November 13, 2020

Kerecis Limited
Gudmundur Sigurjonsson
CEO
Eyrargata 2
400 Isafjordur
ICELAND

Re: K192612
Trade/Device Name: Kerecis Gingiva Graft
Regulation Number: 21 CFR 872.3930
Regulation Name: Bone Grafting Material
Regulatory Class: Class II
Product Code: NPL
Dated: October 9, 2020
Received: October 13, 2020

Dear Gudmundur Sigurjonsson:

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,

for Srinivas Nandkumar, Ph.D.
Director
DHT1B: Division of Dental Devices
OHT1: Office of Ophthalmic, Anesthesia, Respiratory, ENT and Dental 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)*
K192612

Device Name
Kerecis Gingiva Graft

Indications for Use *(Describe)*

Kerecis Gingiva Graft is indicated for:

– Localized gingival augmentation to increase keratinized tissue (KT) around teeth or implants.

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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510(k) Summary

1 Submitter/510(k) Holder

Address:	Kerecis Limited Eyrargata 2 400 Isafjordur Iceland
Contact Person:	Gudmundur Fertram Sigurjonsson President and CEO
Telephone:	011 354 562 2601
Date Prepared:	November 12, 2020

2 Device Name

Proprietary Name:	Kerecis Gingiva Graft
510(k) Number:	K192612
Classification Name:	Barrier, animal source, intraoral
Classification Product Code:	NPL
Regulatory Number:	872.3930
Class:	II

3 Predicate Devices

Primary Predicate: MUCOGRAFT® Collagen Matrix (K102531)

Reference Devices: Kerecis MariGen Wound Extra (K190528), Kerecis SecureMesh (K153364).

4 Device Description

The subject device is fish skin medical device indicated for localized gingiva augmentation.

The subject device is obtained from cod fish skin by a standardized controlled manufacturing process and supplied in a peel-pouch terminally sterile packaging in the following rectangular sizes:

- 15mm x 20mm
- 20mm x 30mm
- 30mm x 40mm

The subject device becomes completely integrated into the surrounding tissue over time, with corresponding new host tissue deposition. The physical properties of the subject device allow cellular ingrowth for augmentation of keratinized tissue.

The subject device is biocompatible, non-crosslinked, bioresorbable, strong, pliable and supports fixation by sutures.

5 Intended Use

Kerecis Gingiva Graft is indicated for:

– Localized gingival augmentation to increase keratinized tissue (KT) around teeth or implants.

6 Technological Characteristics and Substantial Equivalence

Comparisons of the subject device with the predicate device (K102531), and the reference devices (K153364 and K 190528), demonstrate that it is substantially equivalent with regards to: intended use, materials, design, and operational principles.

See Table 6.1. Kerecis Gingiva Graft in comparison with predicate and references device

Table 6-1 Kerecis Gingiva Graft in comparison with predicate and references devices

	Subject Device	Predicate Device	Discussion
Device Name	**Kerecis Gingiva Graft**	**Geislich MUCOGRAFT® Collagen Matrix**	No discussion required
510(k)	Subject Device	K102531	Predicate device and reference devices are cleared.
Regulation	21 CFR 872.3930	21 CFR 872.3930	Same as predicate
Product Code	NPL	NPL	Same as predicate
Device Classification	Barrier, Animal Source, Intraoral	Barrier, Animal Source, Intraoral	Same as predicate
Intended Use	Kerecis Gingiva Graft is a biocompatible, sterile collagen membrane intended for augmentation and regeneration of soft tissue in oral surgical settings.	MUCOGRAFT® Collagen Matrix is sterile resorbable bilayer extra cellular collagen membrane matrix for soft tissue augmentation, guided tissue regeneration and multiple oral tissue defect regeneration in oral surgical settings.	Subset of the intended use of the predicate device.
Indications	Localized gingival augmentation to increase Keratinized tissue (KT) around teeth and implants.	• Covering of implants placed in immediate extraction sockets; • Localized gingival augmentation to increase keratinized tissue (KT) around teeth and implants;	Subset of the indications of the predicate device

