Summary of Safety and Clinical Performance

for

HydroPearl™ Microspheres

SSCP22-0004E

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DOCUMENT CHANGE HISTORY

SSCP Revision	Change Description	NB approved/verified
A	Initial release	☒Yes ☐ No* Validation language: English
B	Updated SSCP per new template with latest data, updated Hydropearl with HydroPearl throughout	☐ Yes ☒ No* Validation language:
C	Correct MVI UDI number	☐ Yes ☒ No* Validation language:
D	Revised External Standards	☐ Yes ☒ No* Validation language:
E	Revised External Standards	☐ 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	HydroPearl Microspheres
EMDN Code	EMDN: C010402020303
Medical Device Nomenclature (EMDN)	Embolization particles and microspheres
Device Class	IIb
Basic UDI-DI	37015174HYDROPEARL7K (MDR MVE) 08402732HYDROPEARL5X (MDR MVI)
Year when first certificate (CE) was issued for the device	2015
Legal Manufacturer	
Name & Address & Manufacturer SRN	MicroVention, Inc. (referred to as MVI) 35 Enterprise Aliso Viejo, CA 92656, USA SRN: US-MF-000016658 MicroVention Europe SARL (referred to as MVE) 30 bis, rue du Vieil Abreuvoir 78100 Saint Germain-en-Laye, France SRN: FR-MF-000004449
Authorized Representative	
Name & Address Authorized Representative SRN	MicroVention Europe SARL (referred to as MVE) 30 bis, rue du Vieil Abreuvoir 78100 Saint Germain-en-Laye, France SRN: FR-AR-000004448
Notified Body	
Name & Address	DQS Medizinprodukte GmbH August-Schanz-Str. 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	HydroPearl Microspheres are intended to occlude blood vessels for therapeutic or adjunctive purposes in hypervascularized carcinoma, hepatocellular carcinoma, uterine fibroids, benign prostatic hyperplasia, peripheral arteriovenous malformations, tumors of the neck, torso and skeletal system, bleeding and trauma and pre-operative reduction of bleeding.
Indications for Use	HydroPearl Microspheres are intended to occlude blood vessels for therapeutic or adjunctive purposes in hypervascularized carcinoma, hepatocellular carcinoma, uterine fibroids, benign prostatic hyperplasia, peripheral arteriovenous malformations, tumors of the neck, torso and skeletal system, bleeding and trauma and pre-operative reduction of bleeding.
Target Population	The HydroPearl Microspheres are intended to treat patients with the following conditions: • hypervascularized carcinoma • hepatocellular carcinoma • uterine fibroids • benign prostatic hyperplasia • peripheral arteriovenous malformations (AVMs) • tumors of the neck, torso and skeletal system • bleeding, trauma, and pre-operative reduction of bleeding
Contraindications and/or Limitations	<u>Contraindications (General)</u> • Targeted embolization of blood vessels belonging to the central vascular system (pulmonary arteries, ascending aorta, aortic arch, descending aorta to the aortic bifurcation, coronary arteries, common carotid artery, external carotid artery, internal carotid artery, cerebral arteries, brachiocephalic artery, cardiac veins, pulmonary veins, superior vena cava, inferior vena cava) • Presence of any vasculature where spheres could pass directly into the central nervous system. • Patients intolerant to occlusion procedures • Vascular anatomy or blood flow that precludes catheter placement of embolic agent injection • Presence or likely onset of vasospasm • Presence or likely onset of hemorrhage • Presence of severe artheromatous disease

	• Presence of feeding arteries smaller than distal branches from which they emerge • Presence of collateral vessel pathways potentially endangering normal territories during embolization • Presence of arteries supplying the lesion not large enough to accept HydroPearl Microspheres • Vascular resistance peripheral to the feeding arteries precluding passage of HydroPearl Microspheres into the lesion • In large diameter arteriovenous malformations (i.e. where the blood does not pass through an arterial/capillary/venous transition but directly from an artery to vein) • In the Pulmonary vasculature • Patients with known allergies to radiopaque contrast • Pregnant patients <u>Uterine Fibroid Embolization (UFE) Specific Contraindications</u> • Pregnant women • Suspected pelvic inflammatory disease or any other active pelvic infection • Any malignancy of the pelvic region • Endometrial neoplasia or hyperplasia • Presence of one or more submucosal fibroid(s) with more than 50% growth into the uterine cavity • Presence of pedunculated serosal fibroid as the dominant fibroid(s) • Fibroids with significant collateral feeding by vessels other than the uterine arteries <u>Specific Contraindications: Neurological</u> • Presence of patent extra-to-intracranial anastomoses or shunts • Presence of end arteries leading to cranial nerves • In any vasculature where HydroPearl Microspheres could pass directly into the internal carotid, vertebral artery or intra-cranial vasculature or the above listed vessels.

