Summary of Safety and Clinical Performance

for

AZUR™ Vascular Plug

SSCP23-0011

Rev. C

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

MicroVention Europe SARL
30 bis, rue du Vieil Abreuvoir
78100 Saint-Germain-en-Laye, France

DOCUMENT CHANGE HISTORY

SSCP Revision	Change Description	NB approved/verified
A	Initial Release	☐Yes ☒ No* Validation language:
B	External Standards Revised	☐Yes ☒ No* Validation language:
C	External Standards Revised	☐Yes ☒ No* Validation language:

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

TABLE OF CONTENTS

LIST OF TABLES

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	AZUR Vascular Plug
EMDN Code	C010402020301
Medical Device Nomenclature (EMDN)	Embolization Coils
Device Class	Class IIb
Basic UDI-DI	08402732AZURPLUG4X
Year when first certificate (CE) was issued for the device	2019
Legal Manufacturer	
Name & Address	MicroVention, Inc. 35 Enterprise Aliso Viejo, California, 92656 USA
Manufacturer SRN	US-MF-000016658
Authorized Representative	
Name & Address	MicroVention Europe SARL 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 60433 Frankfurt am Main Germany
Notified Body Identification Number	0297

1.2 Intended Purpose of the Device

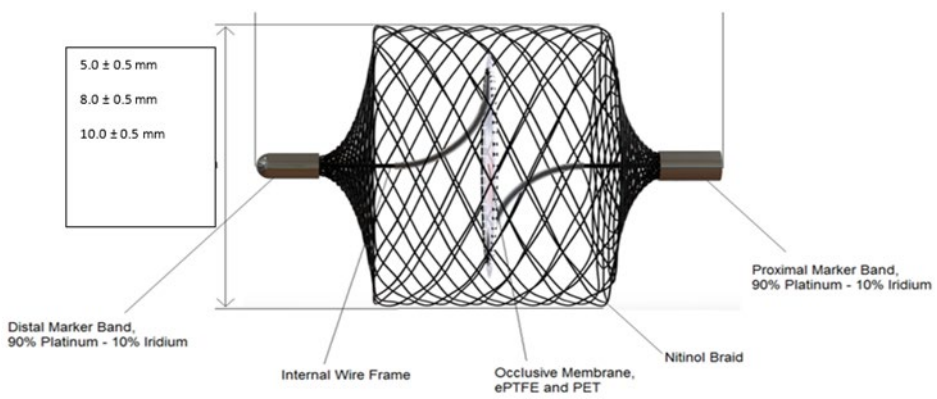
Table 1.2 Intended Use

Intended Purpose	
Intended Purpose	The AZUR Vascular Plug is intended to reduce or block the rate of blood flow in vessels of the peripheral vasculature.
Intended User	This device should only be used by physicians who have undergone training in the use of the AZUR system for embolization procedures as prescribed by a representative from Terumo or a Terumo-authorized distributor.
Target Population	The AZUR Vascular Plug is intended for patients who require a reduction or blockage in flow rate of blood flow in vessels of the peripheral vasculature.
Contraindications and/or Limitations	Use of the AZUR Vascular Plug is contraindicated in any of the following circumstances: • When patient has known hypersensitivity to nickel-titanium. • When end vessels lead directly to nerves. • When vessels supplying the lesion to be treated are not large enough to accept emboli. • In the presence of severe atheromatous disease. • In the presence of vasospasm (or likely onset of vasospasm).

1.3 Device Description

Table 1.3 Device Description

Device Description	
Description of the Device	The AZUR Vascular Plug (Figure 2.1) is an embolization device consisting of a conformable, self-expanding nitinol braided wire frame surrounding a flexible, occlusive membrane. The implant is secured at both ends with radiopaque markers to provide visual confirmation of deployment location during the interventional treatment. The implant proximal marker band is attached to a delivery pusher by a monofilament. The pusher is used to deliver the implant through a microcatheter to the intended treatment site. After satisfactory deployment of the implant at the treatment site, the handheld, battery powered AZUR detachment controller (provided separately) is used to release the implant in the vessel. The AZUR Vascular Plug is used by trained interventionalists to reduce or block the rate of blood flow in the peripheral vasculature. **Figure 1-1: AZUR Vascular Plug Diagram**

	
Design Characteristics of the Device	The AZUR Vascular Plug is an embolization device consisting of a conformable, self-expanding nitinol braided wire frame surrounding a flexible, occlusive membrane (Figure 2.1). The AZUR Vascular Plug is deployed in an appropriately sized vessel to reduce or block the flow of blood. The implant has radiopaque markers to provide visual confirmation of deployment location during the interventional treatment. The implant is deliverable through a microcatheter on a detachable delivery system with a delivery pusher, and AZUR Detachment Controller is used to detach the implant.
Previous Generations or Variants, if applicable	None.
Single use – sterilization method	Single use, EtO Sterilized
Description of Accessories	None.
Description of other Devices or Products intended to be used in combination	The AZUR Vascular Plug implant is deliverable through a microcatheter on a detachable delivery system with a delivery pusher, and AZUR Detachment Controller is used to detach the implant. The microcatheter and AZUR Detachment Controller are provided separately.

1.4 Risks and Warnings

1.4.1 Residual Risks and Undesirable Effects

Hazards associated with the use of the AZUR Vascular Plug are assessed and risks of the resulting harms 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:

1.4.2 Warnings and Precautions

Users and/or patients should report any serious incidents to the manufacturer and the Competent Authority of the Member State or Local Health Authority in which the user and/or patient is established.

