July 16, 2018

BioSphere Medical, S.A.
Rosène Amossé
Senior Regulatory Affairs Specialist
Parc des Nations – Paris Nord 2
383 Rue de la Belle Etoile
95700 Roissy en France
France

Re: K181300
Trade/Device Name: Embosphere Microspheres
Regulation Number: 21 CFR 870.3300
Regulation Name: Vascular Embolization Device
Regulatory Class: Class II
Product Code: KRD, NAJ, NOY, HCG
Dated: May 15, 2018
Received: May 17, 2018

Dear Rosène Amossé:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820);

and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (http://www.fda.gov/DICE) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Brian D. Pullin -S

for Bram D. Zuckerman, M.D.
Director
Division of Cardiovascular Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K181300

Device Name
Embosphere Microspheres

Indications for Use *(Describe)*
Embosphere Microspheres are indicated for use in the embolization of:
- Hypervascular tumors, including symptomatic uterine fibroids
- Prostatic arteries for symptomatic Benign Prostatic Hyperplasia (BPH)
- Arteriovenous malformations
- Blood vessels to occlude blood flow to control bleeding/hemorrhaging in the peripheral vasculature

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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Change in Indication for use

K181300
510(k) Summary

July 13, 2018

General Provisions	Submitter Name: Address: Telephone Number: Fax Number: Contact Person: Registration Number:	Biosphere Medical, S.A. Parc des Nations – Paris Nord 2 383, rue de la Belle Etoile 95700 Roissy-en-France, France +33 (0)1 48 17 25 29 +33 (0)1 49 38 02 68 Alix Fonlladosa 9615728
	Correspondent Name: Address: Telephone Number: Fax Number: Contact Person: Registration Number:	Biosphere Medical, S.A. Parc des Nations – Paris Nord 2 383, rue de la Belle Etoile 95700 Roissy-en-France, France +33 (0)1 48 17 25 29 +33 (0)1 49 38 02 68 Alix Fonlladosa 9615728
Subject Device	Trade Name: Common/Usual Name: Classification Name:	Embosphere® Microspheres Embolization device 21 CFR 870.3300 – Vascular Embolization Device
Predicate Device	**Predicate Device:** Trade Name: Classification Name: Premarket Notification: Manufacturer: **Reference devices:** Trade Name: Classification Name: Premarket Notification: Manufacturer:	 Embosphere® Microspheres 21 CFR 870.3300 – Vascular Embolization Device K021397 Biosphere Medical, S.A. Embosphere® Microspheres 21 CFR 882.5950 – Neurovascular embolization device 21 CFR 876.5550 – Prostatic artery embolization device K991549, DEN160040 Biosphere Medical, S.A.
Classification	Class II 21 CFR § 870.3300 FDA Product Code: KRD FDA Secondary Product Codes: HCG, NAJ, NOY Division of Cardiovascular Devices	

Intended Use

Embosphere Microspheres are indicated for use in the embolization of:
• Hypervascular tumors, including symptomatic uterine fibroids
• Prostatic arteries for symptomatic benign prostatic hyperplasia (BPH)
• Arteriovenous malformations
• ***Blood vessels to occlude blood flow to control bleeding/hemorrhaging in the peripheral vasculature*** (subject of this Traditional 510(k))

Device Description

Embosphere Microspheres are small, compressible, hydrophilic, biocompatible spheres made of acrylic polymer and porcine-derived gelatin. The microspheres are packaged in 0.9% saline and are provided sterile and non-pyrogenic in a vial or in a syringe.

The product is provided in seven size ranges to allow physicians to choose the calibration necessary for the vessel being embolized. The size ranges available are:

- 50-100 microns
- 40-120 microns
- 100-300 microns
- 300-500 microns
- 500-700 microns
- 700-900 microns
- 900-1200 microns

The principles of operation for the subject device Embosphere Microspheres are the same as the predicate device Embosphere Microspheres (K021397) and reference devices Embosphere Microspheres (K991549, DEN160040). Embosphere Microspheres are permanent implantable devices and are designed for controlled, targeted embolization. All indications for Embosphere Microspheres involve arterial embolization; embolization of uterine fibroids, arteriovenous malformations, hypervascular tumors and benign prostatic hyperplasia involve an embolization of the arteries supplying those areas. The procedure of arterial embolization is similar for all arteries. Appropriately sized microspheres for target vessel occlusion are chosen by the trained interventional radiologist. The delivery procedure involves arterial access through an artery, using a guidewire and microcatheter under fluoroscopic guidance. Once the catheter tip is placed in the artery(ies) supplying the targeted tissue Embosphere Microspheres mixed with a non-ionic contrast agent are delivered in a controlled manner under visualization to occlude the feeding vessel(s) to stop blood flow to the targeted area. The device is intended for single use.

Comparison to Predicate

The technological characteristics of the subject device Embosphere Microspheres are identical to the predicate Embosphere Microspheres (K021397) and the reference devices Embosphere Microspheres (K991549, DEN160040). Only the indications for use change between the subject device and the legally marketed predicate device Embosphere Microspheres (K021397) and reference devices Embosphere Microspheres (K991549, DEN160040). The indications for use statement of the subject Embosphere Microspheres includes a specific indication by identifying "control bleeding / hemorrhaging in the peripheral vasculature" as being the result of embolization since embolization stops arterial blood flow, as established by 21 CFR § 870.3300.

