



Food and Drug Administration
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June 22, 2016

Toyobo Co., Ltd.
% James A. Boiani, MS, JD
Official Correspondent
Epstein Becker & Green, P.C.
1227 25th St. NW, Suite 700
Washington, DC 20037

Re: K152967

Trade/Device Name: Nerbridge™
Regulation Number: 21 CFR 882.5275
Regulation Name: Nerve Cuff
Regulatory Class: Class II
Product Code: JXI
Dated: May 20, 2016
Received: May 23, 2016

Dear Mr. Boiani:

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 yours,

Carlos L. Pena -S 

Carlos L. Peña, PhD, MS
Director
Division of Neurological
and Physical Medicine Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known)

K152967

Device Name

Nerbridge™

Indications for Use (Describe)

Nerbridge™ is intended for the repair of peripheral nerve injuries in which there is no gap or where a gap closure can be achieved by flexion of the extremity.

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

The assigned 510(k) number is: K152967

1. Submitter's Identification:

Toyobo Co., Ltd.
2-8 Dojima Hama 2-chome, Kita-ku,
Osaka 530-8230 Japan
Tel: 81-6-6348-3336
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Contact: Mr. Yuta Kawakatsu

Date Summary Revised: June 21, 2016

2. Name of the Device:

Nerbridge™
Device Common Name: Cuff, Nerve
Device Classification Name: Nerve Cuff
Product Regulation Number: 21 CFR Part 882.5275
Product Code: JXI
Regulatory Class: II
Classification Panel: Neurology

3. Predicate Device Information:

- 1) K103081 – Biom'Up SA. Cova™ ORTHO-NERVE
- 2) K983007 – Neuroregen LLC Neurotube™

4. Device Description:

Nerbridge™ is a product composed of polyglycolic acid and collagen derived from porcine skin. Nerbridge™ is a flexible, resorbable and semipermeable tubular membrane matrix filled with porous collagen that provides a non-constricting encasement for injured peripheral nerves for protection of the neural environment. Nerbridge™ is designed to be an interface between the nerve and the surrounding tissue. When hydrated, Nerbridge™ is a pliable, soft, non-friable, porous conduit. The resilience of Nerbridge allows the product to recover and maintain closure without constricting the nerve once the device is placed around the nerve. Nerbridge™ is manufactured using validated viral inactivation and removal processes for the collagen. The product is provided in a foil pouch, sterile, non-pyrogenic, for single use only, in a variety of sizes, and placed in an outer Tyvek header bag for added protection.

5. Indications for Use:

Nerbridge™ is intended for the repair of peripheral nerve injuries in which there is no gap or where a gap closure can be achieved by flexion of the extremity.

6. Comparison to Predicate Devices:

Device Name		Nerbridge™	Neurotube™	Cova™ORTHO- NERVE
Manufacturer		TOYOBO CO., LTD.	Neuroregen, LLC	Biom'Up S.A.
510(k) No.		K152967	K983007	K103081
Intended Use and Indications for Use		Nerbridge™ is intended for the repair of peripheral nerve injuries in which there is no gap or where a gap closure can be achieved by flexion of the extremity.	The Neurotube™ is intended for single use in patients with an injury to a peripheral nerve in which the nerve gap is more than or equal to 8mm, but less than or equal to 3 cm. The nerve gap may be created primarily at the time of injury or created secondarily at the time of exploration of failed primary repair.	Cova™ORTHO-NERVE is indicated for the repair of peripheral nerve injuries in which there is no gap or where a gap closure can be achieved by flexion of the extremity
Material	Synthetic polyester	Polyglycolic acid (PGA)	PGA	Contains no Synthetic Polyester material
	Collagen	Type	I and III	I
		Origin	Porcine	None
Shape		Cylindrical	Cylindrical	Membrane, rollable if needed
Physical structure		PGA conduit whose outer surface is coated by collagen and with inner porous collagen	PGA conduit	Collagen membrane