- Refer to instructions supplied with all interventional devices to be used with the AZUR Vascular Plug for their intended uses, contraindications, and potential complications.
- This device is intended for single use only. Do not reuse, reprocess, or resterilize. Reuse, reprocessing, or resterilization may compromise the structural integrity of 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.
- Angiography is required for pre-embolization evaluation, operative control, and post-embolization follow up.
- Do not advance the delivery pusher with excessive force. Determine the cause of any unusual resistance, remove the AZUR system, and check for damage.
- Advance and retract the AZUR system slowly and smoothly. Remove the entire AZURsystem if excessive friction is noted. If excessive friction is noted with a second AZUR system, check the catheter for damage or kinking.
- The implant must be properly positioned within a maximum of 3 positioning attempts. If the implant cannot be properly positioned after 3 attempts, simultaneously remove the device and the catheter.
- If repositioning is necessary, take special care to retract the implant under fluoroscopy in a one-to-one motion with the delivery pusher. If the implant does not move in a one-to-one motion with the delivery pusher, or if repositioning is difficult, gently remove and discard the entire device.
- Tortuosity or complex vessel anatomy may affect accurate placement of the implant.
- 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 AZUR Detachment Controllers are available before starting an AZUR system procedure.
- The implant cannot be detached with any power source other than an AZUR Detachment Controller.
- Do NOT place the delivery pusher on a bare metallic surface.
- Always handle the delivery pusher with surgical gloves.
- Do NOT use in conjunction with radio frequency (RF) devices.

1.4.3 Potential Complications / Adverse Effects

Potential complications for AZUR Vascular Plug include but are not limited to: hematoma at the site of entry, vessel perforation, unintended parent artery occlusion, incomplete filling, vascular thrombosis, hemorrhage, ischemia, vasospasm, edema, implant migration or misplacement,

premature or difficult implant detachment, clot formation, revascularization, post-embolization syndrome, and neurological deficits including stroke and possibly death.

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

None.

1.5 Summary of the Clinical Evaluation and PMCF

1.5.1 Equivalent Device Clinical Data

Literature search results demonstrate clinical use of the equivalent device, AZUR Peripheral Embolization Coils System (AZUR PECS) to reduce or block the rate of blood flow in arteries of the peripheral vasculature in 923 patients in 19 published articles included 1 randomized controlled trial, 3 prospective cohort studies, and 15 retrospective case control studies. The overall quality of the data from the published clinical studies was moderate. The analysis of the published literature demonstrates clinical performance outcomes: High to complete technical success rate of 75.0% to 100%. (Yamamoto et al., 2020, Iguchi et al., 2020, Goldstein et al., 2012, Osuga et al., 2014, Perdikakis et al., 2018, Shimohira et al., 2018, Omachi et al., 2021, Shreve et al., 2020, Maruyama et al., 2021, Baba et al., 2022, Maruyama et al., 2022) and high to complete clinical success rate of 68.7% to 94.7% (Iguchi et al., 2020, Della Rocca et al., 2020, Cusumano et al., 2020, Abdelfattah et al., 2021, Poyraz et al., 2017, Hongo et al., 2021, Shreve et al., 2020, Maruyama et al., 2021, Baba et al., 2022, Marcelin et al., 2022, Nishihara et al., 2022) were reported as associated with the use of the AZUR system.

1.5.2 Pre-CE-Mark Clinical Data

There are no pre-market clinical investigations for the AZUR Vascular Plug.

1.5.3 Clinical Data

Post-market surveillance

For the evaluation period of 01 January 2019 to 31 December 2023, 4,850 units of the AZUR Vascular Plug have been sold worldwide. The number of product complaints reported to MicroVention is 41, giving a device complaint rate of 0.8%. The total number of complaints reported to EU vigilance authorities is 10, giving a device reportable complaint rate of 0.2%.

Physician Performance Testing (PPT)

Physicians were asked to use the AZUR Vascular Plug and then complete a PPT evaluation form for each case to evaluate the performance of both devices.

A total of 33 cases were conducted. These cases covered a variety of indications such as PAVM, GDA, Splenic embolization, GI embolization, aneurysm, AVF and Pseudoaneurysm etc.

The scores of AZUR Vascular Plug for all the evaluation metrics met the acceptance criteria (≥75% of Responses must be ≥ 3.0) and the average scores were all ≥ 4. (**Table 1.4**)

In 19 cases, physicians considered AZUR Vascular Plug as a better device compared with their commonly used plugs. No physician rated AZUR Vascular Plug as a worse device.

In 25 cases, physicians were willing to switch to AZUR Vascular Plug from their commonly used coils. No physician answered not willing to switch.

The results from the 33 physician surveys met the acceptance criteria that ≥75% of Responses must be ≥ 3.0.

