Summary of Safety and Clinical Performance

for

BioPearl™ Microspheres

SSCP1102600C

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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	BioPearl Microspheres
EMDN Code	EMDN: C010402020303 - Embolization particles and microspheres
Medical Device Nomenclature (EMDN)	Class III
Device Class	MVI: 08402732BIOPEARLM7
Basic UDI-DI	2020 (EU MDD), 2025 (EU MDR)
Year when first certificate (CE) was issued for the device	BioPearl Microspheres
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 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	BioPearl Microspheres are indicated for embolization of blood vessels supplying hypervascular primary tumors or metastases in the liver. Note: BioPearl Microspheres can be loaded with chemotherapeutic drugs. The BioPearl Microspheres are compatible with Doxorubicin, Epirubicin, and Idarubicin, which can be loaded prior to embolization and then, as a secondary action, elute a local, controlled, and sustained dose to the tumor after embolization. When used for drug loading, drug loading should be done under a physician's direction, choice and responsibility, based on type and dose of drug most beneficial to the patient.
Indications for Use	Embolization of blood vessels supplying hypervascular primary tumors or metastases in the liver
Target Population	Patients with hypervascular primary hepatocellular carcinomas and/or metastases from other cancers to the liver
Contraindications and/or Limitations	The BioPearl Microspheres are contraindicated for use in: • 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) • Patients' intolerance to vascular occlusion procedures • Vascular anatomy or blood flow that precludes catheter placement or embolic agent injection • Presence or likely onset of vasospasm or hemorrhage • Presence of severe atheromatous disease • Presence of collateral vessel pathways potentially endangering normal territories during embolization • Presence of arteries supplying the lesion not large enough to accept BioPearl Microspheres • Vascular resistance peripheral to the feeding arteries precluding passage of BioPearl Microspheres into the lesion • Patient is pregnant • Patient has known allergies to radio-opaque contrast agent, drugs and their additives • Do not use BioPearl Microspheres in the following applications: o Embolization of large diameter arteriovenous shunts (i.e., where the blood does not pass through the arterial/capillary/venous transition but directly from artery to vein) Any vasculature where BioPearl Microspheres could pass directly into non-target territories

1.3 Device Description

Table 1.3 Device Description

Device Description	
Description of the Device	The BioPearl Microspheres are comprised of embolizing microspheres that are hydrophilic, precisely calibrated, and capable of loading and releasing chemotherapeutic agents (such as Doxorubicin) in a controlled manner. The degradation profile of BioPearl Microspheres is designed such that there is an opportunity for increased blood flow to the target implant site for the majority of the treated vessels as early as 2 weeks following implantation, based on fluoroscopic examinations in an animal model.
Design Characteristics of the Device	The BioPearl Microspheres polymer consists of monomers (glycerol mono-methacrylate, Dimethyl acrylamide) that are polymerized using bis(2-(methacryloyloxy) ethyl) O,O'-(propane-1,3-diyl) dioxalate (hydrolytically unstable cross-linker). **Chemical Properties** BioPearl Microspheres is a hydrogel made using a combination of monomers including glycerol mono-methacrylate, Dimethyl acrylamide and a hydrolytically unstable in-house designed cross-linker. These components are polymerized together with a sulfopropyl acrylate salt. BioPearl microspheres are provided in a sterile vial, sealed with a rubber septum and an aluminum flip-tear cap. There are no known chemical interactions between BioPearl microspheres and pharmaceuticals. **Physiochemical Properties** The BioPearl Microspheres are available in a dried state. Once the dry microspheres are reconstituted in saline, the microspheres absorb a certain amount of water to obtain a circular shape and size. The sulfopropyl acrylate salts polymerized within the matrix allow for the controlled loading and elution of chemotherapeutic drugs via ionic exchange. Degradation of this device is designed such that it resorbs over time in a hydrolytic environment.
Previous Generations or Variants, if applicable	N/A
Single use – sterilization method	The product is provided sterile (E-beam sterilization) and is for single use only.
Description of Accessories	Not applicable, as no accessories are provided with the device.
Description of other Devices or Products intended to be used in combination	BioPearl Microspheres can be loaded with chemotherapeutic drugs. When used for drug loading, drug loading should be done under a physician's direction, choice and responsibility, based on type and dose of drug most beneficial to the patient.