1.3 Device Description

Table 1.3 Device Description

Device Description	
Description of the Device	The HydroPearl Microspheres are pre-formed, compressible, precisely calibrated, sphere embolic agent consisting of a biocompatible hydrogel (polyethylene glycol diacrylamide). The microspheres are offered in a variety of diameters ranging from 75 - 1100 µm and each microsphere size is tinted with a different color using organic reactive dye. The HydroPearl Microspheres are provided in a 20 ml sterile syringe pre-filled with 2 ml designated microspheres and 4 ml phosphate buffered saline (PBS).

	HydroPearl Microspheres mechanically obstruct vessels to form clots for the purpose of causing ischemia and cell death at the target tissue (e.g., shrink targeted fibroids, carcinomas, tumors, and other malformations). HydroPearl Microspheres are available in a range of diameters to permit selection of appropriate size for select vessel embolization. HydroPearl Microspheres are intended to be delivered to select vasculature by appropriately sized microcatheters. Accurate placement of HydroPearl Microspheres is conducted with visualization using radiographic (fluoroscopy) imaging. HydroPearl Microspheres are mixed with a radiopacity agent (contrast media) prior to injection for visualization purposes.
Design Characteristics of the Device	HydroPearl Microspheres is a preformed, compressible, precisely calibrated, spherical embolic agent consisting of a biocompatible hydrogel. HydroPearl Microspheres is produced from a biocompatible hydrogel (polyethylene glycol diacrylamide and glycerol monomethacrylate). HydroPearl Microspheres mechanically obstruct vessels to form clots for the purpose of causing ischemia and cell death at the target tissue (e.g. shrink targeted fibroids, carcinomas, tumors, and other malformations). HydroPearl Microspheres are available in a range of diameters to permit selection of appropriate size for select vessel embolization. HydroPearl Microspheres are intended to be delivered to select vasculature by appropriately sized microcatheters. Accurate placement of HydroPearl Microspheres is conducted with visualization using radiographic (fluoroscopy) imaging. HydroPearl Microspheres are mixed with a radiopacity agent (contrast media) prior to injection for visualization purposes.
Previous Generations or Variants, if applicable	Not applicable.
Single use – sterilization method	Sterilized by steam. Do not use if the package is opened or damaged.
Description of Accessories	Not applicable.
Description of other Devices or Products intended to be used in combination	The HydroPearl Microspheres device consists of a syringe with a luer lock fitting tip that is compatible with standard catheter lab accessories such as microcatheters and 3-way stopcocks for mixing and preparation.

1.4 Risks and Warnings

1.4.1 Residual Risks and Undesirable Effects

Hazards associated with the use of the HydroPearl Microspheres 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:

- Vessel/Tissue damage – Residual Level: A
- Additional Procedure/Treatment Required – Residual Level: A
- Ischemic stroke – Residual Level: A
- Infection and/or fever – Residual Level: A
- Death – Residual Level: A

1.4.2 Warnings and Precautions

The warnings / precautions for the HydroPearl Microspheres are:

Warnings

- Do not use HydroPearl Microspheres in conjunction with other embolization devices based on organic solvents such as ethyl alcohol or dimethyl sulfoxide (DMSO), at the same embolization site.
- There is no long-term data on the effect of UFE on the ability to become pregnant and carry a fetus to term, and on the development of the fetus.
- This procedure should only be performed on women who do not intend future pregnancy.
- Women who become pregnant following UFE may be at increased risk for the following:
    - Postpartum hemorrhage
    - Preterm delivery
    - Caesarean delivery
    - Malpresentation
- De-vascularization of the uterine myometrium resulting from UFE may increase the risk of uterine rupture of women who subsequently become pregnant following UFE.

