October 12, 2023

AxoGen Corporation
Shravani Shastry
Senior Regulatory Affairs Specialist
13631 Progress Blvd, Suite 400
Alachua, FL 32615-9409

Re: K231708
Trade/Device Name: Axoguard HA+ Nerve Protector (AGHA12); Axoguard HA+ Nerve Protector (AGHA22); Axoguard HA+ Nerve Protector (AGHA24); Axoguard HA+ Nerve Protector (AGHA36); Axoguard HA+ Nerve Protector (AGHA48)
Regulation Number: 21 CFR 882.5275
Regulation Name: Nerve Cuff
Regulatory Class: Class II
Product Code: JXI
Dated: September 11, 2023
Received: September 11, 2023

Dear Shravani Shastry:

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 (the 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 available 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.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device"

(https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

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 Part 803) for devices or postmarketing safety reporting (21 CFR Part 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 Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 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,

Adam D. Pierce -S

Digitally signed by Adam D. Pierce -S
Date: 2023.10.12 09:41:27 -04'00'

Adam D. Pierce, Ph.D.
Assistant Director
DHT5A: Division of Neurosurgical,
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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)*
K231708

Device Name
Axoguard HA+ Nerve Protector (AGHA12); Axoguard HA+ Nerve Protector (AGHA22);
Axoguard HA+ Nerve Protector (AGHA24); Axoguard HA+ Nerve Protector (AGHA36);
Axoguard HA+ Nerve Protector (AGHA48)

Indications for Use *(Describe)*
Axoguard HA+ Nerve Protector is indicated for the management and protection of peripheral nerve injuries where there is no gap, or following closure of the gap.

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: K231708

1. Submitter

Name:	Axogen Corporation 13631 Progress Blvd, Ste 400 Alachua, FL, 32615
Contact Person:	Shravani Shastry
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Date Prepared:	October 12th, 2023

2. Device Information	Axoguard HA+ Nerve Protector
Trade/Device Name:	Nerve Cuff
Common/Usual Name:	Nerve Cuff
Classification Name:	Class II
Regulatory Class:	JXI
Product Code:	21 CFR 882.5275
Regulation Number:	

3. Predicate Device

Device	Company	Predicate 510(k)	Clearance date
Axoguard HA+ Nerve Protector	Axogen	K223640	April 7, 2023

4. Device Description

Axoguard HA+ Nerve Protector is a surgical implant that provides non-constricting protection for peripheral nerve injuries. Axoguard HA+ Nerve Protector is designed to aid in coaptation and protection of peripheral nerve injuries by serving as an interface between the nerve and the surrounding tissue and also providing tension relief when used as a coaptation aid. Axoguard HA+ Nerve Protector is comprised of an extracellular matrix (ECM) and is fully remodeled during the healing process. When hydrated, Axoguard HA+ Nerve Protector is easy to handle, soft, pliable, nonfriable, and porous. The lubricant coating on Axoguard HA+ Nerve Protector is composed of sodium hyaluronate and sodium alginate. When hydrated, the lubricant coating reduces friction between the nerve and the surrounding tissue. Axoguard HA+ Nerve Protector is flexible to accommodate movement of the joint and has sufficient mechanical strength to hold sutures. Axoguard HA+ Nerve Protector is provided sterile, for single use only, and in a variety of sizes to meet the surgeon's needs.

5. Indications for Use

Axoguard HA+ Nerve Protector is indicated for the management and protection of peripheral nerve injuries where there is no gap, or following closure of the gap.

6. Comparison of Technological Characteristics with the Predicate Device

Axoguard HA+ Nerve Protector is similar in intended use, design, principle of operation, and material (ECM base membrane) as Axoguard HA+ Nerve Protector. **Table 7-1** below summarizes the comparison between Axoguard HA+ Nerve Protector and its predicate.