		• Alveolar ridge reconstruction for prosthetic treatment • Guided tissue regeneration procedures in recession defects for root coverage • Guided tissue regeneration procedures in recession defects for root coverage.	
Animal Origin Material	North Atlantic Cod fish: skin tissue, single layer sheet	Porcine skin and connective tissue, double layer sheet	Different animal source, same anatomical tissue
Biocompatibility	Yes	Yes	Same as predicate
NON-Pyrogenic	Yes	Yes	Same as predicate
Resorbable	Yes	Yes	Same as predicate
Sizes	15mm x 20mm 20mm x 30mm 30mm x 40mm	15mm x 20mm 20mm x 30mm 30mm x 40mm	Same as predicate
Sterilization	Ethylene Oxide	Gamma Irradiation	Traditional Sterilization Method
Sterility Assurance Level	10^{-6}	10^{-6}	Same as predicate
Shelf life	3 years	3 years	The shelf life of the product has been validated

7 Performance Testing – Bench

The following performance studies were conducted on representative products to verify that material properties remain unchanged and support the substantial equivalence determination:

7.1 Morphology Observation

The subject device and the predicate device are based on the collagen rich animal tissue, piscine and porcine, respectively. Based on H&E staining, both materials are rich in collagen and porous, therefore favoring cellular infiltration. Scanning Electron Microscope (SEM) shows equivalent preserved collagen structure of the animal origin tissues used for both devices. Cross section of both devices showed that the porous surfaces in the skin derived collagen structure of both materials allows tissue adherence and promotes tissue regeneration by favoring cellular ingrowth when applied to soft tissue defect areas.

7.2. Cellular ingrowth comparison

Both materials were tested for cellular ingrowth capability by fibroblast seeding onto the materials in vitro cellular modes. Both materials showed favorable cellular infiltration of fibroblasts after 14 days which is a key component for tissue augmentation and re-epithelization of defected keratinized tissue in the oral cavity.

7.3. Tensile Strength

The tensile strength of the subject device was determined to be comparable to the predicate device measured by ultimate tensile strength.

7.4. Heavy Metal Analysis

A heavy metal analysis was evaluated to show that the limits of cadmium (Cd), lead (Pb), arsenic (As) and mercury (Hg) contained within the subject device were acceptable under the ICH guidelines: Q3D Elemental Impurities-Guidance for Industry.

7.5. Stability of Kerecis Gingiva Graft in a simulated physiological environment

A stability test was done in a simulated physiological oral environment (artificial saliva buffer) to investigate the dissolution of both material over time and to compare the effects that the products have on the pH levels and conductivity of the buffer over 24 hours. The pH level of the buffer incubated with the two products was stable over time. Incubation of the subject device to the buffer raises the pH slightly, while incubation of the predicate device decreases it slightly. The subject device is structurally more stable than the predicate device since it dissolved slower than the predicate device at neutral pH 7.

7.6. Suture Pull-Out Strength

The suture pull-out strength of the subject device meets or exceeds that of the predicate with a confidence of greater than 95%. For oral surgery and gingival augmentation, the products are equivalent.

7.7. Pin Pull-Out Strength

The pin pull-out strength of the subject device exceeds that of the predicate at a confidence level of greater than 95%. For oral surgery and gingival augmentation, the products are equivalent.

7.8. Compression

The compressive Peak-Load, Load-at-Break, Probe Penetration-at-Break, and Energy-to-Break of the subject device meet or exceed those of the predicate device, with a confidence of greater than 95%. For oral surgery and gingival augmentation, the products are equivalent.