1.4 Risks and Warnings

Hazards associated with the use of the BioPearl 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:

- BioPearl Microspheres fails to achieve satisfactory necrosis
- Biological Hazard
- Implant degrades / fractures during travel through the delivery catheter
- Implant occludes micro catheter
- Implant unable to load drug
- Implant unable to release drug
- Implant degrades too fast
- Implant degrades too slow
- Improper use
- Inability to prepare device for delivery
  - BioPearl Microspheres clumping during preparation
- Device malfunction
- Environment Hazard
- Implant becomes unstable in drug loading solution
- Vasospasm due to vessel wall irritation
- pH level of implant changes before delivery
- Labeling Error
- Label Illegible

1.4.1 Residual Risks and Undesirable Effects

Hazards associated with the use of BioPearl 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.

1.4.2 Warnings and Precautions

The warnings / precautions for BioPearl Microspheres are

WARNINGS:

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 BioPearl Microspheres into normal arteries adjacent to the targeted lesion or through the lesion into other arteries or arterial beds
- Non-target embolization
- Pulmonary embolization
- Ischemia at an undesirable location
- Capillary bed saturation and tissue damage
- Ischemic stroke or ischemic infarction
- Vessel or lesion rupture and hemorrhage
- Neurological deficits including cranial nerve palsies
- Vasospasm
- Death
- Recanalization
- Foreign body reactions necessitating medical intervention
- Infection necessitating medical intervention
- Clot formation at the tip of the catheter and subsequent dislodgement
- 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 a patient's leg
- Thrombosis of the artery at the incision site for arterial access
- Allergic reaction
- Risks of radiation from angiography and fluoroscopy used to visualize the blood vessels during embolization, which may include radiation burn and risks to future fertility
- DO NOT USE BioPearl Microspheres in conjunction with embolization devices based on organic solvents such as ethyl alcohol and dimethyl sulfoxide (DMSO) at the same embolization site

CAUTIONS:

- Do not use if the vial, septum, or aluminum cap appears damaged.
- BioPearl Microspheres MUST NOT be used in their original dry state. They must be reconstituted before use. See the "Device Preparation, Drug Selection and Loading" section for reconstitution steps.
- Embolization with BioPearl Microspheres should only be performed by a physician with appropriate interventional training.
- Each package of BioPearl Microspheres is intended for single patient use only. Discard any unused material**.** Do not re-sterilize.
- The physician should carefully select the size and the quantity of the BioPearl microspheres according to the lesion to be treated, based on the physician's education, training, and currently available scientific evidence.

- Physicians must decide the appropriate time to stop the infusion of BioPearl Microspheres.
- Proximal slowing and termination of flow may indicate that the vessel or the target area is occluded. Careful fluoroscopic monitoring is required.
- Microparticle embolization must be performed slowly. The injection speed and manner must be controlled. Excessive injection rate may result in retrograde flow in the vessel leading to non-targeted embolization of healthy tissue or organs.
- Do not use BioPearl Microspheres that have been improperly stored or mishandled.
- If arteriovenous anastomoses, branch vessels which lead away from the targeted embolization area, or emergent not evident prior to embolization are present, it can lead to non-targeted embolization and cause severe complications for the patient.
- Particles smaller than 100 µm can migrate to distal anastomotic feeders and embolize circulation to distal tissue. For this reason, smaller particles have a greater likelihood of causing unwanted ischemic injury. This should be considered prior to starting the embolization procedure. Possible consequences include, but are not limited to, paralysis, necrosis, swelling, abscess information and severe post-embolization syndrome.
- Ischemia of tissue adjacent to the target area may result from post-embolization swelling. Therefore, special care should be taken to avoid such ischemia of non-tolerant, non-targeted tissue such as a nervous system.
- If there are any symptoms of unwanted embolization during injection, consider stopping the procedure to evaluate the possibility of shunting. Such symptoms may include changes in patient's vital signs, such as hypoxia or central nervous system changes.