Table 6-1: Device Technological Characteristics Comparison Summary

Name	**Axoguard HA+ Nerve Protector (This submission)**	**Axoguard HA+ Nerve Protector (Predicate)**
510(k)#	K231708	K223640
Manufacturer	Axogen Corporation	Cook Biotech Inc.
Common Name	Nerve Cuff	Nerve Cuff
Device Class	Class II	Class II
Classification Name and Number	Nerve Cuff; 21 CFR 882.5275	Nerve Cuff; 21 CFR 882.5275
Classification Product Code	JXI	JXI
Prescription/Over the Counter Use	Rx only	Rx only
Intended Use	Designed to be an interface between the peripheral nerve and the surrounding tissue.	Designed to be an interface between the peripheral nerve and the surrounding tissue.
Indications for Use	Axoguard HA+ Nerve Protector is indicated for the management and protection of peripheral nerve injuries where there is no gap, or following closure of the gap.	Axoguard HA+ Nerve Protector is indicated for the management of peripheral nerve injuries where there is no gap
Dimensions	Width (cm) / Length (cm) / Area (cm2) 1 / 2 / 2 2 / 2 / 4 2 / 4 / 8 3 / 6 / 18 4 / 8 / 32	Width (cm) / Length (cm) / Area (cm2) 1 / 2 / 2 2 / 2 / 4 2 / 4 / 8 3 / 6 / 18 4 / 8 / 32

	Thickness: 100µm to 1000µm SIS thickness range (manufacturing specification).	Thickness: 100µm to 1000µm SIS thickness range (manufacturing specification).
Material	Porcine SIS 2.0 decellularized extracellular matrix supplied by Cook Biotech, Inc., with a 2.2mg/cm^2 dry coating of sodium hyaluronate and sodium alginate applied to both sides of the device in a 1:1 ratio.	Porcine SIS 2.0 decellularized extracellular matrix supplied by Cook Biotech, Inc., with a 2.2mg/cm^2 dry coating of sodium hyaluronate and sodium alginate applied to both sides of the device in a 1:1 ratio.
Configuration	Flat Sheet	Flat Sheet
Sterile/Single Use	Single use only	Single use only
Sterility / Sterilization Method	SAL 10^{-6} / Ethylene Oxide	SAL 10^{-6} / Ethylene Oxide

7. Performance Data

7.1 Bench testing

The following performance data are provided in support of the substantial equivalence determination: biocompatibility testing in compliance with ISO 10993-1 *Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process* (FDA Recognized Consensus Standard 2-258), and bench testing including coefficient of friction, suture retention, ultimate tensile strength, bubble emission (packaging), seal strength (packaging). **Table 7.1-1** summarizes the testing performed for the Axoguard HA+ Nerve Protector.

Table 7.1-1: Axoguard HA+ Nerve Protector Testing Summary

Test	Test Method Summary	Summary Result
Coefficient of Friction	Aged and unaged devices were evaluated for their static coefficient of friction (lubricity) based on ASTM D1894-14.	Test articles met the acceptance criteria.
Suture Retention Strength	Aged and unaged devices were evaluated for their suture retention strength by placing a suture through the devices and the force required to pull free was measured, based on ANSI/AAMI/ISO 7198.	Test articles met the acceptance criteria.
Ultimate Tensile Strength	Aged and unaged devices were evaluated for their ultimate tensile strength by placing the devices between two grips. The separation force required resulting in device failure was measured, based on ASTM D882-18.	Test articles met the acceptance criteria.

Bubble Emission (Packaging)	Aged and unaged devices underwent ethylene oxide sterilization, and visual inspection prior to bubble leak testing. The test articles underwent evaluation in accordance with ASTM F2096-11(2019).	Test articles met the acceptance criteria.
Seal Strength (Packaging)	Aged and unaged devices underwent ethylene oxide sterilization, and visual inspection prior to seal strength testing. The test article sample sets were subjected to seal strength testing in accordance with ASTM F88/F88-21.	Test articles met the acceptance criteria.

7.2 Biocompatibility

Biocompatibility endpoints for the subject device are in compliance with ISO 10993-1 Biological evaluation of medical devices – Part 1: Evaluation and testing within risk management process (FDA Recognized Consensus Standard 2-258) was assessed. All necessary endpoints according to the standard were met (Table 8.2-1).

