SigmaGraft Inc.
% Dave Kim
Medical Device Regulatory Affairs
Mtech Group
7505 Fannin St.
Ste 610
Houston, Texas 77054

March 18, 2023

Re: K221808
Trade/Device Name: InterOss® Collagen
Regulation Number: 21 CFR 872.3930
Regulation Name: Bone Grafting Material
Regulatory Class: Class II
Product Code: NPM
Dated: March 8, 2023
Received: March 8, 2023

Dear Dave Kim:

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,

Andrew I. Steen -S

Andrew I. Steen
Assistant Director
DHT1B: Division of Dental and ENT 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: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K221808

Device Name
InterOss® Collagen

Indications for Use *(Describe)*

InterOss® Collagen is indicated for filling of extraction sockets to enhance preservation of the alveolar ridge. InterOss Collagen is recommended for:

Filling of extraction sockets to enhance preservation of the alveolar ridge
Filling of periodontal defects in extraction sockets in conjunction with products intended for Guided Tissue Regeneration (GTR) and Guided Bone Regeneration (GBR)

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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FDA Traditional 510(k) Summary

K221808

1. Submitter's Information

Submitter:	SigmaGraft, Inc. 575 Sally Place Fullerton, CA 92831, USA
Contact Person:	Elcin Chang
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Fax Number:	+1-714-525-0116
Prepared by:	Elcin Chang, General Manager
Email:	e.chang@sigmagraft.com
Date Prepared:	March 17, 2023

2. Name of the Device

Trade Names:	InterOss Collagen
Common Name:	Bone Grafting Material
Classification Name:	Bone Grafting Material, Collagen
Regulation Number:	§872.3930
Device Classification:	II
Product Code(s):	NPM
Classification Panel:	Dental

3. Predicate Device

Primary Predicate:	OCS-B Collagen® (K142040)
Common Name:	Bone Grafting Material
Classification Name:	Bone Grafting Material, Collagen
Regulation Number:	§872.3930
Device Classification:	II
Product Code(s):	NPM
Classification Panel:	Dental

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4. Reference Device

Primary Predicate:	InterOss® (K151209)
Classification Name:	Bone Grafting Material
Regulation Number:	§872.3930
Device Classification:	II
Product Code(s):	NPM
Classification Panel:	Dental

5. Device Description

InterOss Collagen is a combination of InterOss®, an anorganic hydroxyapatite bone substitute, and collagen fibers for use in periodontal, oral and maxillofacial surgery. This product is a composite of 90% InterOss® (granules of size 0.25-1mm) and 10% porcine collagen fibers. InterOss®, which is already a cleared device by the FDA (K151209), is a hydroxyapatite material derived from Australian bovine bone. The osteoconductive mineral structure is produced from bone through a multi-step purification process. Following placement in bony voids or gaps InterOss® acts as an osteoconductive scaffold for the ingrowth of adjacent viable bone. InterOss® gradually resorbs and is replaced with bone during the healing process. The collagen component facilitates the adaptation of InterOss® to the defect site allowing easier handling. The product is non-pyrogenic, single use only, and terminally sterilized via gamma-irradiation.

The product is available in the following shapes and sizes:

Type	Weight (mg)	Dimension (mm)	Ref#
Block	50	6 x 6 x 3	IOC-50
Block	100	6 x 6 x 6	IOC-100
Block	250	7 x 9 x 8	IOC-250
Block	350	8 x 10 x 9	IOC-350
Block	500	10 x 12 x 10	IOC-500
Plug	150	6 x 10	IOC-P150
Plug	250	8 x 10	IOC-P250
Plug	400	11 x 9	IOC-P400
Plug	450	10 x 12	IOC-P450

6. Intended Use

InterOss® Collagen is indicated for filling of extraction sockets to enhance preservation of the alveolar ridge. InterOss® Collagen is recommended for:

- Filling of extraction sockets to enhance preservation of the alveolar ridge
- Filling of periodontal defects in extraction sockets in conjunction with products intended for Guided Tissue Regeneration (GTR) and Guided Bone Regeneration (GBR)

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7. Summary/Comparison of Technical Characteristics

The subject device and the predicate device have the same indications for use. The subject device has substantially equivalent technological characteristics to the marketed predicate device.