Table 1.4 Physician Performance Testing Results

Performance Criteria	Average	Percentage of Score ≥ 3.0	Acceptance Criteria	Pass/Fail
Package/device prep	4.6	100%	≥75% of Responses must be ≥ 3.0	Pass
Clarity of label	4.4	88%	≥75% of Responses must be ≥ 3.0	Pass
Ease of intro into MC	4.6	97%	≥75% of Responses must be ≥ 3.0	Pass
Ease of tracking	4.4	91%	≥75% of Responses must be ≥ 3.0	Pass
Radiopacity	4.5	94%	≥75% of Responses must be ≥ 3.0	Pass
Ease of deployment	4.7	97%	≥75% of Responses must be ≥ 3.0	Pass
Placement accuracy	4.5	97%	≥75% of Responses must be ≥ 3.0	Pass
Conformability	4.7	97%	≥75% of Responses must be ≥ 3.0	Pass
Ease of recapture	4.8	100%	≥75% of Responses must be ≥ 3.0	Pass
Ease of re-deployment	4.8	100%	≥75% of Responses must be ≥ 3.0	Pass
Ease of detachment	4.8	100%	≥75% of Responses must be ≥ 3.0	Pass
Stability post detachment	4.8	97%	≥75% of Responses must be ≥ 3.0	Pass
Acute occlusion	4.3	97%	≥75% of Responses must be ≥ 3.0	Pass
Overall performance	4.6	100%	≥75% of Responses must be ≥ 3.0	Pass

1.5.4 Clinical Performance and Safety

For the evaluation period of 01 January 2019 to 31 December 2023, 4,850 units of the AZUR Vascular Plug have been sold worldwide. The number of product complaints reported to MicroVention is 41, giving a device complaint rate of 0.8%. The total number of complaints reported to EU vigilance authorities is 10, giving a device reportable complaint rate of 0.2%.

The literature search detailed in the CER presents relevant clinical studies in the published literature for this CER. The literature search was performed with high methodological quality, scientific validity, and relevance to the fields of use in 923 patients in 19 published articles included 1 randomized controlled trial, 3 prospective cohort studies, and 15 retrospective case control studies. The overall quality of the data from the published clinical studies was moderate.

The analysis of the published literature demonstrates clinical performance outcomes: High to complete technical success rate of 75.0% to 100%. (Yamamoto et al., 2020, Iguchi et al., 2020, Goldstein et al., 2012, Osuga et al., 2014, Perdikakis et al., 2018, Shimohira et al., 2018, Omachi et al., 2021, Shreve et al., 2020, Maruyama et al., 2021, Baba et al., 2022, Maruyama et al., 2022) and high to complete clinical success rate of 68.7% to 94.7% (Iguchi et al., 2020, Della Rocca et al., 2020, Cusumano et al., 2020, Abdelfattah et al., 2021, Poyraz et al., 2017, Hongo et al., 2021, Shreve et al., 2020, Maruyama et al., 2021, Baba et al., 2022, Marcelin et al., 2022, Nishihara et al., 2022) were reported as associated with the use of the AZUR system.

Physician performance testing showed in 19 out of the 33 cases, physicians considered AZUR Vascular Plug as a better device compared with their commonly used plugs. No physician rated AZUR Vascular Plug as a worse device. Acceptance criteria was met for assess performance criteria.

1.5.5 Post-Market Clinical Follow-up

The manufacturer continuously monitors published clinical data for the device to ensure the benefits of the use of the device for the patient do not outweigh any possible risk that include systematic literature searches for published clinical data.

1.6 Possible Diagnostic or Therapeutic Alternatives

1.6.1 Treatment Options and Interventions

Alternatives to the use of embolization therapeutics for the forementioned clinical conditions and applications typically include more invasive surgical techniques such as clipping, ligation, or surgical resection, and can often result in deleterious outcomes, as is the case for arteriovenous malformations(Greene and Burrows, 2020, Hawkins and Chewning, 2019, Kim et al., 2020b, Bouwman et al., 2020). Treatment options for AVMs consists of conservative measures, such as compression garments and pain medication, transcatheter and percutaneous embolization, and surgical resection.(Strübing et al., 2022) In smaller, localized lesions, resection with primary wound closure may be feasible, whereas extensive AVMs regularly require the reconstruction of the resulting soft tissue defect and possibly affected functional structures by means of free tissue transfer. The surgical resection of an AVM lesion carries the risks of extensive intraoperative hemorrhage, incomplete removal of the AVM nidus, surrounding organ or tissue injuries, and high recurrence rates(Kim et al., 2021). Instead, treatment with endovascular embolization therapeutics is recommended as they can be delivered with precision to the target vasculature and with minimal invasiveness. While the transarterial approach remains the most commonly employed route for peripheral AVM embolization, the role of transvenous and direct percutaneous approach is ever increasing and the final decision on the approach depends on angioarchitecture of the AVM.(Malik et al., 2022) Below is a discussion of the various options for embolization therapy that can be

considered according to target vasculature size and type, desired outcome, flow characteristics, embolization permanence, and potential for complications(Hawkins and Chewning, 2019, Kim et al., 2020b, Hu et al., 2019). These options are also commonly used in conjunction with one another to achieve the desired clinical effect(Kim et al., 2021, Strübing et al., 2022).