Device Name		Nerbridge™	Neurotube™	Cova™ORTHO- NERVE
Sizes		ID: 0.5, 1.0, 1.5, 2.0, 2.5, 3.0, 3.5, 4.0mm Length: 30, 50 mm	ID: 2.0,3.0, 4.0, 8.0mm Length: 20, 40mm	Rectangular sheets of 15 x 25 mm, 20 x 30 mm, 30 x 40 mm and 40 x 60 mm
Sterilization		Ethylene oxide	Ethylene oxide	Gamma irradiation
Clinical testing		Yes	Yes	No
Non-clinical animal testing		Yes	Unknown	Yes
Biocompatibility		ISO 10993	Unknown	ISO 10993
Performance	Suture retention strength	Yes	Unknown	Yes
	Mechanical compression and rebound	Yes	Yes	Yes
	Porosity	Yes	Unknown	Unknown
	Permeability	Yes	Yes	Unknown
	In vitro degradation	Yes	Yes	Yes
	Tensile strength	Yes	Unknown	Yes
	pH	Yes	Unknown	Yes
	Swelling rate	Yes	Unknown	Yes
	Visual inspection	Yes	Unknown	Unknown
	Bending stiffness	Yes	Yes	Unknown
	Endotoxin	Yes	Unknown	Yes
	Packaging	Foil pouch within protective outer pouch	Double peel packages	Double peel packages
	Shelf Life	3 years	5 years	24 months

The Nerbridge™ and the predicate devices have the same intended use: to act as a conduit to assist the nerve in repairing itself following damage.

The Nerbridge™ and the predicate devices are sutured to the nerve and nerve tissue and surround the damaged nerve to protect the damaged area, allowing it to heal. At a high level, the subject and predicate devices are based on the following same technological elements:

- Provided or can be made into a cylindrical shape
- Flexible
- Smooth
- Wettable
- Resorbable material

Certain technological differences exist between the subject and predicate devices as detailed in the above. In particular, the subject device is a PGA tube with an outer coating and internal filling of a porous Type I and III collagen blend; the Neurotube is a PGA tube that does not contain collagen; the Cova Ortho-Nerve is a Type I collagen membrane. While having some technological differences with the predicates, the Clinical and Non-Clinical tests performed on the Nerbridge™ show that it is safe and effective for its intended use and substantially equivalent to the predicate devices.

7. **Discussion of Non-Clinical Tests Performed for Determination of Substantial Equivalence:**

The following functional performance verification and product characterization testing was conducted on finished sterile Nerbridge™ devices using known standards and/or clinically relevant criteria:

- Suture retention strength
- Mechanical compression and rebound
- Porosity
- Permeability
- In vitro degradation
- Tensile strength
- pH
- Swelling rate
- Visual inspection
- Bending stiffness
- Endotoxin

The testing supports and further characterizes Nerbridge™ that was studied in the Nerbridge™ Clinical Study, and shown to be clinically safe and effective for its intended use as a nerve conduit, and supporting substantial equivalence to other nerve conduits with the same intended use.

Test	Test Method Summary	Results
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Test	Test Method Summary	Results
Suture retention strength	Testing according to ISO 7198:1998 Acceptance criteria: Suture must fail before the Nerbridge	Acceptance criteria met
Mechanical compression and rebound	Testing according to JIS T0401:2013 Acceptance criteria: Nerbridge must maintain mechanical strength after continuous compression and rebound loading	Acceptance criteria met
Porosity	Testing according to ISO 845:2006 and JIS Z8807:2012 Acceptance criteria: Porosity of Nerbridge must be greater than or equal to porosity of PGA tube alone	Acceptance criteria met
Permeability	Devices were filled with protein solution and then immersed in saline. At periods of time up to 96 hours, saline was measured for protein particles Acceptance criteria: Protein must permeate the wall of the Nerbridge	Acceptance criteria met
In vitro degradation	Testing according to ISO 15814:1999 and ISO 527-1:2012 Acceptance criteria: Nerbridge must maintain a tensile strength greater than that of suture for 8 weeks	Acceptance criteria met
Tensile strength	Testing according to ISO 527-1:2012 Acceptance criteria: Nerbridge tensile strength is at least as much as the predicate	Acceptance criteria met
pH	Testing according to JIS T 3211:2011 Acceptance criteria: Nerbridge satisfies the acceptance criteria as specified in JIS T 3211:2011	Acceptance criteria met
Swelling rate	Testing according to ISO 10545-3:1995 Acceptance criteria: Swelling rate of Nerbridge must be greater than or equal to swelling rate of PGA tube alone	Acceptance criteria met
Visual inspection	Visual inspection with a magnifying glass Acceptance criteria: No observation of significant streaks, wrinkles, uneven, scratches and cracks, bubbles or other abnormalities	Acceptance criteria met

Test	Test Method Summary	Results
Bending stiffness	Testing according to JIS T0401:2013 Acceptance criteria: Bending stiffness of Nerbridge must be greater than or equal to bending stiffness of PGA tube alone	Acceptance criteria met
Endotoxin	Testing according to Japanese Pharmacopoeia 16 th edition and FDA Guidance for Industry: Pyrogen and Endotoxin Testing: Questions and Answers (June 2012) Acceptance criteria: Endotoxin level is less than or equal to 20 EU/device	Acceptance criteria met

Biocompatibility Testing

The biocompatibility evaluation for the Toyobo Nerbridge device was performed according to ISO 10993 to demonstrate that the device was both safe for implantation and establish substantial equivalence among the predicate device.

