DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
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July 27, 2017

Novus Scientific AB
c/o Mr. Fedrik Bohman
Quality Assurance & Regulatory Affairs Manager (*acting*)
Virdings Allé 2
SE 754 50 Uppsala
Sweden

Re: K163005
Trade/Device Name: TIGR® Matrix Surgical Mesh
Regulation Number: 21 CFR 878.3300
Regulation Name: Surgical Mesh
Regulatory Class: Class II
Product Code: OWT
Dated: June 26, 2017
Received: June 26, 2017

Dear Mr. Bohman:

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 Part 801); 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" (21 CFR 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,

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)*
K163005

Device Name

TIGR® Matrix Surgical Mesh

Indications for Use *(Describe)*

TIGR® Matrix Surgical Mesh is intended for use in reinforcement of soft tissue where weakness exists.

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

Submitter's Information

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Date of preparation

26 July 2017

Device Name

Trade Name:	TIGR® Matrix Surgical Mesh
Common Name:	Surgical Mesh
Classification:	Mesh, Surgical, Polymeric
Classification Product Code:	OWT
Regulatory number:	§878.3300

Predicate Device Name

TIGR® Matrix Surgical Mesh (K092224)

Device Description

TIGR® Matrix Surgical Mesh is knitted from two different synthetic resorbable fibers, possessing different degradation characteristics. The fast-resorbing fiber, making up approximately 40% of the matrix by weight, is a copolymer of glycolide, lactide, and trimethylene carbonate. The slow-resorbing fiber, making up approximately 60% of the matrix by weight, is a copolymer of lactide, and trimethylene carbonate. Both fibers degrade by bulk hydrolysis once implanted, resulting in a decreasing strength retention followed by mass loss of the fibers. *In vitro* testing showed that the fast-resorbing fiber (glycolide, lactide and trimethylene carbonate) loses its mechanical strength after 2 weeks and *in vivo* studies in the abdominal wall of sheep showed that the fast-resorbing fiber is fully absorbed after 4 months. The same *in vitro* testing showed that the slow-resorbing fiber (lactide and trimethylene carbonate) maintains its mechanical strength for 6 months and in vivo studies in the abdominal wall of sheep indicated that the slow-resorbing fiber is absorbed after approximately 36 months.

Intended Use

TIGR® Matrix Surgical Mesh is intended for use in reinforcement of soft tissue where weakness exists. The indication for use of the subject device is identical compared to the predicate device.

Feature	Subject Device TIGR® Matrix Surgical Mesh	Predicate Device (K092224) TIGR® Matrix Surgical Mesh
Classification	Class II: polymeric surgical mesh	Class II: polymeric surgical mesh
Indication for use	TIGR® Matrix Surgical Mesh is indicated for use in reinforcement of soft tissue where weakness exists.	TIGR® Matrix Surgical Mesh is indicated for use in reinforcement of soft tissue where weakness exists.
Contraindications	Not suitable for reconstruction of cardiovascular defects.	Not suitable for reconstruction of cardiovascular defects.
	TIGR® Matrix Surgical Mesh must always be separated from the abdominal cavity by peritoneum.	TIGR® Matrix Surgical Mesh must always be separated from the abdominal cavity by peritoneum.
	Not for use following planned intra-operative or accidental opening of the gastrointestinal tract.	Not for use following planned intra-operative or accidental opening of the gastrointestinal tract.

Technical Characteristics

The predicate device and the subject device have substantially equivalent technology characteristics, e.g. Design, Material, Sterility etc. The shelf-life is increased to two (2) years compared to the predicate device. The size range has been narrowed for the subject device compared to the predicate device. The measured thickness is also slightly higher for the subject device.