Table 7.2-1: Axoguard HA+ Nerve Protector Testing Summary

Test	Test Method Summary	Summary Result
Sensitization	Test article extracts of the device were evaluated for their potential to cause delayed dermal contact sensitization in a guinea pig maximization test based on ISO 10993-10.	Test article extracts showed no evidence of causing delayed dermal contact sensitization in the guinea pig.
Irritation	Test article extracts of the device were evaluated for their potential to cause irritation following intracutaneous injection in rabbits based on ISO 10993-23.	Test article extracts met the requirements of the test and were considered non-irritants.
Acute Systemic Toxicity	Test article extracts of the device were evaluated for acute systemic toxicity in mice based on ISO 10993-11.	There was no mortality or evidence of systemic toxicity from the test article extracts. Each test article extract met the requirements of the study.
Pyrogenicity	Test article extracts of the device were evaluated for their potential to induce a pyrogenic response following intravenous injection in rabbits based on USP 43- NF38, General Chapter <151>, ISO 10993-11.	The test article met the requirements for the absence of pyrogens.
Genotoxicity (Ames)	Test article extracts of the device were evaluated for their mutagenic potential in a tryptophan-dependent strain of *Escherichia coli* or in one or more strains of histidine-dependent *Salmonella typhimurium* in the presence or absence of S9 metabolic activation based on ISO 10993-3.	Test article extracts met the requirements of the test and were considered non-mutagenic.

Genotoxicity (Mouse Lymphoma Assay)	Test article extracts of the device were evaluated for their mutagenic potential using the mouse lymphoma forward gene mutation assay based on ISO 10993-3.	Test article extracts met the requirements of the test and were considered non-mutagenic.
Endotoxin	Test article extracts were evaluated for bacterial endotoxins using the Kinetic-Turbidimetric test method in accordance with USP 43- NF38, General Chapter <85>, USP43-NF38, General Chapter <161> and ANSI/AAMI ST72.	Test article extracts met USP requirement.
Cytotoxicity	Test article extracts of the device were evaluated for their potential to cause cytotoxic effects using an in vitro mammalian cell culture test based on ISO 10993-5.	Test article extracts showed no evidence of causing cell lysis or toxicity and each had a grade of 0 (no reactivity).

7.3 Non-Clinical GLP Studies

The objective of this GLP study was to evaluate the effects of the Axoguard HA+ Nerve Protector (Next Generation Protection device or NGP) device on nerve regeneration after implantation in a rat sciatic nerve transection injury model. A total of sixty (60) Lewis Rats, were enrolled and divided between three (3) groups of 20 (10 males and 10 females). The 3 groups were Sham device, Test device, and Control device, groups. Animals underwent a single surgical procedure on Day 0 in which the right sciatic nerve was exposed and transected. Following transection, the two nerve ends were loosely approximated using two non-resorbable 10-0 Nylon sutures approximately 180 degrees apart, creating a standard direct nerve repair (neurorrhaphy). Animals were allowed to heal for six- or twelve weeks post-implantation. All animals were successfully implanted and survived until appointed endpoints. Most animals maintained or gained body weight except three (3) that lost a small percentage (≤ 7%) of weight in Sham and Control device groups. There were no significant abnormal clinical observations for any animal in any group. There were no systemic effects to Axoguard HA+ Nerve Protector as indicated by animal health observations, body weight, hematology, serum chemistry or necropsy. Based on the histology endpoints for axonal outgrowth, axonal myelination and gastrocnemius muscle weight, the study met set acceptance criteria regarding safety and local effects related to nerve regeneration following implantation of Axoguard HA+ Nerve Protector in a rat sciatic nerve transection and repair model. The nerve regeneration-related outcomes in the Test device, Axoguard HA+ Nerve Protector, the group were not statistically significantly different when compared to the Control device.

Conclusion:

The non-clinical data support the safety of the device and demonstrate that the Axoguard HA+ Nerve Protector performs as intended in its specified use conditions, is substantially equivalent to its predicate device, and does not raise different questions of safety and effectiveness.