Test	Test Method Summary	Results
Cytotoxicity	ISO Direct contact Cytotoxicity Assay	Non-cytotoxic
Sensitization	ISO Guinea pig Maximization test with device extracts (saline and sesame oil extracts)	No evidence of sensitization
Acute intracutaneous Reactivity	ISO Acute intracutaneous Reactivity Test in rabbits with device extracts (saline and sesame oil extracts)	No evidence of irritation
Acute Systemic Toxicity	ISO Acute System Toxicity in Mice with device extracts (saline and sesame oil extracts)	No mortality or evidence of systemic toxicity
Rabbit Pyrogen Study	USP Material-mediated Rabbit pyrogen test with saline extract of the device	No evidence of material-mediated pyrogenicity
Hemolysis	Hemolysis test by direct contact with human red blood cells	No hemolytic activity
Genotoxicity	ISO Ames Mutagenicity Assay with device extracts (saline and ethanol extracts)	No evidence of mutagenicity

Test	Test Method Summary	Results
Genotoxicity	ISO Mouse bone marrow micronucleus with device extracts (saline and sesame oil extracts)	No evidence of clastogenicity
Genotoxicity	CHL/IU cells with device extracts (MEM & 10%CS/MEM)	No evidence of inducing chromosomal aberrations or polyploid cells
Implantation Absorption	Subcutaneous implantation in rats	Absorption of material by 13 weeks. No inflammation observed
Implantation (safety and performance)	In vivo safety and performance study in rats after 3, 30 and 90 days	Protection during nerve repair. No fibrous perinevous tissue was observed after 3, 30 or 90 days.
Subchronic / Chronic toxicity	13-week systemic toxicity and local tolerance study in rats following subcutaneous implantation	No adverse tissue reaction to the implant up to 13 weeks of implantation No systemic toxicity

Viral Inactivation Study

Viral Inactivation steps were validated for collagen extracted from tissues used in the manufacture of the device. For the validation, different viruses were selected according to their physio-chemical resistance and representativeness. The viral inactivation steps are routinely performed in process using appropriate treatment. It was demonstrated that the inactivation steps reduced down the final viral load to the limit of detection.

8. Clinical Tests Performed

A multi-center joint randomized evaluator-blinded comparative clinical study was conducted on the Nerbridge™ device where the Nerbridge™ device was used in 60 subjects at 20 trial sites with hand injuries. The primary efficacy endpoint was evaluated on the Full Analysis Set (58 subjects) and the Per Protocol Set (54 subjects). The control group consisted of 6 subjects implanted with an autogenous free nerve graft. The mean percentage of improvement in primary evaluation in the sensory function test by the Semmes-Weinstein method for the Nerbridge™ device was higher than that in the autogenous free nerve grafting group. The incidence of adverse events were lower for the Nerbridge™ device than the control. Therefore, the Nerbridge™ device is safe

and effective for its intended use and substantially equivalent to the predicate devices.

9. Animal Tests Performed

An animal study was conducted in rabbit model to evaluate the performance and safety (local tissue effects) of the Nerbridge™ after nerve section and direct suture in the rabbit sciatic nerve. Nerbridge™ resorbed by day 72, there was evidence of nerve regeneration, and the histological reactions at the site of introduction of the device were slight.

10. Conclusions

The subject device, the Nerbridge™, has the same intended use as the predicate devices, Biom'Up SA. Cova™ ORTHO-NERVE (K103081) and Neuroregen LLC, Neurotube™ (K983007). The Clinical and Non-Clinical testing supplied within our submission demonstrates that there are not any significant differences in their technological characteristics thereby not raising any new questions of safety and effectiveness. Therefore, the Nerbridge™ is substantially equivalent to the predicate devices, Biom'Up SA. Cova™ ORTHO-NERVE (K103081) and Neuroregen LLC, Neurotube™ (K983007).