Feature	InterOss Collagen	OCS-B Collagen (K142040)	InterOss ® (K151209)
Indications for Use	• Filling of extraction sockets to enhance preservation of the alveolar ridge • Filling of periodontal defects in extraction sockets in conjunction with products intended for Guided Tissue Regeneration (GTR) and Guided Bone Regeneration (GBR)	• Augmentation for reconstructive treatment of alveolar ridge • Filling of infrabony periodontal defects • Filling of defects after root resection, apicoectomy, and cystectomy • Filling of extraction sockets to enhance preservation of the alveolar ridge • Elevation of maxillary sinus floor • Filling of periodontal defects in conjunction with products intended for Guided Tissue Generation (GTR) and Guided Bone Regeneration (GBR) • Filling of peri-implant	• Augmentation or reconstructive treatment of the alveolar ridge • Filling of infrabony periodontal defects • Filling of defects after root resection, apicoectomy, and cystectomy • Filling of extraction sockets to enhance preservation of the alveolar ridge • Elevation of the maxillary sinus floor • Filling of periodontal defects in conjunction with products intended for Guided Tissue Regeneration (GTR) and Guided Bone

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		defects in conjunction with products intended for Guided Bone Regeneration	Regeneration (GBR) • Filling of peri-implant defects in conjunction with products intended for Guided Bone Regeneration (GBR)
Physical Form	Block and plug shaped	Block and plug shaped	White granules in vial and syringe
Color	White to off-white	White to off-white	White to off-white
Material Composition	• Anorganic bone mineral (calcium phosphate) • Type I Collagen	• Anorganic bone mineral (calcium phosphate) • Type I Collagen	• Anorganic bone mineral (calcium phosphate)
Size (Dimension and weight)	Block (6x6x3mm, 50 mg) Block (6x6x6mm, 100 mg) Block (7x8x9mm, 250 mg) Block (8x9x10mm, 350 mg) Block (10x10x12mm, 500 mg) Plug (6x10mm, 150mg) Plug (8x10mm, 250mg) Plug (11x9mm, 400mg) Plug (10x12mm, 450mg)	Block (6x6x3mm, 50 mg) Block (6x6x6mm, 100 mg) Block (7x8x9mm, 250 mg) Block (9x10x11mm, 500 mg) Cylinderic (4.6x40mm, 250mg) Cylinderic (5.6x45mm, 500 mg)	Via Small granules (0.25-1.00mm): 0.25g, 0.5g, 1.0g, 2.0g or 5.0g Large granules (1.00-2.00mm): 0.5g, 1.0g, or 2.0g Syringe Small granules (0.25-1.00mm): 0.25cc, 0.5cc, or 1.0cc Large granules (1.00-2.00mm): 0.5cc, 1.0cc, or 1.5cc
Source of bone	Bovine	Bovine	Bovine
Source of collagen	Porcine	Porcine	Not applicable
Physical morphology	Trabecular, interconnecting macro and micro pores	Trabecular, interconnecting macro and micro pores	Trabecular, interconnecting macro and micro pores
pH	7.18	6.96	7.86
Swell ratio % (w/w)	179.8	116.8	Not applicable
Surface area	77.41 m^2/g	52.10 m^2/g	114.45 m^2/g
Moisture content	3.1%	3.12%	2.04%
Biocompatibility	Biocompatible	Biocompatible	Biocompatible
Performance	Bone formation	Bone formation	Bone formation
Pyrogenicity	Non-pyrogenic	Non-pyrogenic	Non-pyrogenic
Sterility	Sterile, Sal 10-6 Gamma irradiation	Sterile, Sal 10-6 Gamma irradiation	Sterile, Sal 10-6 Gamma irradiation

8. Non-clinical Testing

A series of *in vivo* and *in vitro* testing of the subject device was conducted to demonstrate chemical and physical properties, biocompatibility, and substantial equivalence of the subject device to its predicate device. The following

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performance data are provided in support of the substantial equivalence determination.

Physical/Chemical Properties

Collagen component was assessed for collagen stability, purity, resistance to trypsin, amino acid analysis, and ELISA assays were performed on collagen samples. Amino acid analysis showed that the collagen contains 80-87% protein (w/w) and the hydroxyproline content within range from 9.4-10.04% (w/w), and ELISA confirmed the presence of predominantly Type I collagen. SDS PAGE on porcine collagen showed signature alpha bands while exposure to collagenase showed no bands confirming collagen purity. Resistance to trypsin was confirmed by a temporal trypsin resistance test.

InterOss Collagen was evaluated for the porous structure/interconnected pores via scanning electron microscopy. Porosity measurement was performed using mercury porosimetry and confirmed porosity greater than 75% while the average pore diameter ranged from 0.12-0.15 μm. Surface area was measured using Brunauer-Emmett-Teller method that confirmed that the article measures the area greater than 75 m^2/g. Compressive and elastic modulus testing showed the values of >1 MPa and >3 MPa respectively at 50% compressive strain. Total residual crude fat analysis using chemical ether extraction showed fat content to be less than 3% (w/w). The moisture content in InterOss Collagen measured using thermogravimetric analyzer showed values of approximately 3.1% (w/w). Peak denaturation temperature was measured to be between 210-230°C using Differential Scanning Calorimetry. No heavy metals within the detection limit (1 ppm) were found in InterOss Collagen when measured using ICP-MS. Water absorption testing showed InterOss Collagen absorbs more than 100% of its weight when immersed in deionized water at room temperature. Water solubility test found InterOss Collagen to be not soluble.

