DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
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Silver Spring, MD 20993-0002

October 1, 2015

Cook Biotech Incorporated
Mr. Perry W. Guinn
Vice President/Quality Assurance and Regulatory Affairs
1425 Innovation Place
West Lafayette, Indiana 47906

Re: K142887
Trade/Device Name: SIS Inguinal Hernia Repair Graft
Regulation Number: 21 CFR 878.3300
Regulation Name: Surgical mesh
Regulatory Class: Class II
Product Code: FTM
Dated: September 10, 2015
Received: September 11, 2015

Dear Mr. Guinn:

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. 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 [SELECT ONE: Part 801 [or, for IVDs only] Parts 801 and

809]); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 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 the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

David Krause -S

for Binita S. Ashar, M.D., M.B.A., F.A.C.S.
Director
Division of Surgical 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: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*

K142887

Device Name

SIS Inguinal Hernia Repair Graft

Indications for Use *(Describe)*

The Inguinal Hernia Repair Graft is intended for implantation to reinforce soft tissues where weakness exists, including the repair of inguinal hernias. The graft is supplied sterile and intended for one time use.

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)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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510(k) Summary

Sep. 30, 2015

Cook Biotech Incorporated

SIS Inguinal Hernia Repair Graft

Manufacturer Name: Cook Biotech Incorporated
1425 Innovation Place
West Lafayette, Indiana 47906
Telephone: +1 (765) 497-3355
FAX: +1 (765) 807-7709

Official Contact: Perry W. Guinn

DEVICE NAME AND CLASSIFICATION:

Trade/Proprietary Name:	SIS Inguinal Hernia Repair Graft
Common Name:	Surgical graft
Classification Regulations:	Class II, 21 CFR §878.3300 (FTM)

INTENDED USE:

The SIS Inguinal Hernia Repair Graft is intended for implantation to reinforce soft tissues where weakness exists, including the repair of inguinal hernias. The graft is supplied sterile and is intended for one-time use.

DEVICE DESCRIPTION:

The SIS Inguinal Hernia Repair Graft is a flat sheet constructed of an animal sourced bioabsorbable, extracellular matrix collagen membrane derived from porcine Small Intestinal Submucosa, (SIS). It is intended for soft tissue repair with sizes and shapes appropriate for the repair of inguinal hernias. SIS Inguinal Hernia Repair Graft contains collagens I, III, IV and VI. The device is packaged in a dried state and supplied sterile in a sealed double pouch system.

EQUIVALENCE TO MARKETED DEVICES:

The SIS Inguinal Hernia Repair Graft is similar with respect to intended use, materials and technological characteristics to its predicate devices in terms of section 510(k) Substantial Equivalence, as shown in pre-clinical (biocompatibility, conducted in accordance to ISO 10993-1 standards), mechanical, and clinical testing.

Biocompatibility Testing

The following biocompatibility tests were performed on sterilized SIS devices, which are identical in composition to the SIS Inguinal Hernia Repair Graft (according to the ISO 10993-1 standard):

- Genotoxicity
- Direct contact *in vitro* hemolysis
- Cytotoxicity
- Muscle implantation
- Acute intracutaneous reactivity
- ISO Sensitization
- Acute systemic toxicity
- Pyrogenicity
- LAL endotoxins
- Subchronic systemic toxicity

The results of these tests provide evidence that the SIS Inguinal Hernia Repair Graft meets the biocompatibility requirements of the ISO standard.

Mechanical Testing

The SIS Inguinal Hernia Repair Graft material was tested for the following:

- Suture retention strength
- Burst strength
- Tensile strength

The results of the mechanical tests provide evidence that the SIS Inguinal Hernia Repair Graft provides adequate mechanical strength for its application.

Clinical Testing

The SIS Inguinal Hernia Repair Graft (also known as Surgisis Inguinal Hernia Matrix SIHM) was implanted in 95 patients in 3 separate clinical studies and the results were published in 3 peer reviewed articles. The results address the durability of repair with resorbable SIS Inguinal Hernia graft as used for open, tensionless repairs of inguinal hernias. One of the studies was a recent US randomized clinical trial comparing the use of SIS Inguinal Hernia Repair Graft (SIHRG) to polypropylene mesh (PP) using the Lichtenstein hernia repair procedure. This repair included bridging the defect. Results showed hernia recurrence rates of 6.7% (3/45 patients) and 0% (0/50 patients) at 1 year follow-up in the treatment (SIHRG) versus control groups. A difference in hernia recurrence rate was also seen at 3 years with 15.6% (7/45 patients) and 4.0% (2/50 patients) for the SIHRG and PP groups, respectively*[1]. In addition, post-operative pain was assessed with a 1 year follow-up. Persistent pain trended higher in the PP group (6% vs. 4%). Authors of the U.S. study note that factors other than device performance could influence hernia recurrence outcomes, e.g., surgical approach, surgical experience, etc.