Liquids/Gel

Liquid/gel embolic agents use in peripheral interventions have the ability to penetrate into smaller or more complex vascular targets where catheters and larger embolic therapeutics cannot(Hu et al., 2019, Santoro et al., 2019, Jiang et al., Ko et al., Young et al., 2022). Liquid/gel embolics block blood flow by forming permanent cast and do not depend on the patient's coagulations system for thrombosis formation. One type of liquid/gel embolics are sclerosings agents, ethanol being the most common, which functions by denaturing vessel endothelium and causing necrosis of vascular structures, such as AVMs(Kim et al., 2020b, Bouwman et al., 2020, Kim et al., 2021, Waters et al.). Other forms of liquid/gel embolic include in-situ polymerization (TruFill) which is commonly known as "glue" and in-situ precipitating fluids (Onyx, Micro Therapeutics; PHIL, MVI) which create casts when exposed to body fluids in the target vasculature. A meta-analysis by Lilje et al. 2022 showed curing rate of transarterial ethanol embolization for intraosseous AVM was 83% with a complication rate of 58% and curing rate of ethanol combined with NBCA or Onyx in soft tissue AVM was 18% with a complication rate of 87%.(Lilje et al., 2022) Another review showed an overall patient satisfaction rate of 91%, with a complete cure rate of 64.7%.(Waters et al.) Drawbacks of liquid/gel embolics include cardiopulmonary complications (ethanol), necrosis of non-target tissue, nerve injury, distal thrombolysis, as well as with agents such as Onyx, high cost, radiopacity, and residual mass effect(Kim et al., 2020a, Bouwman et al., 2020). The reported complication rates of ethanol embolotherapy in treatment of AVMs are 23% overall, 20% for minor complications, and 3% for major complications(Kim et al., 2021).

Particulates

Particulates are the most commonly used embolic agent due to the variety of available sizes, shapes, and properties (permanent, biodegradable, natural, synthetic, etc.) (Hu et al., 2019, Santoro et al., 2019), with microspheres often preferred due to their controllable shape and size distribution. Particulates are delivered proximally to the target vasculature via catheter. After leaving the catheter, blood flow drives the particles into the smallest vessels they can pass. Once lodged within the vessel, they mechanically obstruct flow and thrombus formation begins. Particulates are typically used when the target vasculature for thrombosis formation are small vessels including capillaries. Drawbacks include unintentional occlusion of larger proximal vessels due to clumping of particles and downstream embolization due to size and shape irregularity.

Mechanical

Mechanical embolization devices include coils and vascular plugs that allow complete occlusion of a specific vascular site and are used in small to large vessels with high flows(Hu et al., 2019, Santoro et al., 2019). Coils and plugs are typically permanent implants with bioinert metallic cores (e.g., stainless steel, platinum, nitinol). During procedures, a catheter is steered through the blood stream to the target vasculature. Once positioned, the implant is pushed through the catheter using a delivery system, which deploys the expandable device into its preformed geometry in the vessel lumen. The expansion of the device creates radial force for vessel wall apposition, anchoring the device in place. The embolization of the vessel is achieved by filling the space with coils, or in the use of plugs, by an occlusive membrane supported by a braided wire mesh core(Ghosh et al., 2022). The positioning of the coils or plug is then confirmed by radiography. Both coils and plugs are also used in conjunction in some cases(Adachi et al., 2020, Jardinet et al., 2020, Ghosh et al., 2022, Malik et al., 2022).

Mechanical embolization devices are used to treat pulmonary and peripheral AVMs(Adachi et al., 2020, Bailey et al., 2019, Greene and Burrows, 2020, Gupta et al., 2020, Hawkins and Chewning, 2019), (Kim et al., 2020b), (Kim et al., 2021), aneurysms(Santoro et al., 2019), hemorrhage in visceral organs or extremities from trauma prior to surgery(Santoro et al., 2019), and embolization during both open and endovascular surgical procedures (e.g., structural heart repair, aortic repair, renal pathologies)(Bertoglio et al., 2020, Catelli et al., 2020, Jain et al., 2020, Jardinet et al., 2020, Kubicki et al., 2019, Matsumoto et al., 2019, Wehbe et al., 2020).

Although coils are the most commonly used mechanical embolization device, vascular plugs were developed in large part to address a number of concerns associated with the use of coils in large vessels(Hu et al., 2019). In large vessels, multiple coils are required to achieve successful embolization with an increased risk of complication due to coil placement and migration, longer procedure times, and extended radiation exposure. Advantages of using a vascular plug in these situations include achieving complete vascular occlusion in less time using fewer devices and cost savings(Jardinet et al., 2020, Matsumoto et al., 2019). Other advantages of vascular plugs include, resheathability, immediate occlusion despite procedural anticoagulation, and diminished metal artifact compared with coils on followup- computed tomography imaging(Conrad et al., 2015). In a comparative retrospective study by Botsfort et al. 2023, they reported PAVM embolization with coils was safe, but persistence rate with PAVM embolization was significantly higher than that with plugs. Hence, they concluded plugs should be preferred whenever possible.

The first vascular plug was FDA approved in 2004(Ghosh et al., 2022). Common sizes for vascular plugs are 3-15 mm for use in vessels 1.5-17mm. Vascular plugs have been shown to be successful in the treatment of emergent and elective procedures that include pre-surgical embolizations, AVMs, hemorrhage, hematoma, pseudoaneurysm, aneurysms.

Potential complications include persistent patency, migration, and recanalization. Potential adverse events include non-target vessel embolization, hematoma at entry site, vessel perforation/dissection, hypertension, AVFs, skin erosion of superficial vessels, ischemia,

pulmonary embolism, thrombosis, stroke, infarction, mortality(Ghosh et al., 2022, Gunn et al., 2021, Bailey et al., 2019, Kubicki et al., 2019, Giurazza et al., 2021, Prasad et al., 2021, Kalogeras et al., 2021, Mailli et al., 2023, Botsford et al., 2024).

1.6.2 Available Technologies

Peripheral vascular plugs such as the AZUR Vascular Plug, are well established medical devices with numerous types and styles available from a variety of manufacturers. A few examples of peripheral vascular plugs similar to the AZUR Vascular Plug are listed in **Table 1.5**.

