



January 16, 2024

NeuroSigma, Inc.
% Blake Wilson
Regulatory Counsel
Hogan Lovells US LLP
1735 Market Street, Suite 2300
Philadelphia, Pennsylvania 19103

Re: K233293

Trade/Device Name: Generation 2.0 Monarch external Trigeminal Nerve Stimulation (eTNS) System®

Regulation Number: 21 CFR 882.5898

Regulation Name: Transcutaneous Electrical Nerve Stimulator For Attention Deficit Hyperactivity Disorder

Regulatory Class: Class II

Product Code: QGL

Dated: October 17, 2023

Received: October 18, 2023

Dear Blake Wilson:

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.

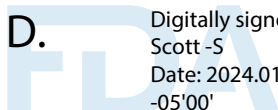
Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's 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,

Pamela D.
Scott -S



Digitally signed by Pamela D.
Scott -S
Date: 2024.01.16 18:33:34
-05'00'

Pamela D. Scott
Assistant Director
DHT5B: Division of Neuromodulation
and Rehabilitation Devices
OHT5: Office of Neurological
and Physical Medicine Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known)

Device Name

Generation 2.0 Monarch external Trigeminal Nerve Stimulation (eTNS) System®

Indications for Use (Describe)

The Generation 2.0 Monarch external Trigeminal Nerve Stimulation (eTNS) System® (“Monarch Gen 2”) is indicated for treatment of pediatric Attention Deficit Hyperactivity Disorder (ADHD) as a monotherapy in patients ages 7 through 12 years old who are not currently taking prescription ADHD medications. The device is used for patient treatment by prescription only and is intended to be used in the home under the supervision of a caregiver during periods of sleep.

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.

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

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 79 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human
Services Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA)
Staff PRASStaff@fda.hhs.gov

“An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number.”

510(k) SUMMARY

NeuroSigma, Inc.'s

Generation 2.0 Monarch external Trigeminal Nerve Stimulation (eTNS) System®

Submitter's Name, Address, Telephone Number, Contact Person and Date Prepared

NeuroSigma, Inc.
10960 Wilshire Blvd., Suite 1910
Los Angeles, CA 90024

Phone: (310) 479-3100
Facsimile: (310) 479-3114
Contact Person: Colin Kealey, M.D.
Date Prepared: September 29, 2023

Name of Device

Generation 2.0 Monarch external Trigeminal Nerve Stimulation (eTNS) System®

Common or Usual Name: Monarch Gen 2

Classification Name: Transcutaneous Nerve Stimulator For ADHD, Neurology

Regulatory Class: Class II

Product Code: QGL

Predicate Device

DEN180041 - NeuroSigma, Inc., Monarch eTNS System

Intended Use / Indications for Use

The Generation 2.0 Monarch external Trigeminal Nerve Stimulation (eTNS) System® ("Monarch Gen 2") is indicated for treatment of pediatric Attention Deficit Hyperactivity Disorder (ADHD) as a monotherapy in patients aged 7 through 12 years old who are not currently taking prescription ADHD medications. The device is to be used for patient treatment by prescription only and is intended to be used in the home under the supervision of a caregiver during periods of sleep.

Device Description

The Monarch Gen 2 eTNS System is a non-invasive device that uses electrical signals to therapeutically stimulate the Trigeminal nerve. The primary components of the device are:

- The *Monarch® Gen 2* external pulse generator, which controls the electrical stimulation, and
- The *Monarch® NS-2* external (cutaneous) electrical patches, which are single-use disposable patches worn on the forehead (**Figure 3**).

Figure 3: NeuroSigma's Monarch eTNS System®



A) The Monarch Gen 2.0 external pulse generator

B) B) The Gen 2.0 Monarch eTNS System held in a representative human hand for scale.



C) The Monarch NS-2 external (cutaneous) electrical patch beside the Gen 2.0 Monarch eTNS System.

The Monarch External Pulse Generator

The *Monarch Gen 2* pulse generator is housed in a sealed protective case and powered by a rechargeable lithium-ion polymer battery. The Monarch Gen 2 stimulation parameters are shown in **Table 1** below, and are nearly identical to the first generation Monarch eTNS System. The only differences in output between the two devices are: i) Gen 2 has a maximum output current of 8.0mA, as opposed to 10.0mA in Gen 1, and ii) Patients can adjust the current in increments of 0.1 mA as opposed to 0.2 mA in Gen 1. The sponsor believes that these changes makes the Gen 2 Monarch a more user-friendly device than the Gen 1, and actually improve patient safety. The parameters reported in **Table 1** are fixed, except for amplitude. The current amplitude is controlled by the patient's caregiver. Using the device's digital interface, the caregiver is able to set the current amplitude anywhere between 0 and 8 mA, under the physician's supervision.