Feature	Subject Device TIGR® Matrix Surgical Mesh	Predicate Device (K092224) TIGR® Matrix Surgical Mesh
Mesh Thickness (mean; mm)	0.687	0.573
Area weight/density (mean; g/m^2)	$125 \leq x \leq 170$	$125 \leq x \leq 170$
Porosity (%)	$20 \leq x \leq 40$	$20 \leq x \leq 40$
Weave characteristics	Multifilament Warp knitted, Mesh	Multifilament Warp knitted, Mesh
Ranges of sizes (mm)	100x150 to 200x300	120x65 to 200x300
Materials	Copolymers (Glycolide, L-lactide and Trimethylene carbonate)	Copolymers (Glycolide, L-lactide and Trimethylene carbonate)
Sterility	Sterile EO, SAL 10^-6	Sterile EO, SAL 10^-6
Shelf Life	2 years	1 year

Nonclinical performance data

Performance testing was initially evaluated for predicate device in (K092224). Additional/new testing has been performed for the subject device as part of process qualification and validation activities during the manufacturing site change. The predicate device and the subject device have substantially equivalent performance characteristics.

Parameter	Standard test method referenced	Subject Device TIGR® Matrix Surgical Mesh	Predicate Device (K092224) TIGR® Matrix Surgical Mesh
Ball burst strength/Force (Mean; N)	ASTM D3787 (2015)	≥ 250	≥ 250
Suture pull-out strength (Mean; N)	Novus internal test method TI-0208	≥ 20	≥ 20
Tear Strength (Mean; N)	ISO 9073-4 (1997)	≥ 30	≥ 30
Stiffness (Bending Modulus; MPa)	ASTM D1388 (2014)	≥ 10 MPa	≥ 10 MPa
Relative Distention at 16N (%)	ASTM D6775 (2013)	≤ 8	≤ 8
Degradation Characteristics	ISO 15814:1999	Established as equivalent *in-vitro*.	
Biocompatibility	ISO 10993, Biological evaluation of Medical Devices, Part 1: Evaluating and Testing	Established	Established
Electrical Safety	NA	NA	NA
Chemical Safety	NA	NA	NA
Thermal Safety	NA	NA	NA
Radiation Safety	NA	NA	NA
Shelf life	Novus internal test methods	2 years	1 year

Biocompatibility testing

Biocompatibility testing and classification has been selected and performed in accordance with ISO 10993, Biological evaluation of Medical Devices, Part 1: Evaluating and Testing. TIGR Matrix Surgical Mesh is classified as an *implant* with *permanent contact*. Testing has been performed on sterilized devices. The biocompatibility was initially assessed in premarket notification (K092224), since; additional tests, as a result of changes in manufacturing facility and altered standard requirements, have been performed. These additional tests are denoted with a * in the table below. Studies have been conducted at contract laboratories BIOMATECH and NAMSA, in accordance with applicable GLP requirements. Tests are summarized in the table below.

Test to be considered	**Action**	**Evaluation**
ISO 10993-3 Test for genotoxicity, carcinogenicity and reproductive toxicity Ames Test (mutagenicity)	The bacterial Reverse Mutation Test (Ames Test) was performed.	The test article extracts were not toxic and not mutagenic.
ISO 10993-3 Test for genotoxicity, carcinogenicity and reproductive toxicity Chromosomal aberration induction in human cells (genotoxicity)	Human lymphocyte cultures were exposed to the test article extract.	The extract of the test article did not induce a significant number of chromosomal aberrations in human lymphocytes in culture in the presence or absence of metabolic activations. The extract of the test article met the requirement of the test.
ISO 10993-5 Tests for Cytotoxicity	The test extract was placed onto triplicate confluent monolayers of L-929 mouse fibroblast cells.	The extract of the test articles showed no evidence of causing cell lysis or toxicity greater than a grade 2 (mild reactivity), grade 0 for these test articles. The extract of the text articles met the requirements of the USP and part 5 of ISO 10993 standard.
	*L-929 mouse fibroblast cells were incubated with test article extracts and evaluated with phase contrast microscopy.	*The full strength test article extract showed no cytotoxic potential to L-929 mouse fibroblast cells.
ISO 10993-6 Test for local effects after implantation 1. Collagen and tissue formation 2. Local tolerance degradation kinetics	The objective of this study was to evaluate collagen tissue formation and remodeling (1, 3 and 6 months within the test implant. Two groups of 5 rats were implanted with the test and control article (total of 30 rats, n=5 sites per product and per time-period). Test mesh (2x3) cm was sutured onto (1cm x 1cm) full thickness defect created within the abdominal musculature of each animal.	Colonization and the local tolerance of the test implant were good and similar or greater as compared to the control implant in terms of degradation at 6 months. The degradation of the large fibers of the test article seemed to be complete at 6 months. The multifilament fiber of the test article showed signs of initial degradation.
ISO 10993-7 Ethylene oxide sterilization residuals	Each sterilized batch is tested for Ethylene oxide and Ethylene chlorohydrin residuals, via gas chromatography according to ISO 10993-7, Annex A.4.	Each batch is evaluated against the limits of exposure defined in ISO 10993-7 section 4.3.2. Product release is conditioned to conformance to the requirements of the standard.