Table 1.5 Similar Devices

Device	Manufacturer	Intended Use
MVP Microvascular Plug Systems	Medtronic	The MVP micro vascular plug system is indicated to obstruct or reduce the rate of blood flow in the peripheral vasculature.
Amplatzer™ Vascular Plug	Abbott	The Amplatzer™ Family of Vascular Plugs are indicated for arterial and venous embolization in the peripheral vasculature.
AZUR Peripheral Embolization Coil System	MicroVention	The AZUR Peripheral Embolization Coil System is intended to reduce or block the rate of blood flow in vessels of the peripheral vasculature. It is intended for use in the interventional radiologic management of arteriovenous malformations, arteriovenous fistulae, aneurysms, and other lesions of the peripheral vasculature.

1.7 Suggested Profile and Training for Users

This device should only be used by physicians who have undergone training in the use of the AZUR system for embolization procedures as prescribed by a representative from Terumo or a Terumo-authorized distributor.

1.8 Reference to any Harmonized Standards and CS

Standard Number	Edition	Standard Title (equivalent edition)
EN ISO 13485	2016/A11:2021	Medical devices - Quality management systems - Requirements for regulatory purposes (ISO 13485:2016)
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)
EN 62366-1	2015/A1:2020	Medical devices - Part 1: Application of usability engineering to medical devices (IEC 62366-1:2015/A1:2020)

Standard Number	Edition	Standard Title (equivalent edition)
ISO/TR 20416	2020	Medical devices - Post-market surveillance for manufacturers
EN ISO 15223-1	2021	Medical devices - Symbols to be used with 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 (ISO 20417:2021, Corrected version 2021-12)
EN ISO 11607-1	2020/A1:2023	Packaging for terminally sterilized medical devices - Part 1: Requirements for materials, sterile barrier systems and packaging systems (ISO 11607-1:2019/Amd 1:2023)
EN ISO 11607-2	2020/A1:2023	Packaging for terminally sterilized medical devices - Part 2: Validation requirements for forming, sealing and assembly processes (ISO 11607-2:2019/Amd 1:2023)
ISTA 3A	2018	Packaged-Products for Parcel Delivery System Shipment 70 kg (150 lbs) or Less
ASTM D4169	2023e1	Standard Practice for Performance Testing of Shipping Containers and Systems
ASTM D4332	2022	Standard Practice for Conditioning Containers, Packages, or Packaging Components for Testing
ASTM F88	2023	Standard Test Method for Seal Strength of Flexible Barrier Materials
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)
ASTM F1980	2016	Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices
EN ISO 10993-1	2020	Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process (ISO 10993-1:2018, 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)

Standard Number	Edition	Standard Title (equivalent edition)
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 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 10993-17	2023	Biological evaluation of medical devices - Part 17: Toxicological risk assessment of medical device constituents (ISO 10993-17:2023)
EN ISO 10993-18	2020/A1:2023	Biological evaluation of medical devices - Part 18: Chemical characterization of medical device materials within a risk management process (ISO 10993-18:2020/Amd 1:2022)
EN ISO 10993-23	2021	Biological evaluation of medical devices - Part 23: Tests for irritation (ISO 10993-23:2021)
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

Standard Number	Edition	Standard Title (equivalent edition)
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)
ISO 11737-3	2023	Sterilization of health care products - Microbiological methods - Part 3: Bacterial Endotoxin testing
EN ISO 11138-1	2017	Sterilization of health care products - Biological indicators - Part 1: General requirements (ISO 11138-1:2017)
EN ISO 11135	2014/A1:2019	Sterilization of health-care products - Ethylene oxide - Requirements for the development, validation and routine control of a sterilization process for medical devices (ISO 11135:2014/Amd 1:2018)
EN ISO 10993-7	2008/A1:2022	Biological evaluation of medical devices - Part 7: Ethylene oxide sterilization residuals (ISO 10993-7:2008/Amd 1:2019)
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

Standard Number	Edition	Standard Title (equivalent edition)
		Determine the Corrosion Susceptibility of Small Implant Devices
ASTM F3044	2020	Standard Test Method for Evaluating the Potential for Galvanic Corrosion for Medical Implants
ASTM G16	2013	Standard Guide for Applying Statistics to Analysis of Corrosion Data
ASTM F640	2023	Standard test methods for determining radiopacity for medical use
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

ABDELFATTAH, O. M., SAAD, A. M., KASSIS, N., SHEKHAR, S., ISOGAI, T., GAD, M. M., AHUJA, K. R., HARIRI, E., KAUR, M., FARWATI, M., KHATRI, J., KRISHNASWAMY, A. & KAPADIA, S. R. 2021. Utilization and outcomes of transcatheter coil embolization for various coronary artery lesions: Single-center 12-year experience. *Catheter Cardiovasc Interv,* 98**,** 1317-1331.

ADACHI, A., OHTA, K., JAHANGIRI, Y., MATSUI, Y., HORIKAWA, M., GEERATIKUN, Y., CHANSANTI, O., YATA, S., FUJII, S. & STEINBERGER, J. 2020. Treatment of pulmonary arteriovenous malformations: Clinical experience using different embolization strategies. *Japanese journal of radiology***,** 1-5.