UFE Specific Potential Complications

Potential post-procedure complications include:

- Abdominal pain
- Discomfort
- Fever

- Nausea
- Constipation
- Premature ovarian failure (i.e. menopause)
- Amenorrhea
- Infection of the pelvic region
- Uterine/ovarian necrosis
- Phlebitis
- Deep vein thrombosis with or without pulmonary embolism
- Vaginal discharge
- Tissue passage, fibroid sloughing, or fibroid expulsion post UFE
- Post-UFE intervention to remove necrotic fibroid tissue
- Vagal reaction
- Transient hypertensive episode
- Hysterectomy

Other UFE Warning

- When using HydroPearl Microspheres for uterine fibroid embolization, do not use beads smaller than 500 microns.
- An appropriate gynecologic work-up should be performed on all patients presenting for embolization of uterine fibroids (e.g. gynecologic history, fibroid imaging, and endometrial sampling to rule out carcinoma in patients with abnormal menstrual bleeding).
- The diagnosis of uterine sarcoma could be delayed by taking a non-surgical approach (such as UFE) to treating fibroids. It is important to pay close attention to warning signs for sarcoma (e.g., rapid tumor growth, postmenopausal with new enlargement, MRI findings) and to conduct a more thorough work-up of such patients prior to recommending UFE. Recurrent or continued tumor growth following UFE should be considered a potential warning sign for sarcoma and surgery should be considered.

Precautions

- Do not use if the syringe or packaging appears damaged.
- Select the size and quantity of HydroPearl Microspheres appropriate for the pathology to be treated.
- Embolization with HydroPearl Microspheres should only be performed by physicians who have received appropriate interventional occlusion training in the region intended to be embolized.

UFE Specific Precautions

- There is an increased chance of reflux of HydroPearl Microspheres into unintended blood vessels as uterine artery flow diminishes. Comparison of angiographic endpoint &

  infarction rate in individual patients indicates that best results were obtained with an endpoint close to stasis.

- The long-term outcome of UFE is at present unknown.

1.4.3 Potential Complications / Adverse Effects

The potential complications / adverse effects for the HydroPearl Microspheres are:

Complications

Vascular Embolization is a high-risk procedure. The procedure should be performed by physicians trained in vascular embolization procedures. Complications can occur at any time during or after the procedure and may include, but not limited to:

- Undesirable reflux or passage of HydroPearl Microspheres into normal arteries adjacent to the targeted lesion or through the lesion into other arterial beds or arteries
- Embolization of the wrong artery or migration of the microspheres to the other parts of the body, which may necessitate further treatment.
- Hematoma, or bruising, at the incision site for arterial access
- Arterial aneurysm at the incision site for arterial access
- Deep vein thrombosis, or clotting of a deep vein in patient(s) leg
- Pulmonary embolization
- Ischemia at an undesired location
- Capillary bed saturation and tissue damage
- Vessel or lesion rupture and hemorrhage
- Neurological deficits including cranial nerve palsies
- Vasospasm
- Recanalization
- Foreign body reactions necessitating medical intervention
- Infection necessitating medical intervention
- Clot formation at the tip of the catheter and subsequent dislodgement
- Allergic reaction
- Risks of radiation from angiography and fluoroscopy used to visualize blood vessels during embolization, which may include radiation burn and risks to future fertility
- Death
- For gynecological embolization, including fibroid embolization, risks include expulsion of a fibroid tumor or embolization materials from the uterus through vagina after procedure, amenorrhea following the procedure, worsening of fibroid-related symptoms or the onset of new symptoms, premature menopause, infection of the endometrium or other structures in the pelvis, which, if severe, could require a hysterectomy, and rupture of the uterus.

1.4.4 Other Aspects of Safety

Data relevant to the clinical safety and performance of the HydroPearl Microspheres was collected and evaluated from routine data sources from PMS such as complaints, Corrective and

Preventative Action (CAPA), as well as post-market clinical follow-up (PMCF). The data has demonstrated the clinical safety of the subject devices.

- From 01 November 2020 to 31 October 2024, there were a total of 101,467 units shipped worldwide and 31 complaint records, for an overall complaint rate of 0.030%.
- From 01 November 2019 to 31 October 2024, eight (8) CAPAs were opened or in process that pertained to the HydroPearl Microspheres
- From 01 November 2020 to 31 October 2024, there was one (1) Field Action involving the HydroPearl

The clinical evidence generated through this PMS will be used in the clinical evaluation of the HydroPearl Microspheres with the aim of confirming the safety and performance throughout the expected lifetime of the device, of ensuring the continued acceptability of identified risks and of detecting emerging risks.