1.4.3 Potential Complications / Adverse Effects

The potential complications / adverse effects for the BioPearl Microspheres include, but not limited to:

- Undesirable reflux or passage of BioPearl Microspheres into normal arteries adjacent to the targeted lesion or through the lesion into other arteries or arterial beds
- Non-target embolization
- Pulmonary embolization
- Ischemia at an undesirable location
- Capillary bed saturation and tissue damage
- Ischemic stroke or ischemic infarction
- Vessel or lesion rupture and hemorrhage
- Neurological deficits including cranial nerve palsies

- Vasospasm
- Death
- Recanalization
- Foreign body reactions necessitating medical intervention
- Infection necessitating medical intervention
- Clot formation at the tip of the catheter and subsequent dislodgement
- 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 a patient's leg
- Thrombosis of the artery at the incision site for arterial access
- Allergic reaction
- Risks of radiation from angiography and fluoroscopy used to visualize the blood vessels during embolization, which may include radiation burn and risks to future fertility
- DO NOT USE BioPearl Microspheres in conjunction with embolization devices based on organic solvents such as ethyl alcohol and dimethyl sulfoxide (DMSO) at the same embolization site

1.4.4 Other Aspects of Safety

There are currently no Field Safety Corrective Actions to report for BioPearl Microspheres

1.5 Summary of the Clinical Evaluation and PMCF

There is one ongoing Post Market Clinical Follow-up (PMCF) study of BioPearl Microspheres. The protocol for this study has been published in a peer-reviewed journal (Verset et al., 2025). Thus far, 18 patients have been enrolled in the study. Preliminary reports show 100 % technical success, and 13 total adverse events (one serious and 12 non-serious). There were zero deaths reported.

One paper has been published from the BioPearl-1 study including 13 patients (Iezzi et al., 2025). The authors of this study observed 100% technical success, one case of intra-procedural catheter blockage and two post-treatment bilomas that required intervention. The one-month overall disease control rate was 90.9%, with six complete responses.

Limited data demonstrating the safety and performance of BioPearl Microspheres are available at this time. The data that are available show that BioPearl Microspheres is safe and performs as intended.

1.5.1 Equivalent Device Clinical Data

No equivalence for BioPearl Microspheres is claimed.

1.5.2 Pre-CE-Mark Clinical Data

There is no pre-market clinical data available for BioPearl Microspheres.

1.5.3 Clinical Data

There is one ongoing Post Market Clinical Follow-up (PMCF) study of BioPearl Microspheres. The protocol for this study has been published in a peer-reviewed journal (Verset et al., 2025). Thus far, 18 patients have been enrolled in the study. Preliminary reports show 100 % technical success, and 13 total adverse events (one serious and 12 non-serious). There were zero deaths reported.

One paper has been published on BioPearl Microspheres treatment of patients with hepatocellular carcinoma including 13 patients (Iezzi et al., 2025). The authors of this study observed 100% technical success, one case of intra-procedural catheter blockage and two post-treatment bilomas that required surgical intervention. The one-month overall disease control rate was 90.9%, with six complete responses.

1.5.4 Clinical Performance and Safety

There are limited clinical safety data available for the BioPearl Microspheres at this time from published literature (Iezzi et al., 2025), and post-market clinical studies for evaluation of the overall safety of the subject device. A preliminary report published from the BioPearl-1 study shows that the 13 patients treated with BioPearl Microspheres had 90.9% overall disease control at one month and, 6/13 (46.2%) of patients had a complete response to the treatment. The ongoing PMCF study has enrolled 18 patients. Preliminary reports show 100 % technical success, and 13 total adverse events (one serious and 12 non-serious). There were zero deaths reported.

These results support the conclusion that BioPearl Microspheres is safe and performs as indicated.

1.5.5 Post-Market Clinical Follow-up

One Post-Market Clinical Follow-up (PMCF) study for BioPearl Microspheres is currently enrolling patients. Thus far, 18 patients have been enrolled in the study. Preliminary reports show 100 % technical success, and 13 total adverse events (one serious and 12 non-serious). There were zero deaths reported.

1.6 Possible Diagnostic or Therapeutic Alternatives

There have been significant advances in Hepatic Cell Carcinoma (HCC) treatment over the past years. ASSLD (American Association for the Study of Liver Diseases) guidelines divide treatment options into curative and noncurative interventions. Curative treatment offers the chance of long-term response and improved survival such as surgical resection, liver transplantation, and ablative techniques. Non-curative treatment attempts to prolong survival by slowing tumor progression such as trans-arterial chemoembolization, trans-arterial radioembolization, stereotactic body radiation therapy and systemic chemotherapy. **Table 1.4** below describes the available standard of care described in the clinical literature.