BABA, K., KONDO, M., EITOKU, T., SHIGEMITSU, Y., HIRAI, K., OTSUKI, S., KANAZAWA, T., IWASAKI, T., IGUCHI, T., TOH, N., KOTANI, Y. & KASAHARA,

S. 2022. Vascular occlusion with 0.035-inch hydrogel expandable coils in congenital heart diseases and vascular anomalies. *J Cardiol,* 80**,** 249-254.

BAILEY, C. R., ARUN, A., TOWSLEY, M., CHOI, W. K., BETZ, J. F., MACKENZIE, S., ABOU AREDA, M., DUVVURI, M., MITCHELL, S. & WEISS, C. R. 2019. MVP™ micro vascular plug systems for the treatment of pulmonary arteriovenous malformations. *Cardiovascular and interventional radiology,* 42**,** 389-395.

BERTOGLIO, L., SALVATI, S., FITTIPALDI, A., MELLONI, A., KAHLBERG, A., CAMBIAGHI, T., MELISSANO, G. & CHIESA, R. 2020. Carotid to subclavian bypass and Amplatzer vascular plug subclavian endovascular occlusion before thoracic open or endovascular repair. *Journal of vascular surgery,* 71**,** 1480-1488. e1.

BOTSFORD, A., TRADI, F., LOUBET, A., TANTAWI, S., SOULEZ, G., GIROUX, M. F., FAUGHNAN, M. E., GAUTHIER, A., PERREAULT, P., BOUCHARD, L., HOLDERBAUM DO AMARAL, R., CHARTRAND-LEFEBVRE, C. & THERASSE, E. 2024. Transarterial Embolization of Simple Pulmonary Arteriovenous Malformations: Long-Term Outcomes of 0.018-Inch Coils versus Vascular Plugs. *J Vasc Interv Radiol,* 35**,** 349-360.

BOUWMAN, F. C., BOTDEN, S. M., VERHOEVEN, B. H., KOOL, L. J. S., VAN DER VLEUTEN, C. J., DE BLAAUW, I. & KLEIN, W. M. 2020. Treatment Outcomes of Embolization for Peripheral Arteriovenous Malformations. *Journal of Vascular and Interventional Radiology,* 31**,** 1801-1809.

CATELLI, A., LOIUDICE, G., CORVINO, A., BRACALE, U. M., QUARANTELLI, M. & VENETUCCI, P. 2020. Amplatzer vascular plug in renal artery embolization: case report and review of the literature. *Egyptian Journal of Radiology and Nuclear Medicine,* 51**,** 1-5.

CONRAD, M. B., ISHAQUE, B. M., SURMAN, A. M., KERLAN, R. K., JR., HOPE, M. D., DICKEY, M. A., HETTS, S. W. & WILSON, M. W. 2015. Intraprocedural Safety and Technical Success of the MVP Micro Vascular Plug for Embolization of Pulmonary Arteriovenous Malformations. *J Vasc Interv Radiol,* 26**,** 1735-9.

CUSUMANO, L. R., DUCKWILER, G. R., ROBERTS, D. G. & MCWILLIAMS, J. P. 2020. Treatment of Recurrent Pulmonary Arteriovenous Malformations: Comparison of Proximal Versus Distal Embolization Technique. *Cardiovasc Intervent Radiol,* 43**,** 29-36.

DELLA ROCCA, D. G., HORTON, R. P., DI BIASE, L., BASSIOUNY, M., AL-AHMAD, A., MOHANTY, S., GASPERETTI, A., NATALE, V. N., TRIVEDI, C., GIANNI, C., BURKHARDT, J. D., GALLINGHOUSE, G. J., HRANITZKY, P., SANCHEZ, J. E. & NATALE, A. 2020. First Experience of Transcatheter Leak Occlusion With Detachable Coils Following Left Atrial Appendage Closure. *JACC Cardiovasc Interv,* 13**,** 306-319.

GHOSH, A., XIAO, N., GORDON, A. C., FUNAKI, B. & LEWANDOWSKI, R. J. 2022. Embolic Agents: Vascular Plugs. *Seminars in Interventional Radiology,* 39**,** 526-532.

GIURAZZA, F., IERARDI, A. M., CONTEGIACOMO, A., CORVINO, F., CARRAFIELLO, G. & NIOLA, R. 2021. Embolization with MVP (Micro Vascular Plug((R))): experience on 104 patients in emergent and elective scenarios. *CVIR Endovasc,* 4**,** 59.

GOLDSTEIN, B. H., AIYAGARI, R., BOCKS, M. L. & ARMSTRONG, A. K. 2012. Hydrogel expandable coils for vascular occlusion in congenital cardiovascular disease: a single center experience. *Congenit Heart Dis,* 7**,** 212-8.

GREENE, A. K. & BURROWS, P. E. 2020. Arteriovenous malformation. *Vascular Anomalies.* Springer.

GUNN, A. J., RABORN, J. R., GRIFFIN, R., STEPHENS, S. W., RICHMAN, J. & JANSEN, J. O. 2021. A pilot randomized controlled trial of endovascular coils and vascular plugs for proximal splenic artery embolization in high-grade splenic trauma. *Abdom Radiol (NY),* 46**,** 2823-2832.

GUPTA, M., AGRAWAL, A., IAKOVOU, A., COHEN, S., SHAH, R. & TALWAR, A. 2020. Pulmonary artery aneurysm: a review. *Pulmonary circulation,* 10**,** 2045894020908780.

HAWKINS, C. M. & CHEWNING, R. H. 2019. Diagnosis and Management of Extracranial Vascular Malformations in Children: Arteriovenous Malformations, Venous Malformations, and Lymphatic Malformations. *Semin Roentgenol,* 54**,** 337-348.