1.5 Summary of the Clinical Evaluation and PMCF

A Clinical Evaluation of the HydroPearl Microspheres is continuously updated in conducted in accordance with the requirements in MEDDEV.2.7.1 Revision 4– Guidelines on Medical Devices – Evaluation of Clinical Data: A Guide for Manufacturers and Notified Bodies. It includes the following:

- Literature Based Safety Appraisal
- A search of published relevant and available scientific literature was performed to assess the risks and benefits associated with other similar competitive devices
- Summary of Clinical Studies
- Performance and Safety - Design Verification and Validation Data Analysis
- Product Literature and Instructions for Use
- The CER includes the methodology, literature references and conclusions and are reviewed and signed by an appropriately qualified physician.

The Clinical Evaluation Report, documents available clinical data relevant to the HydroPearl Microspheres. The available clinical data was collected, appraised, and analyzed, and it was determined that there is sufficient clinical evidence on the safety and performance in accordance with the intended purpose.

The Clinical Evaluation Report documents the benefit-risk profile, including side-effects, in the intended target patient populations and medical indications by assessing the clinical evidence against the hazards and patient harms as informed by the Risk Management and Post-Market Surveillance (PMS) documentation. The report also demonstrates the acceptability of the benefit-risk profile based on the current knowledge and state of the art in the concerned medical fields. Therefore, the clinical evaluation has established that the available clinical data are sufficient to establish conformity with all relevant Safety and Performance Requirements (Annex I) of EU MDR 2017/745 and confirm the safety and performance of the HydroPearl Microspheres.

In addition, Post-Market Surveillance (PMS) is a continuous process at MicroVention to gather, record, and analyze relevant data on the quality, performance, and safety of a device throughout its entire lifetime actively and systematically. The planning and execution of PMS are conducted in accordance with the European Medical Device Regulation (MDR (EU) 2017/745), Chapter VII, Section 1 Post-Market Surveillance and MicroVention Post Market Procedures.

Given the evidence and data presented in the clinical evaluation and post market surveillance, and when the HydroPearl Microspheres is used according to the manufacturer's Instructions for Use, the risk to benefit profile is deemed acceptable.

1.5.1 Equivalent Device Clinical Data

Equivalency is not claimed in the clinical evaluation for HydroPearl Microspheres.

1.5.2 Pre-CE-Mark Clinical Data

There were no pre-market clinical studies conducted for HydroPearl Microspheres.

1.5.3 Clinical Data

Scientific Literature Data Source

- The technical success for HydroPearl ranges from 97%-100%. Procedural success is 100%. Clinical success was 78.5% at 12 months. International prostate symptom score (IPSS) improvement at 3 months is 14.6 points. IPSS improvement at 12 months was reported as 14.6 and 14.25 points. Quality of life (QoL) improvement at 3 months is 3.3 points. QoL improvement at 12 months is 3.5 points and 4.17 points. Prostate specific antigen (PSA) reduction at 3 months is 15%-22%. Peak urinary flow rate (Qmax) improvement at 3 months is 6.3 mL/s (+78%) and 8.6 mL/s (+100%) at 12 months. PVR reduction at 3 months is 56% and 58% at 12 months. Prostate volume (PV) at 3 months is 23.4 cm3 (-29%) and 19.6cm3 (-25%) at 12 months. On follow-up, 13/16 patients (81%) and 12/13 patients (92%) experienced improvement in menorrhagia and bulk symptoms. The clinical benefits are similar to that of similar devices**.**
- Complications cited in the published literature were collected. Overall common complications included burning sensation (7.1%), nausea (1% and 7.1%), urinary tract infection (3.7% and 13.3%), erythema (3.3%), hematuria (10%), urinary retention (3.3% and 3.7%), amenorrhea (22%), post embolization syndrome (3.7%), erectile dysfunction (1.2%), femoral artery dissection (1.2%), mortality (2%), spasm (9.1%), hematoma (8.1%), abdominal pain (4%). The complication rates are similar to that of similar devices.

PMS Data Source

- From 01 November 2020 to 31 October 2024, there were a total of 101,467 units shipped worldwide and 31 complaint records, for an overall complaint rate of 0.030%.
- From 01 November 2019 to 31 October 2024, eight (8) CAPAs were opened or in process that pertained to the HydroPearl Microspheres.