1.6.1 Treatment Options and Interventions

Standards of Care: Treatment Options

- Transcatheter arterial chemoembolization (TACE)
- Liver Transplantation
- Microballon Interventions (MBIs)
- Liver Resection or Hepatic Resection
- Transarterial Radioembolization (TARE)
- Thermal Ablation (Radiofrequency ablation (RFA) and Microwave ablation (MWA))
- Medical Management (Multikinase Inhibitors, Sorefenib, Regorafenib, Lenvatinib, Cabozantinib)
- Hepatic Artery Infusion Chemotherapy (HAIC)
- Immunotherapy

Table 1.4 Treatment Options - Benefits/Risks

Treatment Option	Benefits/Pros	Risks/Cons	Notes
Transcatheter arterial chemoembolization (TACE)(Chen, 2019), (Lee, 2019)	TACE is recognized as the first-line treatment for Hepatocellular Carcinoma (HCC) and its efficacy is widely reported. TACE is a mixed emulsion of iodized oil and chemical agents, which could embolize the tumor supplying artery and cause hypoxia and locally high concentrations of chemotherapeutic agents to induce tumor necrosis.	Patients with HCC often need to undergo repeated TACE treatments, in which the Hepatic Fibrosis may be induced by repeated lipiodol embolization	TACE, an intra-arterial catheter-based chemotherapy, selectively delivers high doses of cytotoxic drugs to the tumor bed together with the induction of ischemic necrosis via arterial embolization. This treatment is one of the preferred modalities for HCC patients who are not suitable for curative therapy and is the standard of care for non-surgical patients with tumors limited to the liver because it preserves liver function. TACE also is recommended for late-stage HCC as the first

Treatment Option	Benefits/Pros	Risks/Cons	Notes
			option for palliative treatment. The most common sole-agent anticancer drug used in published TACE studies is doxorubicin (36%), followed by cisplatin (31%), epirubicin (12%), mitoxantrone (8%), mitomycin (8%), and SMANCS (5%).
Liver Transplantation (Lee, 2019)	Improvements in surgical techniques and the growing acceptance of organ transplantation have made liver transplantation a feasible, curative treatment for HCC.	The shortage of available organs limits transplantation to 30% of patients who meet the criteria.	Not feasible for all types of patients.
Microballoon Interventions (MBIs) (Lucatelli, 2022)	MBIs consists of the execution of an embolization procedure immediately after the temporary occlusion of a vascular territory. The advantages of this novel technique lie in the possibility of preventing the reflux of embolic material into non-target territories as well as in giving the operator the capability to perform a pressure gradient driven embolization, which could not be otherwise achieved.	The only reported complication directly related to the employment of a microballoon was vascular dilatation at the site of balloon inflation.	The underlying mechanism of action that permits this technical advantage is the following: the opening of the intersegmental arterial arcades determines a restoration of blood flow beyond the occluded segment, restoring hepatoportal flow towards lower resistance areas such as the tumoral hypertrophic vasculature. Recent literature has been focused on the flow and concomitant pressure alterations associated with several different antireflux devices. This novel technique, introduced by Irie in 2012, has been applied to the treatment of both primary and secondary liver tumors, as well as to different modalities of transarterial therapies: conventional and drug-eluting embolic transarterial chemoembolization (c-TACE and DEE-TACE, balloon-occluded-c-TACE -b-c-TACE- and balloon occluded-DEE-