HONGO, N., KIYOSUE, H., OTA, S., NITTA, N., KOGANEMARU, M., INOUE, M., NAKATSUKA, S., OSUGA, K., ANAI, H., YASUMOTO, T., TANOUE, S., MARUNO, M., KAMEI, N., KICHIKAWA, K., ABE, T., HASEBE, T. & ASAYAMA, Y. 2021. Vessel Occlusion using Hydrogel-Coated versus Nonhydrogel Embolization Coils in Peripheral Arterial Applications: A Prospective, Multicenter, Randomized Trial. *J Vasc Interv Radiol,* 32**,** 602-609.e1.

HU, J., ALBADAWI, H., CHONG, B. W., DEIPOLYI, A. R., SHETH, R. A., KHADEMHOSSEINI, A. & OKLU, R. 2019. Advances in biomaterials and technologies for vascular embolization. *Advanced Materials,* 31**,** 1901071.

IGUCHI, T., HIRAKI, T., MATSUI, Y., FUJIWARA, H., SAKURAI, J., BABA, K., TOYOOKA, S., GOBARA, H. & KANAZAWA, S. 2020. Embolization using hydrogel-coated coils for pulmonary arteriovenous malformations. *Diagn Interv Imaging,* 101**,** 129-135.

JAIN, S. M., PRADHAN, P. M., SEN, S. & DALVI, B. V. 2020. Transcatheter closure of elongated and pulmonary hypertensive patent arterial duct in infants using Amplatzer vascular plug II. *Cardiology in the young,* 30**,** 243-248.

JARDINET, T., BONNE, L., OYEN, R. & MALEUX, G. 2020. Initial Experience With the Microvascular Plug in Selective Renal Artery Embolization. *Vascular and endovascular surgery,* 54**,** 240-246.

JIANG, Y., ZHANG, Y., LU, Z., WANG, X., BAI, S., CHEN, Y., CHEMPHYSMATER, J. M. & UNDEFINED Liquid embolic agents for interventional embolization. *Elsevier*.

KALOGERAS, K., NTALEKOU, K., AGGELI, K., MOLDOVAN, C., KATSIANOS, E., KALANTZIS, C., BEI, E., MOURMOURIS, C., SPARGIAS, K., CHRISSOHERIS, M., DARDAS, P., AZNAOURIDIS, K., TZIFA, A., THEOFILOGIANNAKOS, E., SIASOS, G., TOUSOULIS, D. & VAVURANAKIS, M. 2021. Transcatheter closure of paravalvular leak: Multicenter experience and follow-up. *Hellenic J Cardiol,* 62**,** 416-422.

KIM, R., DO, Y. S. & PARK, K. B. 2020a. How to Treat Peripheral Arteriovenous Malformations. *Korean J Radiol*.

KIM, R., DO, Y. S. & PARK, K. B. 2020b. How to Treat Peripheral Arteriovenous Malformations. *Korean Journal of Radiology,* 21.

KIM, R., DO, Y. S., PARK, K. B., KIM, D. I., HEO, S. H., PARK, H. S., SHIN, S. W., CHO, S. K. & HYUN, D. H. 2021. Therapeutic outcomes of embolotherapy of extremity bone intraosseous arteriovenous malformation with ethanol, coils, and n-butyl cyanoacrylate. *J Vasc Surg,* 73**,** 2090-2097 e5.

KO, G., CHOI, J. W., LEE, N., KIM, D., HYEON, T., BIOMATERIALS, H. C. K. & UNDEFINED Recent progress in liquid embolic agents. *Elsevier*.

KUBICKI, R., STILLER, B., HUMMEL, J., HÖHN, R., FLECK, T. & GROHMANN, J. 2019. Collateral closure in congenital heart defects with Amplatzer vascular plugs: single-center experience and a simplified delivery technique for exceptional cases. *Heart and vessels,* 34**,** 134-140.

LILJE, D., WIESMANN, M., HASAN, D., RIABIKIN, A., RIDWAN, H., HÖLZLE, F. & NIKOUBASHMAN, O. 2022. Interventional therapy of extracranial arteriovenous malformations of the head and neck-A systematic review. *PLoS ONE,* 17.

MAILLI, R., CHEVALLIER, O., MAZIT, A., MALAKHIA, A., FALVO, N. & LOFFROY, R. 2023. Embolisation Using Microvascular Plugs for Peripheral Applications: Technical Results and Mid-Term Outcomes. *Biomedicines,* 11.

MALIK, V., KRAMADHARI, H., RATHOD, J., MUNDE, Y. W. & KOVILAPU, U. B. 2022. Peripheral Arteriovenous Malformations: Imaging and Endovascular Management Strategies. *Journal of Clinical Interventional Radiology ISVIR,* 6**,** 43-51.

MARCELIN, C., PARK, A. W., GILBERT, P., BOUCHARD, L., THERASSE, E., PERREAULT, P., GIROUX, M. F. & SOULEZ, G. 2022. Management of Pancreatico-duodenal arterio-venous malformation. *CVIR Endovasc,* 5**,** 2.

MARUYAMA, M., YOSHIZAKO, T., ANDO, S., NAKAMURA, M., TAJIMA, Y. & KITAGAKI, H. 2021. Coil volume embolization ratio for preventing recanalization after portal vein embolization. *Diagn Interv Radiol,* 27**,** 366-371.