7.9. User Evaluation of Device for Cutting and Shaping

The subject device was evaluated in comparison to the predicate by four dental clinicians for use in the oral environment using a questionnaire to assess: ease of placement, stability over the site, robustness of the device, and satisfaction with handling the device. The questionnaire results showed a favorable usability that was substantially equivalent to the predicate for cutting and shaping the device for use as a dental barrier membrane.

7.10.Biocompatibility, Sterilization, Shelf-life and Animal origin.

Testing from the applicant's own predicate device (K190528 and K153364) were leveraged in support of substantial equivalence.

- Biocompatibility per ISO 10993 series
    - Cytotoxicity
    - Sensitization
    - Irritation or Intracutaneous reactivity
    - Acute systemic toxicity
    - Subacute/sub-chronic toxicity
    - Genotoxicity
    - Implantation
    - Materials-Mediated Pyrogenicity
    - Chronic Toxicity
    - Carcinogenicity

- Sterilization validation per ISO 11135, ISO 11737-1, Ethylene Oxide residual test following ISO 10993-7
- Endotoxin validation (<20 EU/device) of sterilization method per LAL turbidimetric kinetic method following ISO 10993-11
- Shelf life per ASTM F1980 and Q5C (R2)[ICH] using accelerated and real-time aged samples
- Packaging per ISO 11607-series, ASTM F88 and ASTM F1886
- Animal Origin and Viral inactivation per ISO 22422 series

Based upon our assessment of the design and applicable performance data, the subject device has been determined to be substantially equivalent to the identified predicate device.

8 Performance Testing – Animal

Kerecis performed preclinical testing in canines to demonstrate the capacity of the device to facilitate guided tissue repair (GTR) in mucogingival defects in the oral environment. Each animal received four oral defects: two smaller soft tissue defects in the mandibular canines and two larger soft tissue+GTR defects on the maxillary defects. In both cases, the oral membranes (subject or predicate devices, respectively) were inserted between the exposed tooth and the soft tissue and secured by suturing the defect. Three animals were terminated at 30 days after surgery, three animals at 60 days after surgery

and four animals at 90 days after surgery. The study endpoints were as follows:

Primary analyses outcome variable:

- Histomorphometric measurements (thickness and length of keratinized tissue (KT))
- Histological analysis (inflammation, healing, remodeling)

Secondary analyses outcome variable(s):

- Thickness of keratinized tissue measured by Periodontal Probe (*in vivo* and *postmortem)*.

Overall, the findings of the study support the conclusion that all animals remained in good general health throughout the duration of the study and gross pathological findings suggest an acceptable safety profile for the subject device. For all the parameters analyzed, including KT thickness, KT length, root coverage, inflammation and membrane degradation, no statistically significant difference was detected between the subject and predicate devices after 90 days of healing. *In vivo* measurements indicate that both the subject and predicate device were able to increase keratinized tissue around teeth for both the smaller (mandibular) and larger (maxillary) defects.

The overall conclusion is that regarding the thickness and length of keratinized tissue 90 days after the creation of a soft tissue defect, the subject device is equivalent to the predicate device.

9 Performance Testing – Clinical

The clinical study (and the respective publications) provided safety and clinical evidence supporting the device use for gingival augmentation. The device was tested in six individuals in an open label, non-comparative study. All the subjects completed the clinical investigation. There were no adverse effects or complications during the duration of the clinical study. Three patients were treated for unilateral deformities and the other three patients were treated for bilateral deformities. An increased in the in the width of the KT was noticed for all treated sites. This average gain has been reported as adequate to maintain long-term periodontal health. During the 12-month follow up, the device showed stability as the KT slowly replaced the piscine xenograft. In addition, the results with the subject device are similar to published results reported for the predicate device.

10 Conclusion

Based on the data provided within this 510(k) submission, as summarized above, it can be concluded that the subject device is substantially equivalent to the predicate device with regard to intended use, indications for use, and technological characteristics, including principles of operation and performance characteristics as shown in a series of biocompatibility, bench, and clinical testing. Thus, the subject device is substantially equivalent.