Biocompatibility Testing

A series of *in vitro* and *in vivo* biocompatibility testing was performed to assess the safety of the subject device. Testing was determined in accordance with ISO 10993-1 and FDA Guidance on Use of International Standard ISO 10993-1 for the biological evaluation of medical devices within a risk management process.

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The biocompatibility testing performed is summarized in the table below.

Test	Standards	Results
Mouse Lymphoma forward mutation assay	ISO 10993-3, OECD 476, OECD 490	Non-mutagenic
Kligman Maximization Sensitization Test	ISO 10993-10	Non-sensitizer
Genotoxicity (Mammalian Erythrocyte Micronucleus) Test	ISO 10993-3, OECD Test No. 474.	Non-mutagenic
Primary buccal irritation Test	ISO 10993-10	Non-irritant
Acute Systemic Toxicity Test	ISO 10993-11	Non-toxic
Cytotoxicity L929 Neutral Red uptake test	ISO 10993-5	Non-cytotoxic
Genotoxicity (Ames: Bacterial Reverse Mutation) Test	ISO 10993-3	Non-mutagenic
90 day Subchronic Toxicity Test	ISO 10993-11	Non-toxic
Local effects after Implantation Test	ISO 10993-6	Minimum tissue reaction at 4, 8, and 13 weeks of implantation and no adverse tissue reaction to the host

Animal Testing

The performance of the device in a canine two-wall intrabony defect model was compared to the performance of the predicate device, OCS-B Collagen. The objective of this study was to evaluate the in vivo performance, local effects following implantation, and systemic toxicity of the test article, InterOss Collagen, in comparison to a predicate and empty control in beagle dogs with mandibular defects as a dental application.

By all the parameters evaluated in the study, biocompatibility, performance, and healing of InterOss Collagen treated defects were indistinguishable from those treated with the predicate. The results demonstrate performance substantially equivalent to the predicate device OCS-B Collagen when used as intended.

9. Animal Tissue Management

Animal tissues are managed in accordance with the following standards and guidance documents:

- ISO 22442-1 Animal Tissues and Their Derivatives Utilized in the Manufacture of Medical Devices – Part 1: Analysis and Risk Management
- ISO 22442-2 Animal Tissues and Their Derivatives Utilized in the Manufacture of Medical Devices – Part 2: Controls on Sourcing, Collection, and Handling
- ISO 22442-3 Animal Tissues and Their Derivatives Utilized in the Manufacture of Medical Devices – Part 3: Validation of the Elimination and/or Inactivation of Viruses and Transmissible Agents
- Medical Devices Containing Materials Derived from Animal Sources (Except for In Vitro Diagnostic Devices) Guidance for Industry and Food and Drug Administration Staff, CDRH, FDA, March 15, 2019
- FDA Guidance for Industry – Q5A Viral Safety Evaluation of Biotechnology Products Derived from Cell

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Lines of Human or Animal Origin, CDER, CBER, September 1998

10. Sterilization

Sterilization validation was performed in accordance with ISO 11137-1 Sterilization of health care products – Radiation Part 1 Requirements for development, validation and routine control of a sterilization process for medical devices, ISO 11137-2 Sterilization of health care products – Radiation Part 2 Establishing the sterilization dose, and ISO 11737 Sterilization of Medical Devices – Microbiological Method – Determination of the Population of Microorganisms on Products.

11. Pyrogenicity

This device is non-pyrogenic. Each batch of product manufactured is tested for endotoxin per the Limulus Amebocyte Lysate (LAL) endotoxin test, USP <85> . Material mediated pyrogenicity was evaluated by USP <161> testing, as finished product release test.

12. Shelf Life and Stability

Product and packaging stability was determined using real-time aging data. Performance testing of packaging system was tested in accordance with ASTM D4169 Standard Practice for Performance Testing of Shipping Containers and Systems. Selection, qualification, and validation of packaging were conducted in accordance with ISO 11607 Packaging for Terminally Sterilized Medical Devices – Requirements for Materials, Sterile Barrier Systems, and Packaging Systems.

13. Viral Inactivation

Viral inactivation studies were performed in accordance with ISO 22442-3 to ensure the viral safety of the product.

14. Clinical Studies

Clinical performance data was not required to determine substantial equivalence.

15. Conclusion

Chemical, physical, and biocompatibility tests as well as pre-clinical data show that the subject device is substantially equivalent to the predicate device. Comparison with the predicate device shows that the device has similar specifications and performance. Therefore, the conclusions drawn from the nonclinical and preclinical tests demonstrate that the device is substantially equivalent to its predicate device.

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