ISO 10993-10 Tests for irritation and delayed-type hypersensitivity Part 7.4 Maximization Test for delayed hyper sensitivity	Maximization test for delayed hypersensitivity was performed.	No delayed sensitization was induced with either extracts. The score became grade 0.
	* A guinea pig maximization test was performed to evaluate the potential for delayed dermal contact sensitization.	*The topical application of the 0.9% NaCl extract and sesame oil extract evaluated at concentration of 100%, according to the ISO 13993-10 standard, did not induce delayed senstitization in the guinea pig (grade 0).
ISO 10993-10 Tests for irritation and delayed-type hypersensitivity Annex B.B. 2 Intracutaneous (Intradermal) Reactivity Test	Two (2) adult albino rabbits were clipped on both flanks. The rabbits received five intracutaneous injections of 0.2 mL of the 0.9% NaCl extract on one side and five injections of 0.2 mL of the corresponding vehicle as negative control. Similarly, the rabbits received five injections of 0.2 mL of the sesame oil extract, and five injections of the corresponding vehicle. The sites were examined at 24, 48 and 72 hours after injection for gross evidence of tissue reactions, such as erythema, edema or necrosis.	The irritation indexes for the 0.9% NaCl extract became 0 and for the sesame oil extract 0.08, i.e. the difference between the test and control sites was lower than 1.
	*An intracutaneous test was performed to evaluate the potential of the material to produce irritation following intradermal injection. Three (3) rabbits received intracutaneous injections. The sites were examined immediately, 24, 48 and 72 hours after injection for gross evidence of tissue reactions, such as erythema, edema or necrosis.	*The extracts of the test article met the requirements of the intracutaneous injection test in the rabbit according to the procedure described in the ISO 10993-10 standard.
ISO 10993-11 Tests for systemic toxicity Acute Systemic Toxicity	A single dose of each extract was injected into five (5) mice per extract, by either intravenous route or intraperitoneal route. Animals were observed immediately and at 4, 24, 48 and 72 hours after systemic injection.	Under the conditions of the test, there was no evidence of significant systemic toxicity or mortality after test article extracts injection and therefore meets the requirements of the test.
ISO 10993-3 Test for genotoxicity, carcinogenicity and reproductive toxicity Carcinogenicity	Not performed	Chronic toxicity and carcinogenicity studies as suggested in ISO 10993-1 as supplementary tests were not considered necessary as the chemical structure of the two polymers as well as their degradation products do not suggest a carcinogenic potential. Neither of the two polymeric materials used in mesh nor their degradation products are in a class that has produced positive carcinogenic results; furthermore prior studies, in vitro and in vivo, of the mutagenic potential for this type of materials do not indicate the need for additional testing.
ISO 10993-11 Tests for systemic toxicity Chronic Toxicity	Not performed	