The Monarch NS-2 Electrical Patch

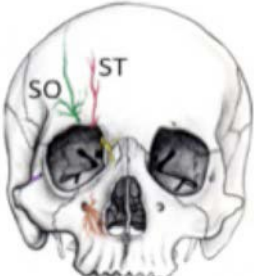
The Monarch eTNS patch attaches to the skin of the forehead by both hypoallergenic hydrogel and medical grade foam and adhesive and allows for bilateral stimulation of both the right and left supraorbital (SO) and supratrochlear (ST) branches of the trigeminal nerve (V1), located above the eyebrows in the forehead. The caretaker places the patch in the midline of the patient's forehead and applies the patch to the forehead directly above the eyebrows.

The gel, foam, and adhesive have undergone skin sensitization and histocompatibility studies in animals according to ISO 10993-1: Biological Evaluation of Medical Devices – Part 1: Evaluation and Testing. The electrical patch is connected to the pulse generator via a lead wire.

Stimulation Parameters

Electrical Stimulation parameters generated by the Monarch eTNS System are summarized in the table below:

Table 1: Stimulation Parameters and Anatomic Targets for the Monarch eTNS System

Parameter	Outcome
Waveform	Symmetrical Square Wave
Frequency of stimulation	120 Hz
Pulse width	250 μ sec
Duration between pulses	8 msec
Maximum stimulus intensity	8 mA, under patient control
Current Increment	0.1 mA
Maximum output voltage	4.14 V at maximum stimulus intensity
Hours of use	7 - 9 hours, while asleep, as prescribed by treating physician
Cycling	30 sec on : 1 sec ramp down : 30 sec off : 1 sec ramp up
Net charge per pulse	2 microcoulombs per pulse
Maximum current density	1.1 mA/cm ²
Maximum average power density	4.5 mW/cm ²
Maximum average current	8 mA
Anatomical target	<p>Supraorbital (SO) and Supratrochlear (ST) nerves of the V1 division of the Trigeminal Nerve bilaterally</p> 

Technological Characteristics

Both the subject device and predicate device function as non-invasive eTENS devices that use electrical signals to therapeutically stimulate the Trigeminal nerve. The primary components of the device are:

- The Monarch® Gen 2 external pulse generator, which controls the electrical stimulation, and
- The Monarch® NS-2 external (cutaneous) electrical patches, which are single-use disposable patches worn on the forehead (**Figure 3**).

Table 2 provides a comparison between the key functional features of the Monarch® Gen 2 and predicate device.

Table 2: Comparison between subject and predicate devices

	Monarch Gen 2 (Subject Device)	Monarch eTNS System (DEN180041)
Manufacturer	NeuroSigma, Inc.	NeuroSigma, Inc.
Regulation Number	N/A – Subject Device	DEN180041
Regulation Description	21 CFR 882.5898	21 CFR 882.5898
Regulatory Class	Class II	Class II
Product Code	QGL	QGL
Intended Use	Monarch Gen 2 is Transcutaneous electrical nerve stimulator for Attention Deficit Hyperactivity Disorder.	Monarch eTNS System is Transcutaneous electrical nerve stimulator for Attention Deficit Hyperactivity Disorder.
Indications for Use	The Generation 2.0 Monarch external Trigeminal Nerve Stimulation (eTNS) System® (“ <i>Monarch Gen 2</i> ”) is indicated for treatment of pediatric Attention Deficit Hyperactivity Disorder as a monotherapy in patients ages 7 through 12 years old who are not currently taking prescription ADHD medications. The device is used for patient treatment by prescription only and is intended to be used in the home under the supervision of a caregiver during periods of sleep.	The Monarch external Trigeminal Nerve Stimulation (eTNS) System is indicated for treatment of pediatric Attention Deficit Hyperactivity Disorder as a monotherapy in patients ages 7 through 12 years old who are not currently taking prescription ADHD medications. The device is used for patient treatment by prescription only and is intended to be used in the home under the supervision of a caregiver during periods of sleep.
User Population	Ages 7 through 12 years old who are not currently taking prescription ADHD medications.	Ages 7 through 12 years old who are not currently taking prescription ADHD medications.
Physical State	Electrical stimulation unit with leads and cutaneous electrodes.	Electrical stimulation unit with leads and cutaneous electrodes.

