August 7, 2019

BonAlive Biomaterials Ltd.
% Elisa Maldonado-Holmertz
RA/QA Consultant
Obelix Biotech Solutions
12416 Fairfax Ridge Place
Austin, Texas 78738

Re: K191274
Trade/Device Name: BonAlive® Granules
Regulation Number: 21 CFR 888.3045
Regulation Name: Resorbable calcium salt bone void filler device
Regulatory Class: Class II
Product Code: MQV
Dated: May 10, 2019
Received: May 15, 2019

Dear Ms. Maldonado-Holmertz:

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/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 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 https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, 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).

Sincerely,

Laurence D. Coyne, Ph.D.
Assistant Director
DHT6C: Division of Restorative, Repair
and Trauma Devices
OHT6: Office of Orthopedic Devices
Office of Product Evaluation and Quality
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)*
K191274

Device Name

BonAlive® Granules

Indications for Use *(Describe)*

BonAlive® granules is indicated only for bony voids or gaps that are not intrinsic to the stability of the bony structure. BonAlive® granules is indicated to be gently packed into bony voids or gaps of the skeletal system (i.e. the extremities and pelvis). These defects may be surgically created osseous defects or osseous defects created from traumatic injury to the bone. The product contains a bone void filler that resorbs and is replaced with bone during the healing process. When used in the extremities and pelvis, BonAlive® granules is intended to be used alone.

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.

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Section 005 - 510(k) Summary

1. Submission Sponsor

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3. Date Prepared

10 May 2019

4. Device Identification

Type of 510(k) Submission:	Traditional
Trade or Proprietary Name:	BonAlive Granules
Common or Usual Name:	Filler, Bone Void, Calcium Compound
Regulation Description:	Resorbable calcium salt bone void filler device
Regulation Classification:	888.3045
Product Code:	MQV
Class of Device:	Class II
Review Panel:	Office of Device Evaluation (ODE) Division of Orthopedic Devices (DOD) Restorative and Repair Devices Branch (RRDB)
Reason for Submission:	New device
Prior Related Submissions:	Submission K110024 received NSE due to osteostimulation and antibacterial claims. This current submission has removed such claims.
Multiple Devices:	None

5. Legally Marketed Predicate Device(s)

K071199 (Rx Only) BonAlive Granules by Vivoxid Ltd. (now called BonAlive Biomaterials, Ltd.)

6. Device Description

BonAlive® granules is composed of osteostimulative calcium-phosphorous-sodium-silicate (glass S53P4) granules (size 0.5-0.8 mm or 1.0-2.0 mm) and is a sterile medical device. This synthetic, osteoconductive material is comprised of SiO_2, Na_2O, CaO and P_2O_5. Bioactive glass is characterized by its ability to attach firmly to living tissue. Other properties include its ability to facilitate bone tissue growth, bond chemically with surrounding bone, and promote new bone formation in the implanted area.

In aqueous solution (e.g. body fluids), bioactive glass works by leaching out ions and developing a silica-gel layer which acts as a template for a calcium phosphate (CaP) precipitation. The CaP crystallizes to hydroxyapatite, which resembles the mineral phase of natural bone in its chemical composition and structure, thus enabling bonding of the bioactive glass to the surrounding bone.

The BonAlive® granules resorb and are replaced with bone slowly over a period of years. The bioactive glass in the BonAlive® granules is radiodense thus enabling postoperative radiologic evaluation.

Best results are obtained by ensuring close contact of the device with surrounding bone tissue and by carefully following the Instructions for Use.

BonAlive® granules is sterilized by irradiation and is available in different granule and unit sizes.

7. Indication for Use Statement

BonAlive® granules is indicated only for bony voids or gaps that are not intrinsic to the stability of the bony structure. BonAlive® granules is indicated to be gently packed into bony voids or gaps of the skeletal system (i.e. the extremities and pelvis). These defects may be surgically created osseous defects or osseous defects created from traumatic injury to the bone. The product contains a bone void filler that resorbs and is replaced with bone during the healing process. When used in the extremities and pelvis, BonAlive® granules is intended to be used alone.

RX Only

8. Substantial Equivalence Discussion

The following table compares the DEVICE to the predicate device with respect to intended use, technological characteristics and principles of operation, providing more detailed information regarding the basis for the determination of substantial equivalence.

Comparison of Characteristics

Manufacturer	**SUBJECT DEVICE** BonAlive Biomaterials, Ltd	**PREDICATE DEVICE** Vivoxid Ltd (now called BonAlive Biomaterials, Ltd.)	**SIGNIFICANT DIFFERENCES**
Trade Name	BonAlive Granules	BonAlive Granules	None
510(k) Number	-	K071199	
Product Code	MQV	MQV	None
Regulation Number	888.3045	888.3045	None
Regulation Name	Resorbable calcium salt bone void filler device	Resorbable calcium salt bone void filler device	None
Indications for Use	BonAlive® granules is indicated only for bony voids or gaps that are not intrinsic to the stability of the bony structure. BonAlive® granules is indicated to be gently packed into bony voids or gaps of the skeletal system (i.e. the extremities and pelvis). These defects may be surgically created osseous defects or osseous defects created from traumatic injury to the bone. The product contains a bone void filler that resorbs and is replaced with bone during the healing process. When used in the extremities and pelvis, BonAlive® granules is intended to be used alone.	BonAlive® granules is indicated only for bony voids or gaps that are not intrinsic to the stability of the bony structure. BonAlive® granules is indicated to be gently packed into bony voids or gaps of the skeletal system (i.e. the extremities and pelvis). These defects may be surgically created osseous defects or osseous defects created from traumatic injury to the bone. The product provides a bone void filler that resorbs and is replaced with bone during the healing process. When used in the extremities and pelvis, BonAlive® granules is intended to be used alone. The device is not intended for use in posterolateral spine applications. BonAlive® granules is not	None