- From 01 November 2020 to 31 October 2024, there was one (1) Field Action involving the HydroPearl Microsphere.

PMCF Report

Relevant data collected from PMCF activities in the PMCF Report described as routine data sources were integrated into the above data sections. These data sources include:

- Scientific Literature
- Post-market clinical studies
- There were no additional PMCF activities initiated to address specific findings of the previous clinical evaluation.

1.5.4 Clinical Performance and Safety

The clinical safety data presented in this document, collected from published literature, clinical investigations, and post-market surveillance, demonstrates the overall safety of the HydroPearl Microspheres. The literature review demonstrated acceptable clinical safety outcomes with no new hazards found. The post-market surveillance data demonstrates low rates of reportable complaints, showing the safety of the device. The data collected is considered sufficient to determine that the HydroPearl Microspheres does not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons. Overall common complications included burning sensation (7.1%), nausea (1% and 7.1%), urinary tract infection (3.7% and 13.3%), erythema (3.3%), hematuria (10%), urinary retention (3.3% and 3.7%), amenorrhea (22%), post embolization syndrome (3.7%), erectile dysfunction (1.2%), femoral artery dissection (1.2%), mortality (2%), spasm (9.1%), hematoma (8.1%), abdominal pain (4%). The complication rates are similar to that of similar devices.

The clinical performance data presented in this document, collected from published literature, clinical investigations, and post-market surveillance, demonstrates the overall performance of the HydroPearl Microspheres. The literature review demonstrated acceptable clinical performance outcomes. The clinical investigations demonstrated acceptable clinical performance outcomes. The post-market surveillance data demonstrates very low overall complaint rate. The data collected is considered sufficient to determine that the HydroPearl Microspheres achieves the performance intended and is suitable for the intended purpose. The technical success for HydroPearl ranges from 97%-100%. Procedural success is 100%. Clinical success was 78.5% at 12 months. International prostate symptom score (IPSS) improvement at 3 months is 14.6 points. IPSS improvement at 12 months was reported as 14.6 and 14.25 points. Quality of life (QoL) improvement at 3 months is 3.3 points. QoL improvement at 12 months is 3.5 points and 4.17 points. Prostate specific antigen (PSA) reduction at 3 months is 15%-22%. Peak urinary flow rate (Qmax) improvement at 3 months is 6.3 mL/s (+78%) and 8.6 mL/s (+100%) at 12 months. PVR reduction at 3 months is 56% and 58% at 12 months. Prostate volume (PV) at 3 months is 23.4 cm3 (-29%) and 19.6cm^3 (-25%) at 12 months. On follow-up, 13/16 patients (81%) and 12/13

patients (92%) experienced improvement in menorrhagia and bulk symptoms. The clinical benefits are similar to that of similar devices.

1.5.5 Post-Market Clinical Follow-up

From the evidence provided in this clinical evaluation, there are some gaps for peripheral arteriovenous malformations, tumors of the neck, torso and skeletal system, bleeding and trauma and pre-operative reduction of bleeding. Additional PMCF activities related to the indications are recommended.

1.6 Possible Diagnostic or Therapeutic Alternatives

1.6.1 Treatment Options and Interventions

Hepatocellular carcinoma (HCC)/ Liver Cancer

Treatment options for HCC include transcatheter arterial chemoembolization (TACE), liver transplantation, microballoon interventions (MBIs), liver resection (LR)/ hepatic resection (HR), thermal, radiofrequency, or microwave, ablation, medical management, transarterial radioembolization (TARE), hepatic artery infusion chemotherapy (HAIC), and immunotherapy. LR is considered the gold standard therapy for HCC but is an invasive procedure that carries the risk of Surgical complications, blood loss, the need for transfusion, and increased rate of infections. Because of these risks, less invasive procedures like TACE have become increasingly popular. (Lee, 2019, Lucatelli, 2022) (Glassberg, 2019) (Yang, 2020) (Dou, 2022) (Haubold, 2020) (Liu, 2022a) (Cao, 2019)

Benign Prostatic Hyperplasia (BPH)