Technological Characteristics Comparison Table

Attribute	Predicate Device Embosphere Microspheres (K021397) and Reference devices Embosphere Microspheres (K991549, DEN160040)	Subject Device Embosphere Microspheres	Comment
Shelf Life (single use)	Three years (36 months)	Three years (36 months)	Same
Material (spheres)	Acrylic polymer and porcine-derived gelatin	Acrylic polymer and porcine-derived gelatin	Same
Physical Characteristics	Biocompatible, hydrophilic, compressible, non-resorbable	Biocompatible, hydrophilic, compressible, non-resorbable	Same
Microspheres Size	• 50-100 microns • 40-120 microns • 100-300 microns • 300-500 microns • 500-700 microns • 700-900 microns • 900-1200 microns	• 50-100 microns • 40-120 microns • 100-300 microns • 300-500 microns • 500-700 microns • 700-900 microns • 900-1200 microns	Same
Sterilization	Steam sterilized	Steam sterilized	Same
Pyrogenicity	Non-pyrogenic	Non-pyrogenic	Same
Performance	Designed for controlled, targeted embolization at the desired level of vessel occlusion	Designed for controlled, targeted embolization at the desired level of vessel occlusion	Same
Principle of Operation	The microspheres are administered with contrast medium into the patient's artery via a catheter	The microspheres are administered with contrast medium into the patient's artery via a catheter	Same
Volume of microspheres per container	1 ml or 2 ml of microspheres in 0.9% saline solution	1 ml or 2 ml of microspheres in 0.9% saline solution	Same
Packaging	8-mL glass vial, or 20-mL plastic syringe Microbial barrier: Blister tray sealed by a Tyvek® peel-away lid	8-mL glass vial, or 20-mL plastic syringe Microbial barrier: Blister tray sealed by a Tyvek® peel-away lid	Same

No performance standards have been established under Section 514 of the Food, Drug and Cosmetic Act for these devices. However, vascular and neurovascular embolization devices are subject to the special controls specified in "*Guidance for Industry and FDA Staff – Class II Special Controls Guidance Document: Vascular and Neurovascular Embolization Devices*", issued on December 29, 2004. In addition, the subject device follows the FDA Draft Guidance on "*Medical Devices Containing Materials Derived from Animal Sources (Except for In Vitro Diagnostic Devices)"*, issued on January 23, 2014.

Non-clinical performance testing conducted on the predicate device includes:
- Chemical analysis
- Size range
- Catheter compatibility
- Packaging performance
- Shelf Life
- Sterility
- Biocompatibility

Biocompatibility evaluation was performed in accordance with ISO 10993-1:2009 for permanent implants in contact with blood for the predicate device Embosphere Microspheres (K021397) and the reference devices Embosphere Microspheres (K991549, DEN160040), and is being adopted for this subject device based upon the fact that all devices are made from the same materials using the same manufacturing and sterilization processes.

Safety & Performance Tests

No new testing was performed since predicate device Embosphere Microspheres (K021397) / reference devices Embosphere Microspheres (K991549, DEN160040), and subject device Embosphere Microspheres have identical technological characteristics, manufacturing, processing and sterilization.

Clinical data from the literature were reviewed on the use of Embosphere Microspheres for embolization of blood vessels to occlude blood flow to control bleeding / hemorrhaging in the peripheral vasculature. The retrieved clinical data consisted of 40 publications from 2000 to 2018, including eight prospective trials and thirty-two retrospective trials. The total number of patients treated with Embosphere Microspheres was 662 (at least). The majority of patients were adults of both genders. Some publications listed age ranges below adult (from 1 to 17 years).

The extensive clinical data provide relevant information about the safety and effectiveness of the subject Embosphere Microspheres in the proposed indication for use. Embolization of arteries with Embosphere was found to be an effective method to control bleeding / hemorrhaging in the peripheral vasculature, with a low complication rate.

Adverse events that were found related to the procedure are mostly complications related to catheterization, post-embolization syndrome and non- targeted embolization. The raised events found are addressed in the predicate device Embosphere Microspheres (K021397) and the reference devices Embosphere Microspheres (K991549, DEN160040) IFU as warnings or potential complications.

The proposed indication for use does not raise a safety or effectiveness issue that was not raised by the predicate device, or have the potential to significantly increase a safety or effectiveness concern raised by the predicate device. The

	function of both the subject device and predicate device (K021397) is to occlude blood vessel(s) in order to stop blood flow to a targeted area, which is the clinical endpoint for both devices. The safety and effectiveness of the device are related to size, shape, compressibility and biocompatibility for both general and specific indications. These characteristics do not change from the predicate to the subject Embosphere Microspheres.
Summary of Substantial Equivalence	Based on the same intended use (other than the requested change that is the objective of this submission), design, fundamental scientific technological characteristics, fundamental operational characteristics and safety and performance testing, the BioSphere Medical subject Embosphere Microspheres device meets the requirements that are considered essential for its intended use and is substantially equivalent to the predicate device Embosphere Microspheres (K021397).