	Monarch Gen 2 (Subject Device)	Monarch eTNS System (DEN180041)
Technical Method	Applies an electrical current through electrodes on patient's skin.	Applies an electrical current through electrodes on patient's skin.
Target Area	Trigeminal nerve	Trigeminal nerve
Technological Characteristics		
Waveform	Symmetrical Square Wave	Symmetrical Square Wave
Frequency of stimulation	120 Hz	120 Hz
Pulse width	250 μ sec	250 μ sec
Duration between pulses	8 msec	8 msec
Maximum stimulus intensity	8 mA, under patient control	10 mA, under patient control
Current Increment	0.1 mA	0.2 mA
Maximum output voltage	4.14 V at maximum stimulus intensity	5.36 V at maximum stimulus intensity

Performance Data

The Monarch® Gen 2's design elements and performance is similar to that of the predicate device. The subject device presents a few minor upgrades, including a built-in rechargeable battery, amplitude of current controlled in increments of 0.1mA, and the user interface is simplified. The company conducted internal bench tests and external lab testing to verify and validate the battery's safety, software and firmware testing and validation, biocompatibility, and device performance were performed on the Monarch® Gen 2. In all instances, the Monarch® Gen 2 functioned as intended and functions as expected. Conformance to IEC 60601-1, IEC 60601-1-2, IEC 60601-1-11, IEC 60601-2-10, IEC 62304, and IEC 62133-2 was established.

The testing is summarized below:

Electrical Safety

Electrical safety testing was conducted according to FDA-recognized consensus standard IEC 60601-1.

Electromagnetic Compatibility

Electromagnetic compatibility (EMC) testing was conducted according to FDA-recognized consensus standard IEC 60601-1-2:2014 +AMD1:2020. No modifications to the proposed device were required to pass the test. EMC specifications based on the test results were included in the device labeling.

Home Environment Testing

Electrical safety in the home environment was evaluated according to FDA-recognized consensus standard IEC 60601-1-11:2015/AMD1:2020. Testing under this standard demonstrated that the device meets the safety requirements necessary for use in the uncontrolled home environment (e.g., storage temperature, continuous operating conditions, shock temperature, etc.).

Bench Testing

Bench testing was conducted to evaluate the performance of the subject device according to applicable consensus standards and device characterization testing:

Battery design analysis: Testing was conducted to analyze the number of therapy sessions per single charge of device performed to determine number of consecutive days the battery/device can perform therapy. The test results showed that the device can perform two therapy sessions before needing to charge the device and the cycle life of the battery is 300 charge cycles.

Nerve and muscle stimulator test: The safety and performance of the Monarch® Gen 2 were evaluated per FDA-recognized consensus standard IEC 60601-2-10:2012+AMD1:2016, Medical electrical equipment – Particular requirements for the basic safety and essential performance of nerve and muscle stimulators. The device met all applicable requirements.

Substantial Equivalence

The Monarch® Gen 2 is as safe and effective as the Monarch eTNS System. The Monarch® Gen 2 has the same intended uses and similar indications, technological characteristics, and principles of operation as its predicate device. The minor technological differences between the Monarch® Gen 2 and its predicate devices raise no new issues of safety or effectiveness. Performance data demonstrate that the Monarch® Gen 2 is as safe and effective as Monarch eTNS System. Thus, the Monarch® Gen 2 is substantially equivalent.

Clearance of the first-generation Monarch eTNS System as a monotherapy for pediatric ADHD was largely based on results from two clinical trials. The first was an 8-week open label trial of 24 subjects ages 7 - 14 and the second was a 4-week double-blind randomized controlled trial of 62 subjects ages 8 – 12. In both trials subjects underwent stimulation titration during their first clinic visit to find the intensity when stimulation first became perceptible and when the stimulation became too intense for comfort; the resulting range from this exercise was between 2 – 4 mA (i.e., lowest perceptible was 2 mA and the highest setting upon reaching discomfort was 4 mA). While investigators in these two trials did not collect the exact level of stimulation used by patients on a nightly basis, clinical experience shows that pediatric patients are more sensitive to stimulation than adults and tend to use the device between 2 – 4 mA simply because this is comfortable. Importantly, both of these pediatric ADHD studies achieved a statistically significant outcome on the primary endpoint, thereby supporting the effectiveness of nightly stimulation with eTNS administered at settings well below the maximum intensity of 10 mA. Therefore, based on a combination of factors, including, historical development of the Monarch eTNS system, evidence from the clinical trials used to support clearance of the first-generation eTNS system, and neuroimaging and electrophysiology findings, we believe the technological differences raise no new issues of safety or effectiveness.

Conclusions

The Monarch® Gen 2 is has the same intended use and indications for use and substantially similar technological characteristics as its predicate device. The modifications to the device and minor changes to user interface, magnitude increments, and to the rechargeable battery do not raise different questions of safety or effectiveness. Performance data demonstrate that the Monarch® Gen 2 is as safe and effective as the predicate device. Thus, the Monarch® Gen 2 is substantially equivalent to its predicate device.