Treatment Option	Benefits/Pros	Risks/Cons	Notes
			TACE -b-DEE-TACE) as well as selective internal radiation therapies (SIRT and b-SIRT). In specific indications and clinical scenarios, microballoon TACE has been applied in combination with percutaneous ablation.
Liver Resection (LR)/ Hepatic Resection (HR) (Glassberg, 2019)	HR is the gold standard treatment for liver cancer for patients in whom surgery is not contraindicated and whose tumors are resectable. The Barcelona Clinic Liver Cancer staging system, endorsed by many HCC associations, recommends LR for very early and early-stage HCC. Larger liver tumors (including metastases) may be better suited for HR. Resection is also the preferred treatment for tumors on the surface or edges of the liver.	Surgical complications, blood loss, the need for transfusion, and increased rate of infections. HCC patients may experience severe liver cirrhosis, and excessive liver resection may increase the risk of liver failure after hepatic surgery.	The distinguishing factor between resectable and non-resectable tumors is whether a resection could be designed that would remove all residual disease with appropriate margins and leave the patient with sufficient liver remnant to support post hepatectomy liver function. Most patients are not resectable (up to 80%); thus, HR is complemented by local ablative therapies such as radiofrequency ablation (RFA) and microwave ablation (MWA) for liver cancer treatment.
Transarterial Radioembolization (TARE) (Yang, 2020)	TARE seems to be tumor-selective based on natural disruptions to the microvasculature surrounding liver tumors and can be selectively delivered with whole, lobar, or segmental-liver approaches. Mean Overall Survival (OS) is significantly longer with TARE. The respective 1- and 2-year survival rates were higher for TARE.	The main adverse events include nausea/vomiting, pain, fatigue, infection/fever, liver failure, and gastrointestinal bleeding. TARE has significantly lower complications risk.	TARE, using resin microspheres or a glass matrix labeled with yttrium-90, is another regional technique. TARE, which consists of the arterial infusion of microspheres integrated into a radiotherapeutic agent, allows for the concentration of beta-radiation in the tumor parenchyma without damaging the surrounding liver tissue.
Thermal Ablation (Radiofrequency ablation (RFA) and Microwave ablation (MWA))(Dou, 2022).	Ablation therapy is considered as the first choice of treatments for most patients with small hepatocellular carcinoma nodules, or as an alternative treatment for patients who are not suitable for surgical resection or whose chemotherapy has failed.	Major complications of RFA include intraperitoneal bleeding, infections, liver failure, pneumothorax, organ injury, bile duct stenosis, and tumor lysis syndrome, but the major complication rate and procedural mortality rate are significantly low. The	The most commonly used ablation modalities in clinical practice are MWA and RFA. RFA is performed by advancing a specially designed electrode into the lesion and radiofrequency energy emitted from the tip of the electrode is converted into

Treatment Option	Benefits/Pros	Risks/Cons	Notes
	RFA is considered the best therapeutic modality for very early and early-stage HCC according to BCLC staging when resection or liver transplantation is not indicated. Clinically, if the tumor nodule was less than 3 cm, both of the 2 methods may be considered. However, when the HCC diameter of nodules is larger than 3 cm, MWA can remove the nodules more effectively due to its higher temperature and faster heating.	major complications of MWA are bleeding peritoneal hemorrhage, liver abscess, hemothorax, colon perforation, and bile duct stenosis.	heat to create a zone of thermal destruction that encompasses the tumor. MWA uses electromagnetic energy to create an electromagnetic field that heats rapidly the target tissue and induces coagulation necrosis. In comparison with RFA, MWA is more homogenous, and the heat-sink effect is reduced due to the higher temperatures and the faster heating that is produced by electromagnetic energy.
Medical Management (Multikinase Inhibitors, Sorefenib, Regorafenib, Lenvatinib, Cabozantinib)(Haubold, 2020).	Sorafenib significantly prolongs the time to progression without significant differences concerning the median time to symptomatic progression. Regorafenib, Lenvatinib, and Cabozantinib have significantly improved systemic treatment options for advanced HCC.	Occurrence of treatment-related adverse events was as high as 80 % in the Sorafenib group consisting predominantly of Gastrointestinal, Constitutional, or Dermatologic symptoms leading to permanent treatment discontinuation. Limitations of significant drug toxicity and relatively short median survival times during systemic therapy remain.	sorafenib has been determined as a targeted medicine that can significantly extend the survival of patients with advanced HCC. Sorafenib is an orally available active targeted cancer medication that reduces tumor proliferation and angiogenesis by inhibiting the interaction of Raf kinase with vascular endothelial growth factor (VEGF) and platelet-derived growth factor (PDGF) receptors. Thus, sorafenib can improve the radiosensitivity of the tumor.
Hepatic Artery Infusion Chemotherapy (HAIC) (Liu, 2022)	HAIC can be administered by continuous infusion for several days, which can significantly increase the total dose of chemotherapy and prolong the action time of the chemotherapeutic agents in the hepatic lesions and thrombus, thereby maximizing the killing of tumor cells. HAIC is well tolerated by patients.	Side effects include neutropenia, anemia, thrombocytopenia, and vomiting.	HAIC is a locoregional therapy that directly delivers chemotherapeutic agents into tumor-associated arterial branches and increases local drug concentrations. HAIC was first proposed in Japan, and has been carried out in Japan, South Korea, and other Asian countries for more than 30 years and is recommended by the Japan Society of Hepatology (JSH) Consensus-Based Clinical

