September 27, 2018

Biosphere Medical, S.A.
Alix Fonlladosa
Regulatory Affairs Manager
Parc des Nations – Paris Nord 2, 383 rue de la Belle Etoile
Roissy en France, 95700 Fr

Re: K181021
Trade/Device Name: EmboCube Embolization Gelatin
Regulation Number: 21 CFR 870.3300
Regulation Name: Vascular Embolization Device
Regulatory Class: Class II
Product Code: KRD
Dated: September 4, 2018
Received: September 4, 2018

Dear Alix Fonlladosa:

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. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. 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) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; 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,

Misti L. Malone -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)*
K181021

Device Name
EmboCube Embolization Gelatin

Indications for Use *(Describe)*
EmboCube Embolization Gelatin is indicated for use in embolization of hypervascular tumors.

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.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 79 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

510(k) Summary

<table>
<tr><td colspan="3">September 27, 2018</td></tr>
<tr><td>General Provisions</td><td>Submitter Name:
Address:

Telephone Number:
Fax Number:
Contact Person:
Registration Number:</td><td>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</td></tr>
<tr><td>Subject Device</td><td colspan="2">Trade Name: EmboCube Embolization Gelatin
Common/Usual Name: Embolization device
Classification Name: 21 CFR § 870.3300 Vascular Embolization Device</td></tr>
<tr><td>Predicate and Reference Devices</td><td colspan="2">Primary Predicate Device:
Trade Name: Gel-Block 10x Embolization Pledgets
Classification Name: 21 CFR § 870.3300 Vascular Embolization Device
Premarket Notification: K143038
Manufacturer: Vascular Solutions
Reference Device:
Trade Name: Embosphere Microspheres
Classification Name: 21 CFR 870.3300 - Vascular Embolization Device
Premarket Notification: K021397
Manufacturer: Biosphere Medical, S.A.</td></tr>
<tr><td>Classification</td><td colspan="2">Class II
21 CFR § 870.3300
FDA Product Code: KRD
Division of Cardiovascular Devices</td></tr>
<tr><td>Intended Use</td><td colspan="2">EmboCube Embolization Gelatin is indicated for use in embolization of hypervascular tumors.</td></tr>
<tr><td>Device Description</td><td colspan="2">EmboCube Embolization Gelatin is a hydrophilic medical device which consists of pre-cut, dry cubes of resorbable gelatin sponge packaged in a syringe. The device is available in 2 cube sizes and 3 weight configurations.

<table>
<tr><th>Reference code</th><th>Cube size (mm)</th><th>Quantity of dry cubes per syringe</th></tr>
<tr><td>EC2525</td><td>2.5x2.5x2.5</td><td>25 mg</td></tr>
<tr><td>EC2550</td><td>2.5x2.5x2.5</td><td>50 mg</td></tr>
<tr><td>EC25100</td><td>2.5x2.5x2.5</td><td>100 mg</td></tr>
<tr><td>EC5025</td><td>5.0x5.0x5.0</td><td>25 mg</td></tr>
<tr><td>EC5050</td><td>5.0x5.0x5.0</td><td>50 mg</td></tr>
<tr><td>EC50100</td><td>5.0x5.0x5.0</td><td>100 mg</td></tr>
</table>

Once rehydrated, the deformable cubes can be injected into the target vessel with an intravascular catheter or a micro-catheter (depending on the size range) to provide a mechanical barrier to blood flow. Contrast enhancement may be used to monitor the embolization procedure using fluoroscopy. The device is intended for single use and is provided sterile.</td></tr>
<tr><td>Comparison to Predicate</td><td colspan="2">EmboCube Embolization Gelatin is similar in design to the Primary Predicate Device, Gel-Block 10x Embolization Pledgets (K143038) and the Reference Device, Biosphere Embosphere Microspheres (K021397), as all of them provide a mechanical barrier to blood flow in the vasculature and are delivered using catheters. The subject device is available in six sizes, as the Reference Device, Biosphere Embosphere Microspheres (K021397), while the Primary Predicate Device, Gel-Block 10x Embolization Pledgets, K143038 is available in three</td></tr>
</table>

