October 4, 2023

Marizyme, Inc.
% John J. Smith, M.D., J.D.
Partner
Hogan Lovells US LLP
555 13th NW
Washington, District of Columbia 20004

Re: DEN230002
Trade/Device Name: DuraGraft Vascular Conduit Solution
Regulation Number: 21 CFR 876.4100
Regulation Name: Flushing and storage solution for vascular autografts at room temperature
Regulatory Class: Class II
Product Code: QEJ
Dated: July 17, 2023
Received: July 17, 2023

Dear John Smith:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your De Novo request for classification of the DuraGraft Vascular Conduit Solution, a prescription device under 21 CFR Part 801.109 with the following indications for use:

> DuraGraft Vascular Conduit Solution is a solution indicated for adult patients undergoing Coronary Artery Bypass Grafting Surgeries and is intended for flushing and storage of the saphenous vein grafts from harvesting through grafting for up to 4 hours.

FDA concludes that this device should be classified into Class II. This order, therefore, classifies the DuraGraft Vascular Conduit Solution, and substantially equivalent devices of this generic type, into Class II under the generic name flushing and storage solution for vascular autografts at room temperature.

FDA identifies this generic type of device as:

> **Flushing and storage solution for vascular autografts at room temperature**. A flushing and storage solution for vascular autografts is a device that is used for flushing or short-term storage of vascular grafts. This generic type of device is intended to maintain cell viability and structural integrity of vascular grafts during short-term storage at room temperature during the surgical procedure.

Section 513(f)(2) of the Food, Drug and Cosmetic Act (the FD&C Act) was amended by section 607 of the Food and Drug Administration Safety and Innovation Act (FDASIA) on July 9, 2012. This law provides two options for De Novo classification. First, any person who receives a "not substantially equivalent" (NSE) determination in response to a 510(k) for a device that has not been previously classified under the Act may request FDA to make a risk-based classification of the device under section 513(a)(1) of the Act. On December 13, 2016, the 21st Century Cures Act removed a requirement that a De Novo request be submitted within 30 days of receiving an NSE determination. Alternatively, any person who determines that there is no legally marketed device upon which to base a determination of substantial equivalence may request FDA to make a risk-based classification of the device under section 513(a)(1) of the Act without first submitting a 510(k). FDA shall, within 120 days of receiving such a request, classify the device. This classification shall be the initial classification of the device. Within 30 days after the issuance of an order classifying the device, FDA must publish a notice in the Federal Register announcing the classification.

On January 3, 2023, FDA received your De Novo requesting classification of the DuraGraft Vascular Conduit Solution. The request was submitted under section 513(f)(2) of the FD&C Act. In order to classify the DuraGraft Vascular Conduit Solution into class I or II, it is necessary that the proposed class have sufficient regulatory controls to provide reasonable assurance of the safety and effectiveness of the device for its intended use. After review of the information submitted in the De Novo request and provided interactively in response to interactive deficiencies, FDA has determined that, for the previously stated indications for use, the DuraGraft Vascular Conduit Solution can be classified in class II with the establishment of special controls for class II. FDA believes that class II (special) controls provide reasonable assurance of the safety and effectiveness of the device type. The identified risks and mitigation measures associated with the device type are summarized in the following table:

Risks to Health	**Mitigation Measures**
Adverse tissue reaction	Biocompatibility evaluation
Damage to vascular grafts leading to major adverse cardiac events or vascular injury	Clinical performance data Non-clinical performance testing Shelf life testing Labeling
Particulate matter contamination leading to vascular occlusion, coronary artery embolization and occlusion, phlebitis, infarction, and death	Clinical performance data Non-clinical performance testing Shelf life testing Labeling
Infection	Sterilization validation

In combination with the general controls of the FD&C Act, the flushing and storage solution for vascular autografts at room temperature is subject to the following special controls:

(1) Clinical data must evaluate adverse events associated with clinical use of the device. Devices indicated for vascular grafts for coronary artery bypass graft surgeries must include an evaluation of the incidence of major adverse cardiac events, vein graft occlusion, and mortality.

(2) Non-clinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use. The following performance characteristics must be tested:
    (i) Maintenance of cell viability and structural integrity of vascular conduits during storage at the labeled temperature and storage duration; and
    (ii) Evaluation of visible and non-visible particulates in the final mixed solution.
(3) Shelf life testing must demonstrate the stability of the device's chemical components over the identified shelf life.
(4) The device must be demonstrated to be biocompatible.
(5) Performance data must demonstrate the sterility of the device.
(6) Labeling must include:
    (i) The maximum storage duration for vascular autografts in the solution;
    (ii) A description of all additives or supplements that are added at the point of care;
    (iii) The need for visual inspection of the solution for particulate matter prior to use;
    (iv) A statement regarding the duration of stability of the final solution after preparation;
    (v) A summary of the non-clinical performance testing that supports use of the device as a flushing and storage solution for vascular autografts; and
    (vi) A summary of the clinical data that supports use of the device as a flushing and storage solution for vascular autografts.

In addition, this is a prescription device and must comply with 21 CFR 801.109.

Although this letter refers to your product as a device, please be aware that some granted products may instead be combination products. If you have questions on whether your product is a combination product, contact CDRHProductJurisdiction@fda.hhs.gov.

Section 510(m) of the FD&C Act provides that FDA may exempt a class II device from the premarket notification requirements under section 510(k) of the FD&C Act, if FDA determines that premarket notification is not necessary to provide reasonable assurance of the safety and effectiveness of the device type. FDA has determined premarket notification is necessary to provide reasonable assurance of the safety and effectiveness of the device type and, therefore, the device is not exempt from the premarket notification requirements of the FD&C Act. Thus, persons who intend to market this device type must submit a premarket notification containing information on the flushing and storage solution for vascular autografts at room temperature they intend to market prior to marketing the device.

Please be advised that FDA's decision to grant this De Novo request does not mean that FDA has made a determination that your device complies with other requirements of the FD&C Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the FD&C 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/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); 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 FD&C Act; 21 CFR 1000-1050).

A notice announcing this classification order will be published in the Federal Register. A copy of this order and supporting documentation are on file in the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852 and are available for inspection between 9 a.m. and 4 p.m., Monday through Friday.

As a result of this order, you may immediately market your device as described in the De Novo request, subject to the general control provisions of the FD&C Act and the special controls identified in this order.

For comprehensive regulatory information about medical devices and radiation-emitting products, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). 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 (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

If you have any questions concerning the contents of the letter, please contact Jordana Gilbert-Honick, Ph.D., at 301-796-6873.

Sincerely,

Courtney H. Lias -S

Courtney H. Lias, Ph.D.
Office Director
OHT3: Office of GastroRenal, ObGyn,
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