Treatment Option	Benefits/Pros	Risks/Cons	Notes
	After HAIC, chemotherapy drugs will circulate throughout the body, thus playing a certain role in systemic chemotherapy. The well-received advantage of HAIC is a lower overall incidence of grade 3-4 adverse events compared with TACE.		Practice Guidelines as the standard treatment for liver cancer with portal vein tumor thrombus.
Immunotherapy (Cao, 2019)	Immunotherapy was introduced into the field as the ability to escape from immunological surveillance, which forms the basis for tumor progression. The underlying mechanism comprises defective antigen presentation, dysfunction of effector T cells, cytokine disarray, and alterations in immune checkpoints. While conventional chemotherapy exerts its effect by directly reducing tumor volume morphologically, immunotherapy works indirectly and takes longer to induce an effective immune response. However, it provides a more durable antitumor effect. Immune-based approaches include cytokines, vaccines, adoptive cell therapy [based on peripheral blood mononuclear cells or dendritic cells (DCs)], tumor antibody-based immunotherapy, and immune checkpoint inhibitors. Recombinant interferon-α was the first immunotherapeutic agent introduced into the field, although, even with its features of immune stimulation and anti-angiogenesis, it failed to show a significant effect	Although several analyses have supported the beneficial effect of cellular immunotherapy when combined with specific HCC treatment, the efficacy and necessity of cellular immunotherapy after different interventional therapies remains to be interrogated.	Vaccine strategies are carried out on different anti-cancer platforms, including RNA-, peptide- and protein-based vaccines, whole-tumor-cell vaccines, and most widely, DC-based vaccines. DC-based vaccines are adapted more for solid malignancies, including melanoma, renal cancer, and prostate cancer, as well as HCC. As mature DCs prime T cells and boost memory T cells, induction of DC maturation by Toll-like receptor ligands or cytokines is often applied clinically. Adoptive cell therapy is commonly performed with cytokine-induced killer cells (CIKs), tumor-infiltrating lymphocytes, and genetically modified T cells. Among these, CIKs have been used in more clinical trials. CIKs, consisting of NKG2Dhigh T cells, activated natural killer cells, and natural killer T cells[15], are generated ex vivo from peripheral blood mononuclear cells and stimulated with cytokines and antibodies targeting CD3. CIKs harbor a high capacity of proliferation and have a cytolytic effect against cancer cells.

Treatment Option	Benefits/Pros	Risks/Cons	Notes
	in clinical trials of patients with HCC.		

1.6.2 Available Technologies

DSMs (Degradable Starch Microspheres) for TACE (Transarterial Chemoembolization) are well established medical devices with numerous types and styles available from a variety of manufacturers. Examples of DSMs similar to the BioPearl™ Microspheres are listed in **Table 1.5**.

Table 1.5 Similar Device

Device	Manufacturer	Intended Purpose
EmboCept S	Magle PharmaCept	EmboCepts are degradable starch microspheres (DSM) designed for use in transarterial chemoembolization (TACE) for inoperable liver and lung tumors in conjunction with local delivery of chemotherapy.

1.7 Suggested Profile and Training for Users

DSM-TACE (Degradable Starch Microspheres-Transarterial Chemoembolization) is a high-risk procedure. The procedure should be performed by physicians trained in DSM-TACE procedures

1.8 Reference to any Harmonized Standards and CS

Standards and Guidance Documents

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)

Standard Number	Edition	Standard Title (equivalent edition)
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 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 10993-12	2021	Biological evaluation of medical devices - Part 12: Sample preparation and reference materials (ISO 10993-12:2021)

Standard Number	Edition	Standard Title (equivalent edition)
EN ISO 10993-13	2010	Biological evaluation of medical devices - Part 13: Identification and quantification of degradation products from polymeric medical devices (ISO 10993-13:2010)
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
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 11137-1	2015/A2:2019	Sterilization of health care products - Radiation - Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices (ISO 11137-1:2006/Amd 2:2018)
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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

Standard Number	Edition	Standard Title (equivalent edition)
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

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