Manufacturer	**New Product** BonAlive Biomaterials, Ltd	**PREDICATE** Vivoxid Ltd (now called BonAlive Biomaterials, Ltd.)	**SIGNIFICANT DIFFERENCES**
Trade Name	BonAlive Granules	BonAlive Granules	None
		indicated for use in load-bearing applications, therefore, standard internal or external stabilization techniques must be followed to obtain rigid stabilization.	
Rx or OTC	Rx	Rx	None
Physical Form	Amorphous, non-porous random-shaped particles	Amorphous, non-porous random-shaped particles	None
Color	Brown	Slightly pink	Color is different
Materials Composition	SiO_2, Na_2O, CaO and P_2O_5	SiO_2, Na_2O, CaO and P_2O_5	None
Product Sizes	Granule sizes: 0.5-0.8 mm 1.0-2.0 mm Product volumes: 1 cc 2.5 cc 5 cc 10 cc	Granules sizes: 0.5-0.8 mm 1.0-2.0 2.0-3.15 mm Product volumes: 1 cc 2 cc 4 cc 16 cc	Largest granule size 2.0-3.15 mm is obsolete Volumes are different
Biocompatibility	Biocompatible ISO 10993	Biocompatible ISO 10993	None
Sterilization, SAL	Gamma Sterile, SAL 10^{-6}	Dry Heat Sterile, SAL 10^{-6}	None
Pyrogenicity	Non-pyrogenic	Non-pyrogenic	None
Single Use/ Reuse	Single use only	Single use only	None
Mode of action	Works by leaching out ions that react with the body fluids transforming the glass surface chemically into one that by its chemical composition and structure resembles the mineral phase found in natural bone.	Works by leaching out ions that react with the body fluids transforming the glass surface chemically into one that by its chemical composition and structure resembles the mineral phase found in natural bone.	None
Properties	Synthetic	Synthetic	None

Manufacturer	**New Product** BonAlive Biomaterials, Ltd	**PREDICATE** Vivoxid Ltd (now called BonAlive Biomaterials, Ltd.)	**SIGNIFICANT DIFFERENCES**
Trade Name	BonAlive Granules	BonAlive Granules	None
	Osteoconductive	Osteoconductive	

9. Non-Clinical Performance Data

The following testing has been performed to support substantial equivalence to the predicate:

- Apatite
- Composition - Heavy Metals
- Crystallinity
- Particle Size Distribution
- Surface Area
- Manufacturing & Specifications Validation

As part of demonstrating safety and effectiveness of BonAlive Granules, and in showing substantial equivalence to the predicate device, BonAlive completed a number of tests. The BonAlive Granules meets all the requirements for overall design and confirms that the output meets the design inputs and specifications. The BonAlive Granules passed all testing stated above as shown by the acceptable results obtained.

The BonAlive Granules complies with the applicable voluntary, national and international standards and guidance.

10. Biocompatibility

Biocompatibility testing was conducted in accordance with ISO-10993-1, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process" The following biocompatibility studies were successfully performed with the BonAlive® granules: cytotoxicity, sensitization, systemic toxicity, genotoxicity, and muscle implantation.

The granules predicate device was depyrogenated at 250 degrees Celsius for one hour prior to dry heat sterilization. Bacterial endotoxins were investigated in a LAL gel clot test. The analysis was performed according to Ph. Eur. 2.6.14 method A. The log reduction in endotoxin levels in the dry heat depyrogenation cycles was 4.6 logs. The results met USP requirement for bacterial endotoxins.

Similarly, as for the predicate device, a depyrogenation step at 250 degrees Celsius is performed for the granules subject device prior the gamma irradiation. The granules material and the depyrogenation method are the same for the predicate and the subject devices, thus the log reduction in the endotoxin levels for the predicate and the subject devices are equivalent. The testing performed on the predicate device supports the pyrogen status of the subject device. The predicate and subject devices are substantially equivalent in their non-pyrogenic nature.

11. Sterility and Shelf Life

The BonAlive Granules and Applicator (Granules) are sterilized with radiation. The sterility of the Granules was assured by using a validated sterilization method qualified in accordance with EN ISO 11137. After the sterilization cycle was completed, the Granules were placed on real-time shelf-life testing for a length of time to determine any degradation or loss of sterility over the anticipated shelf-life period of five (5) years. The validations and shelf life testing were completed successfully in accordance with ISO 11607.

12. Clinical Performance Data

There was no clinical testing required to support the medical device as the indications for use is equivalent to the predicate device. These types of devices, including the predicate devices, have been on the market for many years with a proven safety and efficacy for the use of the device. The non-clinical testing detailed in this submission supports the substantial equivalence of the device.

13. Statement of Substantial Equivalence

A device is substantially equivalent to a predicate device when the device has the same intended use and the same technological characteristics as the previously cleared predicate device, and that the new device does not raise different questions regarding its safety and effectiveness as compared to the predicate device. BonAlive Granules is substantially equivalent to its predicate.