ISO 10993-18 Chemical characterization of materials	The chemical characterization test performed are: - Exhaustive Extraction (Water, IPA, Hexane) - Inductively coupled plasma spectroscopy (ICP) - IR Spectrum analysis - GC/MS - LC/MS	The initial testing performed in preparation of (k092224) identified that extraction of the WK-6 Surgical Mesh with isopropyl alcohol and hexane resulted in a non-volatile residue of 42.2 and 30.8 mg. From the FT-IR analysis it was clear that part of this residue was polydimethylsiloxane which more frequently is referred to as silicone oil. Silicone oil was used as a spin finisher during the fiber spinning process. After knitting and annealing the mesh is cleaned in isopropyl alcohol to remove the spin finisher. The batches used for the first biocompatibility testing were cleaned for 2 minutes in an ultrasonic bath containing Isopropyl alcohol. Cleaning validation of the mesh was later been performed and the operational qualification showed that cleaning need to be continued for 6 minutes using an ultrasonic Isopropyl alcohol bath to fully get rid of the silicone oil as determined by the characteristic FTIR peaks for silicone oil at 2962 cm-1, 1260 cm-1 and shoulder at 1011 cm-1. This was later verified in a performance qualification of the cleaning process. In addition this was further clarified in the Q&A following the FDA review of (K092224).
	*The chemical characterization test performed are: - Exhaustive Extraction (Water, IPA, Hexane) - Inductively coupled plasma spectroscopy (ICP) - IR Spectrum analysis - GC/MS - UPLC/MS	*Equivalent testing was performed as part of process validation during the manufacturing site change. Silicone oil usage in the manufacturing of the predicate device has been replaced with castor oil in the manufacturing of the subject device. Castor oil is generally recognized as safe and is permitted as a direct food additive to hinder stickiness of hard candy and vitamin and/or mineral tablets 21CFR part 172.876. Both castor oil and its sulphated counterpart is listed as safe in Indirect additives used in food contact 21CFR part 175-178. Castor oil is also listed as a safe chemical for use in laxative sold as OTC drug and the ethoxylated castor oil is used as an excipient in several drug formulations.

Shelf life

Accelerated and real time stability studies of the mesh and packaging have been performed for TIGR® Matrix Surgical Mesh as part of process qualification and validation activities during the manufacturing site change. The conclusion of the performed studies is that there are only no or vague declining trends of quality characteristics defined in the product specification.

Animal studies

Additional testing has not been conducted for the subject device for determination of substantial equivalence. Animal studies conducted for the predicate device (K092224) are summarized below.

Rat

A 6 months implantation study in rats were performed to study local tissue response, tissue remodeling and implant degradation. For each selected time period (1, 3 and 6 months) two groups of five rats were each implanted with test mesh (TIGR® Matrix Surgical Mesh) and control mesh (Prolene®), altogether 30 rats. The surgery was performed by creating a full thickness defect, 10 mm x 10 mm, within the abdominal wall musculature. Degradation of the fast-resorbing fiber of the test mesh seemed to be completed at 6 months whereas the slow-resorbing fibers showed no signs of degradation.

Sheep

An implantation study in sheep, evaluated at 4, 9, 15, 24 and 36 months was performed to study local tissue response, tissue remodeling and degradation of the mesh in a larger animal having a larger tension in the abdominal wall. A total of 13 sheep were implanted with four meshes. Each observation comprised 3 sheep with 10 test meshes (TIGR® Matrix Surgical Mesh) and 2 control meshes (Prolene®). A full thickness, 3 cm x 3 cm square, defect was created within the abdominal wall musculature. The abdominal wall was removed carefully to leave the peritoneum intact. A mesh of 8 cm x 8 cm was used to cover the defect with an overlap. Microscopic observations of the implant sites were performed after termination. Histological analysis was performed to evaluate the local tolerance and material degradation. Degradation of the fast/resorbing fiber of the test mesh seemed to be completed after 4 months while the slow/resorbing fibers showed no signs of degradation and were still present after 9 months. After 36 months, the test mesh was fully resorbed and only microscopic implant residues could be found in the tissue.

Clinical performance data

The changes to labeling proposed in this submission were initiated by the results of a clinical study, where the long-term performance for repair of inguinal hernia was investigated for the predicate device. No clinical study has been conducted for the subject device for determination of substantial equivalence.

Conclusion

Since nonclinical bench performance testing data and biocompatibility studies are well understood for this type of device, nonclinical performance data are deemed sufficient to support substantial equivalence. As shown in this summary, TIGR® Matrix Surgical Mesh is substantially equivalent to the predicate device in intended use, indication for use, fundamental design and technology, and principles of operation. Novus Scientific AB has made this determination of substantial equivalence based on intended use, indications for use, technological characteristics and nonclinical performance. Based on the 510(k) and the information provided herein, we conclude that the Subject Device is substantially equivalent to the Predicate Device under the Federal Food, Drug and Cosmetic Act.