NEC: a prospective registry evaluating the safety, ease of use, and efficacy of the HydroSoft coil as a finishing device." J Neurointerv Surg **10**(1): 83-87.

6. H. J. Cloft (2006). "<1 - Cloft 2006.pdf>."

7. G. Dabus, L. Hacein-Bey, B. Varjavand, R. D. Tomalty, P. P. Han, V. Yerokhin, I. Linfante, J. Mocco, T. Oxley, A. Spiotta, M. I. Chaudry, R. D. Turner and A. S. Turk (2017). "Safety, immediate and mid-term results of the newer generation of hydrogel coils in the treatment of ruptured aneurysms: a multicenter study." J Neurointerv Surg **9**(4): 419-424.

8. E. M. Deshaies (2007). "<16 - Deshaies 2007.pdf>."

9. N. F. Fanning, Z. Berentei, P. R. Brennan and J. Thornton (2007). "HydroCoil as an adjuvant to bare platinum coil treatment of 100 cerebral aneurysms." Neuroradiology **49**(2): 139-148.

10. T. Gunnarsson, F. C. Tong, P. Klurfan, C. M. Cawley and J. E. Dion (2009). "Angiographic and clinical outcomes in 200 consecutive patients with cerebral aneurysm treated with hydrogel-coated coils." AJNR Am J Neuroradiol **30**(9): 1657-1664.

11. F. Hagen, A. Berlis, M. Skalej and C. J. Maurer (2021). "Endovascular Treatment of Ruptured Middle Cerebral Artery Bifurcation Aneurysms. A Retrospective Observational Study of Short- and Long-Term Follow-Up." Cardiovasc Intervent Radiol **44**(4): 587-595.

12. H. Imamura, N. Sakai, Y. Ito, C. Sakai, A. Hyodo, S. Miyachi, Y. Matsumaru, S. Yoshimura, T. Abe, H. Yamagami, M. Hayakawa, H. Sato, T. Fujinaka, K. Tanabe and J. Collaborators (2019). "Prospective Registry of Embolization of Intracranial Aneurysms Using HydroSoft Coils: Results of the Japanese HydroSoft Registry." World Neurosurg **127**: e631-e637.

13. H. S. Kang (2007). "<17 - Kang 2007.pdf>."

14. P. Klurfan (2006). "<11 - Klurfan.pdf>."

15. R. Lopez-Benitez, P. Hallscheidt, C. Kratochwil, C. Ernst, L. Kara, O. Rusch, P. Vock and J. Kettenbach (2013). "Protective embolization of the gastroduodenal artery with a one-HydroCoil technique in radioembolization procedures." Cardiovasc Intervent Radiol **36**(1): 105-110.

16. J. MacDonell, N. C. Field, P. Entezami, J. Yamamoto, A. S. Boulos, J. C. Dalfino and A. R. Paul (2022). "Comparison of hydrogel coils versus bare platinum coils for the treatment of anterior communicating artery aneurysms." Brain Circulation **8**(1): 6.

17. C. Nickele, C. S. Oravec, D. Morris, D. Hoit, L. Elijovich and A. S. Arthur (2022). "Long-Term Follow-up of Aneurysms Treated with Hydrogel-Coated Coils Shows Progressive Thrombosis and Improvement in Raymond–Roy Classification." Operative Neurosurgery **22**(4): 239-243.

18. C. Nickele, C. S. Oravec, S. D. Morris, D. Hoit, L. Elijovich and A. S. Arthur (2022). "Long-Term Follow-up of Aneurysms Treated With Hydrogel-Coated Coils Shows Progressive Thrombosis and Improvement in Raymond–Roy Classification." Operative Neurosurgery **22**(4): 239-243.

19. S. A. Pineda-Castillo, A. M. Stiles, B. N. Bohnstedt, H. Lee, Y. Liu and C. H. Lee (2022). "Shape Memory Polymer-Based Endovascular Devices: Design Criteria and Future Perspective." Polymers (Basel) **14**(13).

20. W. Poncyljusz, A. Zarzycki, L. Zwarzany and T. H. Burke (2015). "Bare platinum coils vs. HydroCoil in the treatment of unruptured intracranial aneurysms-A single center randomized controlled study." Eur J Radiol **84**(2): 261-265.

21. K. Rotim, V. Kalousek, F. Vrban and B. Splavski (2021). "Microsurgical Management of Recurrent Intracranial Aneurysms Following Endovascular Treatment: A Single Institution Illustrative Case Series and Literature Review." Acta Clin Croat **60**(4): 695-702.

22. E. B. Sousa, L. F. S. Brandao, C. B. Tavares, J. Brito and I. M. Kessler (2019). "Importance of the First Coil in the Embolization of Intracranial Aneurysms : A Case Control Study." Clin Neuroradiol **29**(4): 733-740.

23. C. A. Taschner, R. Chapot, V. Costalat, P. Machi, P. Courtheoux, X. Barreau, J. Berge, L. Pierot, K. Kadziolka, B. Jean, R. Blanc, A. Biondi, H. Brunel, S. Gallas, A. Berlis, D. Herbreteau, J. Berkefeld, H. Urbach, S. Elsheikh, J. Fiehler, H. Desal, E. Graf and A. Bonafe (2018). "Second-Generation Hydrogel Coils for the Endovascular Treatment of Intracranial Aneurysms: A Randomized Controlled Trial." Stroke **49**(3): 667-674.

24. A. Tessitore, A. Paolucci, S. Hohenstatt, A. A. Caragliano, O. Buonomo, E. Mormina, A. Pitrone and S. L. Vinci (2023). "Comparison between second generation HydroSoft coils and bare platinum coils for the treatment of large intracranial aneurysms." Interventional Neuroradiology **29**(3): 321-326.

25. P. M. White, S. C. Lewis, H. Nahser, R. J. Sellar, T. Goddard, A. Gholkar and H. T. Collaboration (2008). "HydroCoil Endovascular Aneurysm Occlusion and Packing Study (HELPS trial): procedural safety and operator-assessed efficacy results." AJNR Am J Neuroradiol **29**(2): 217-223.

26. L. Zhang, X. Chen, L. Dong, P. Liu, L. Jia, Y. Zhang and M. Lv (2021). "Clinical and Angiographic Outcomes After Stent-Assisted Coiling of Cerebral Aneurysms With Laser-Cut and Braided Stents: A Comparative Analysis of the Literatures." Front Neurol **12**: 666481.