Two OUS prospectively randomized clinical investigations were conducted comparing SIHRG to PP using the Lichtenstein Repair. These studies found no hernia recurrences for SIHRG-treated patients at 1 and 3 years, (0/15, 1 year)[2] and 0% (0/35, 3 years)[3], respectively. Recurrence rates for the PP-treated group found hernia recurrences of 0% (0/15, 1 year) [2] and 2.9% (1/35, 3 years) [3]. Both studies found lower post-operative pain and discomfort in the SIHRG patients at 30 days[2, 3]. The reported differences regarding hernia recurrence between the OUS and US clinical investigations may be reflective of many factors, chief among these being the probable difference in surgical procedures.

In clinical studies in which SIHRG was used to repair an inguinal hernia, the mean BMI in patients undergoing inguinal herniorraphy was 26 kg/m^2. Recurrence rates may be higher in obese patients (BMI>30) when using SIHRG in a tensionless inguinal hernia repair. A synopsis of each study is presented in the following tables.

*Three year follow-up data not yet validated or published.

Table 1: Bochicchio GV, *et al.*, Biologic vs Synthetic Inguinal Hernia Repair: 1-Year Results of a Randomized Double-Blinded Trial. *J Am Coll Surg* 2014; 218:751-759.

Number of centers	*One center; Baltimore VA hospital; 7 investigators including 4 surgeons*
Number of patients	*100 male patients randomized in a 1:1 fashion to open Lichtenstein repair of the test groups, Surgisis Inguinal Hernia Matrix (SIHM) and control polypropylene mesh: 50:50 patients* *Note: In SIHM group 5 patients were withdrawn prior to surgery due to emergency surgery or traumatic event resulting in 45:50 patients*
Study inclusion/exclusion criteria	*Exclusion Criteria: life expectancy<3 years, ASA class IV and V, bowel obstruction, strangulation, peritonitis, bowel perforation, local or systemic infection, history of inguinal hernia repair with mesh* *Inclusion Criteria: 18 years of age or older, unilateral hernia, able to provide informed consent.*
Patient Age, BMI and Hernia Types	*All male patients* *Mean Age: 64(24-85) SIHM and 59 (25-97) Polypropylene* *BMI: 36(18-39) SIHM; 25(19-37) Polypropylene* *Hernia type: Direct 20 (44% SIHM) 21(42% Polypropylene)* *Indirect 26(58% SIHM) 29 (58% Polypropylene)* *Sliding 24 (53% SIHM) 19 (38% Polypropylene)* *Non-sliding 26 (58% SIHM) 31 (62% Polypropylene)*
Operative procedure specifics - anesthesia, duration of procedure	*Lichtenstein open repair* *Anesthesia: Spinal: 4 (9% SIHM) 6 (12% Polypropylene)* *General: 42 (93% SIHM) 44 (88% Polypropylene)* *Procedure time (Minutes):* *134 (SIHM) 115 (Polypropylene)*

Patient duration of follow-up outcomes/adverse events	*All patients were followed up for 12 months* *Recurrences:* • *3 hernia recurrences all in the SIHM group incidence 6.7% vs 0% in Polypropylene group* • *All recurrences occurred in patients who originally had direct inguinal hernias (recurrence rate in subset of patients with direct hernias: 3/20 or 15% at 1 year)* • *Unpublished 3 year data recurrence rates: 15.6% (7/45) SIHM vs 4% (2/50) Polypropylene* *Post-operative pain:* *At 2 weeks : 9 (20% SIHM) vs 8 (16% Polypropylene)* *At 1 year : 2 (4% SIHM) vs 3 (6% Polypropylene)* *Adverse events:* *Hematoma: 6 (13% SIHM) vs 1 (2% Polypropylene)* *Incisional pain: 2 (4% SIHM) vs 4 (8% Polypropylene)* *Surgical site reaction : 3 (7% SIHM) vs 0 (0% Polypropylene)* *Seroma : 5 (11% SIHM) vs 0 (0% Polypropylene)* *Neuralgia: 4 (9% SIHM) vs 6 (12% Polypropylene)* *Infection: 0 (0% SIHM) vs 0 (0% Polypropylene)* *Testicular Problems: 5 (11% SIHM) vs 4 (8% Polypropylene)* *Urinary retention: 6 (13% SIHM) vs 3 (6% Polypropylene)* *Spermatic cord injury: 0 (0% SIHM) vs 1 (2% Polypropylene)* **One death in SIHM group due to myocardial infarction.*

Table 2: Ansaloni L, *et al*. Inguinal hernia repair with porcine small intestine submucosa: 3-year follow-up results of a randomized controlled trial of Lichtenstein's repair with polypropylene mesh versus Surgisis Inguinal Hernia Matrix. *Am J Surg* 2009; 198:303-312.