	sizes. The subject and predicate devices differ in shape: EmboCube Embolization Gelatin is a cubic embolic while the Primary Predicate Device, Gel-Block 10x Embolization Pledgets, K143038 are cylindrical and the Reference Device, Biosphere Embosphere Microspheres (K021397) are spherical particles. Both the subject device and the Primary Predicate Device, Gel-10x Block Embolization Pledgets, K143038 are made from resorbable porcine gelatin. The Reference Device, Biosphere Embosphere Microspheres (K021397) consists of a non-resorbable acrylic polymer impregnated with porcine gelatin. The technological differences between the subject and predicate devices have been evaluated through biocompatibility, bench and animal testing to provide evidence of substantial equivalence of the EmboCube Embolization Gelatin to the Primary Predicate Device, Gel-Block 10x Embolization Pledgets, K143038.
Safety & Performance Tests	No performance standards have been established under Section 514 of the Food, Drug and Cosmetic Act for these devices. However, vascular 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. A battery of tests performed on EmboCube Embolization Gelatin were designed to demonstrate that the device meets critical design specifications as well as clinical performance attributes for its intended use. Where appropriate, the tests were based on the requirements of the following documents: • FDA Guidance Class II Special Controls Guidance Document: Vascular and Neurovascular Embolization Devices (December 29, 2004) • ASTM F2096-11, *Standard Test Method for Detecting Gross Leaks in Medical Packaging by Internal Pressurization (Bubble Test)* • ASTM F1140/F1140M-13, *Standard Test Methods for Internal Pressurization Failure Resistance of Unrestrained Packages for Medical Applications* • ASTM F88/F88M-09, *Standard Test Method for Seal Strength of Flexible Barrier Materials* • ASTM D4332-14, *Standard Practice for Conditioning Containers, Packages, or Packaging Components for Testing* • ASTM D4169-16, *Standard Practice for Performance Testing of Shipping Containers and Systems* • ASTM F1980-16, *Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices* • ISO 11137-1:2016, *Sterilization of health care products -- Radiation -Part 1: Requirements for development, validation and routine control of* a *sterilization process for medical devices* • ISO 10993-1 :2009, *Biological Evaluation of Medical Devices Part 1: Evaluation and Testing within* a *risk management process,* and the FDA Modified ISO 10993 Test Profile FDA Memo G95-1

Safety & Performance Tests (Continued**)**	EmboCube Embolization Gelatin was evaluated for various performance attributes to demonstrate the substantial equivalence of the device to the predicate. The following is a list of all testing that was successfully completed: • Macroscopic appearance (visual inspection) • Pepsin digestibility • Size range • Density • Moisture content (H20 analysis) • Hydration test • Effect on pH variation • Sterility • Pyrogenicity (Bacterial endotoxins) • Deliverability with the recommended catheters and radiopaque contrast agents • Flush test Biocompatibility testing included • Cytotoxicity • Sensitization • Irritation • Acute Systemic Toxicity • Material-Mediated Pyrogenicity • Genotoxicity • Hemolysis • Complement Activation • Chemical characterization and toxicological risk assessment were used to assess Subacute/Subchronic Systemic Toxicity, Chronic Systemic Toxicity, and Carcinogenicity An animal study was conducted on eight test (EmboCube Embolization Gelatin) and four control (Gel-Block 10x Embolization Pledgets, K143038) adult female sheep in the renal arteries over a period of 4 weeks. The animal study evaluated vascular safety, local tissue effects, and in vivo degradation of the EmboCube Embolization Gelatin.
Summary of Substantial Equivalence	Based on the indications for use, design and performance testing, the subject EmboCube Embolization Gelatin is substantially equivalent to the Primary Predicate Device, the currently marketed Gel-Block 10x Embolization Pledgets, manufactured by Vascular Solutions, 510(k) K143038.