Treatment options for BPH include medical management, prostatic artery embolization (PAE), various minimally invasive surgical treatments (MISTs), transarterial embolization (TAE), transurethral resection of the prostate (TURP), and holmium laser enucleation of the prostate (HoLEP). Recently, PAE has become widely used as a treatment for BPH because it is a minimally invasive therapy which has been shown to provide significant reductions in International Prostate Symptom Score (IPSS). (Kim, 2018 , Ayyagari, 2019), (Geevarghese, 2019, Spradling, 2020), (Chughtai, 2022), (Liu, 2022b), (Veyg, 2022), (Chughtai, 2022), (Chen, 2023)

Uterine Fibroids (UFs)

These options include uterine artery embolization (UAE), myomecty, and high-intensity focused ultrasound ablation (HIFU). Recently, UAE has become a popular treatment for UF because it is the most established uterus-sparing treatment other than laparoscopic or hysteroscopic surgery among minimally invasive procedures (Ito, 2023, Sofy, 2023, Chen, 2020).

Tumors of the Neck, Torso, and Skeletal System

These treatments include surgical resection and endovascular tumor embolization. Embolization is considered a beneficial treatment over resection because it minimizes blood loss and reduces surgical time. (Wang, 2021, Ahmad, 2021)

1.6.2 Available Technologies

The devices below share similar technology and are designed to perform the same function as Microvention in-scope devices. Analysis of the treatment offered by the identified similar devices provides comparable safety and performance data for the same clinical conditions as the in-scope device. Additionally, data from similar patients at a similar severity and stage of condition fall

within what is generally acknowledged as a typical standard of care within the European Union and/or other regions.

Microspheres are well established medical devices with numerous types and styles available from a variety of manufacturers. Examples of Microspheres similar to the HydroPearl Micropsheres are listed in Table 1.4.

Table 1.4 Similar Devices

Device	Manufacturer	Intended Use
Similar Devices for HydroPearl		
Embozene™ Microspheres	Celonova / Boston Scientific/ Varian	Embozene Microspheres are indicated for embolization under the following conditions: • Hypervascular tumors • Arteriovenous malformations • Uterine fibroids • Hepatocellular carcinoma • Tumors of head, neck, torso, and skeletal system • Bleeding and Trauma • Pre-operative reduction of bleeding other than in the central nervous system This device is not intended for neurovascular use.
Embosphere® Microspheres	Merit Medical	Embosphere Microspheres are indicated for use in the embolization of: • Hypervascular tumors, including symptomatic Uterine Fibroids • Arteriovenous Malformations • BPH (Prostatic arteries for symptomatic benign prostatic hyperplasia in people with medication-refractory urinary obstructive symptoms who are poor surgical candidates or refuse surgical therapy.

1.7 Suggested Profile and Training for Users

Embolization with HydroPearl Microspheres should only be performed by physicians who have received appropriate interventional occlusion training in the region intended to be embolized.

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)
EN ISO 14155	2020	Clinical investigation of medical devices for human subjects - Good clinical practice (ISO 14155:2020)
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

Standard Number	Edition	Standard Title (equivalent edition)
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
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)
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 10993-23	2021	Biological evaluation of medical devices - Part 23: Tests for irritation (ISO 10993-23:2021)

Standard Number	Edition	Standard Title (equivalent edition)
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
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 17665-1	2006	Sterilization of health care products - Moist heat - Part 1: Requirements for the development, validation and routine control of a sterilization process for medical devices (ISO 17665-1:2006)

Standard Number	Edition	Standard Title (equivalent edition)
EN ISO 17665 (supersedes EN ISO 17665-1)	2024	Sterilization of health care products - Moist heat - Requirements for the development, validation and routine control of a sterilization process for medical devices (ISO 17665:2024)
EN ISO 80369-7	2021	Small-bore connectors for liquids and gases in healthcare applications - Part 7: Connectors for intravascular or hypodermic applications (ISO 80369-7:2021)
EN ISO 14630	2012	Non-active surgical implants - General requirements (ISO 14630:2012)
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

AHMAD 2021. Endovascular embolization of highly vascular head and neck tumors.

AYYAGARI, R. 2019. Case-Control Comparison of Conventional End-Hole versus Balloon-Occlusion Microcatheter Prostatic Artery Embolization for Treatment of Symptomatic Benign Prostatic Hyperplasia. 1459–1470.

CAO 2019. Immunotherapy with dendritic cells and cytokine-induced killer cells for hepatocellular carcinoma: A meta-analysis.

CHEN, F. 2023. Comparison of holmium laser enucleation and transurethral resection of prostate in benign prostatic hyperplasia : a systematic review and meta-analysis.

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