MARUYAMA, M., YOSHIZAKO, T., YOSHIDA, R., NAKAMURA, M., TAJIMA, Y. & KITAGAKI, H. 2022. Increased future liver function after modified associating liver partition and portal vein ligation/embolization for staged hepatectomy. *Acta Radiol Open,* 11**,** 20584601221134951.

MATSUMOTO, K., OHUCHI, Y., YATA, S., ADACHI, A., ENDO, M., TAKASUGI, S., FUJII, S., HASHIMOTO, M., KAMINOU, T. & OGAWA, T. 2019. Compressed Amplatzer Vascular Plug II embolization of the left subclavian artery for thoracic endovascular aortic repair is efficient and safety method comparable to conventional coil embolization. *Yonago acta medica,* 62**,** 024-029.

NISHIHARA, T., ISHIKAWA, H., OMACHI, N., YAMAGUCHI, Y., KITAGUCHI, K. & HATTORI, T. 2022. Prevalence of non-bronchial systemic culprit arteries in patients with hemoptysis with bronchiectasis and chronic pulmonary infection who underwent de novo bronchial artery embolization. *Eur Radiol*.

OMACHI, N., ISHIKAWA, H., HARA, M., NISHIHARA, T., YAMAGUCHI, Y., YAMAMOTO, Y., YOUMOTO, M., HATTORI, T., KITAGUCHI, K., YAMAMOTO, S., KAWAGUCHI, T. & FUKUZAWA, M. 2021. The impact of bronchial artery embolisation on the quality of life of patients with haemoptysis: a prospective observational study. *Eur Radiol,* 31**,** 5351-5360.

OSUGA, K., KISHIMOTO, K., TANAKA, K., NAKAMURA, M., ONO, Y., MAEDA, N., HIGASHIHARA, H., NAKAZAWA, T. & TOMIYAMA, N. 2014. Initial experience with use of hydrogel microcoils in embolization of pulmonary arteriovenous malformations. *Springerplus,* 3**,** 609.

PERDIKAKIS, E., FEZOULIDIS, I., TZORTZIS, V. & ROUNTAS, C. 2018. Varicocele embolization: Anatomical variations of the left internal spermatic vein and endovascular treatment with different types of coils. *Diagn Interv Imaging,* 99**,** 599-607.

POYRAZ, N., BALASAR, M., GÖKMEN İ, E., KOÇ, O., SÖNMEZ, M. G., AYDıN, A., GÖGER, Y. E. & ÖZTÜRK, A. 2017. Clinical efficacy and safety of transcatheter embolization for vascular complications after percutaneous nephrolithotomy. *Wideochir Inne Tech Maloinwazyjne,* 12**,** 403-408.

PRASAD, R., ISRARAHMED, A., YADAV, R. R., SINGH, S., BEHRA, M. R., KHUSWAHA, R. S., PRASAD, N. & LAL, H. 2021. Endovascular Embolization in Problematic Hemodialysis Arteriovenous Fistulas: A Nonsurgical Technique. *Indian J Nephrol,* 31**,** 516-523.

SANTORO, J., DI MARTINO, M., PIOTTO, S. & MIDULLA, M. Image-Guided Mini-Invasive Treatments for Vascular and Oncologic Diseases: Embolization Therapy. International Conference on Bio and Nanomaterials, 2019. Springer, 233-242.

SHIMOHIRA, M., KAWAI, T., HASHIZUME, T., MUTO, M., KITASE, M. & SHIBAMOTO, Y. 2018. Usefulness of Hydrogel-Coated Coils in Embolization of Pulmonary Arteriovenous Malformations. *Cardiovasc Intervent Radiol,* 41**,** 848-855.

SHREVE, L., JARMAKANI, M., JAVAN, H., BABIN, I., NELSON, K., KATRIVESIS, J., LEKAWA, M., KUNCIR, E., FERNANDO, D. & ABI-JAOUDEH, N. 2020. Endovascular management of traumatic pseudoaneurysms. *CVIR Endovasc,* 3**,** 88.

STRÜBING, F. F., PORUBSKY, S., BIGDELI, A. K., SCHMIDT, V. J., KREBS, L., KNESER, U. & SADICK, M. 2022. Interdisciplinary management of peripheral arteriovenous malformations: review of the literature and current proceedings. *Journal of Plastic Surgery and Hand Surgery,* 56**,** 1-10.

WATERS, M. J., HINSHELWOOD, J., CLINICS, M. I. C. D. & UNDEFINED Interventional treatment of vascular anomalies. *derm.theclinics.com*.

WEHBE, M. R., SAWAYA, F., SABRA, M., HAMADI, C., HOBALLAH, J. & HADDAD, F. 2020. Vascular Complications in the Era of Transcatheter Treatment of Adult Structural Heart Disease: A Single-Center Early Experience. *Vascular & Endovascular Surgery,* 54**,** 504.

YAMAMOTO, A., JOGO, A., KAGEYAMA, K., SOHGAWA, E., HAMAMOTO, S., HAMURO, M., KAMINO, T. & MIKI, Y. 2020. Utility of Coil-Assisted Retrograde

Transvenous Obliteration II (CARTO-II) for the Treatment of Gastric Varices. *Cardiovasc Intervent Radiol,* 43**,** 565-571.

YOUNG, S., GASPARETTO, A. & GOLZARIAN, J. 2022. Liquid Embolics: A Guide to Currently Available and Pipeline Products. *Digestive Disease Interventions,* 06**,** 013-018.