Number of centers	*1 OUS Center / 2 investigators*
Number of patients	*70 patients randomized to:* • *Polypropylene* • *Porcine small intestinal submucosa (Surgisis)*
Study inclusion/exclusion criteria	*Excluded patients with recurrent hernia, any condition preventing a correct evaluation of pain, hypersensitivity to drugs used in study, intraoperative findings of pathology other than inguinal hernia*
Patient Age, BMI and Hernia Types	*Mean age: 61.3 years for polypropylene (SD 17.7 years)* *56.2 years for SIHM (SD 18.0 years)* *Mean BMI: 26* *Mix of direct and indirect inguinal hernias in each group*
Operative procedure specifics - anesthesia, duration of procedure	*Operative time: SHIM 68.6 Minutes / PP 66.0 Minutes* *Preoperative antibiotics* *General or Spinal anesthesia (patient's choice/ anesthetist's preference)*
Patient duration of follow-up outcomes/adverse events	*36 month follow-up* • *Hernia recurrence:* *0% SIHM / 2.9% PP* • *Chronic pain:* *6 months 11% SIHM / 31% PP* *12 months 8% SIHM / 23% PP* *36 months 3% SIHM / 14% PP* • *Surgical site occurrence at 1 week post-surgery:* *Hematoma: 5.7% SIHM / 5.7% PP* *Seroma: 5.7% SIHM / 17.1% PP*

Table 3: Puccio F, *et al.*. Comparison of three different mesh materials in tension-free hernia repair: Prolene versus Vypro versus Surgisis. *Int Surg* 2005:90:S21-S23.

Number of centers	*1 OUS Center / 5 investigators*
Number of patients	*45 patients with unilateral primary inguinal hernia receiving Lichtenstein repair randomized to:* • *Polypropylene* • *Polyglactin and polypropylene* • *Porcine small intestinal submucosa (Surgisis)*
Study inclusion/exclusion criteria	*Excluded patients with history of major surgery in lower abdomen other than cancer or immune deficiency*
Patient Age, BMI and Hernia Types	*Mean age 54 (range 26-74 years)* *Mean BMI 26* *Mix of direct and indirect inguinal hernias in each group*
Operative procedure specifics - anesthesia, duration of procedure	*Operative time for all patients 45 minutes (range 35-80 min)* *Preoperative antibiotics* *Local anesthesia*
Patient duration of follow-up outcomes/adverse events	*12 mo (1-16 mo)* *All patients received 3 month follow-up, using ultrasound U/S - no evidence of prosthesis in SIS group, prosthesis visible in other groups* • *Polypropylene – early complications (< 30 days): 1 hematoma, 1 seroma, 1 delayed wound healing, 8 discomfort; late complication (> 30 days) 1 hyperesthesia; hernia recurrence 0* • *Polyglactin and polypropylene – early complications: 2 hematoma, 1 prolonged pain, 1 sensory loss, 7 discomfort; long term: 1 hyperesthesia, 1 prolonged pain, 1 sensory loss, hernia recurrence 0* • *Porcine small intestinal submucosa (Surgisis) – early: 1 seroma, 2 discomfort; late – none, hernia recurrence 0*

Substantial Equivalence

See Table 4 for a comparison of the subject device and its predicates.

Table 4 – Substantial Equivalence Comparison

Device	SIS Inguinal Hernia Repair Graft	SurgiMend Collagen Matrix	SIS Hernia Repair Device
Manufacturer	Cook Biotech Incorporated	TEI Biosciences Inc.	Cook Biotech Incorporated
510(k) Number	K142887	K083898	K062697
Intended Use	For implantation to reinforce soft tissues where weakness exists, including the repair of inguinal hernias.	For implantation to reinforce soft tissue where weakness exists and for the surgical repair of damaged or ruptured soft tissue membranes. SurgiMend is specifically indicated for: plastic and reconstructive surgery, muscle flap reinforcement, hernia repair including abdominal, inguinal, femoral, diaphragmatic, scrotal, umbilical, and incisional hernias.	For implantation to reinforce soft tissues where weakness exists. Indications for use include repair of a hernia or body wall defect.
Product code	FTM	FTM	FTL
21 CFR	878.3300	878.3300	878.3300
Material	Porcine small intestinal submucosa (porcine) Primarily Types I, III, IV and VI collagen (constituents of the extracellular matrix)	Collagen based derived from fetal bovine dermis	Porcine small intestinal submucosa (porcine) Primarily Types I, III, IV and VI collagen (constituents of the extracellular matrix)
Dimensions	Rectangular or pre-shaped 6 x 10 cm 8 x 15 cm 10 x 15 cm 12 x 15 cm 13 x 18 cm	3 x 3 cm to 20 x 20 cm square, 0.3 x 25 cm to 25 x 40 cm rectangle, 7 x 17 cm to 10 x 20 rectangle, 8 x 16 cm to 15 x 15 cm semi-oval	5 x 8 cm to 20 x 30 cm
Thickness	0.1 – 1.0 mm	0.5 to 4.4 mm	0.1 – 1.5 mm
EtO Sterilized	Yes	Yes	Yes

CONCLUSION:

The mechanical, pre-clinical, and clinical tests performed on the SIS Inguinal Hernia Repair Graft show that the device is substantially equivalent to its predicates.

REFERENCES:

1.Bochicchio, GV, *et al.*, J Am Coll Surg, 2014. **218**(4): p. 751-7.
2.Puccio, F, *et al.*, Int Surg, 2005. **90**(3 Suppl): p. S21-3.
3.Ansaloni, L, *et al.*, Am J Surg, 2009. **198**(3): p. 303-12.