K133408

MAR 2 8 2014

NEURONETICS

510(k) Summary

NeuroStar® TMS Therapy System

510(k) Owner: Neuronetics, Inc.
3222 Phoenixville Pike
Malvern, PA 19355
Phone: 610-640-4202
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Company Contact: Judy P. Ways, Ph.D.
Vice President,
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Malvern, PA 19355
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Date Prepared: 27 March 2014

Proprietary Name: NeuroStar® TMS Therapy System

Common Name: Transcranial Magnetic Stimulator

Classification Name: Transcranial Magnetic Stimulation System [21 CFR 882.5805, Product Code OBP]

Predicate Device: NeuroStar TMS Therapy® System [K061053/K083538/K130233]

Device Description:

The NeuroStar TMS Therapy System is a computerized, electromechanical medical device that produces and delivers non-invasive, magnetic stimulation using brief duration (185 μsec (nominal)) rapidly alternating, or pulsed, magnetic fields to induce electrical currents directed at spatially discrete regions of the cerebral cortex. This method of cortical stimulation by application of brief magnetic pulses to the head is known as Transcranial Magnetic Stimulation or TMS. NeuroStar TMS Therapy is a non-invasive tool for the stimulation of cortical neurons for the treatment of adult patients with Major Depressive Disorder (MDD) who have failed to receive satisfactory improvement from prior antidepressant medication as described under Intended Use. The NeuroStar System is used for patient treatment by prescription only under the supervision of a licensed physician. It can be used in both inpatient and outpatient settings including physician's offices and clinics, and hospitals.

The NeuroStar TMS Therapy System is an integrated system consisting of a combination of hardware, software, accessories and consumable supplies. It includes a Mobile Console which houses the electronics, includes a software controlled graphical user interface, and gantry that supports the Treatment Coil. The ferromagnetic Treatment Coil delivers the TMS Therapy™. The Head Support System provides accurate positioning of the Treatment Coil using a laser-guided alignment system. A single-use device, the SenStar® Treatment Link, which is applied to the Treatment Coil, provides contact sensing to monitor contact of the treatment coil with the patient's head throughout a treatment session, quality control by monitoring the magnetic field level prior to patient treatment, surface field cancellation to reduce stimulation of the scalp, and acts as a hygiene barrier from patient to patient. The TMS TrakStar™ practice data management system consists of a stand-alone computer and data management software that facilitates recording and retrieval of patient and treatment information and communication of data among multiple NeuroStar TMS Systems.

Intended Use:

The NeuroStar TMS Therapy System is indicated for the treatment of Major Depressive Disorder in adult patients who have failed to receive satisfactory improvement from prior antidepressant medication in the current episode.

Technological Characteristics and Substantial Equivalence:

The subject device, NeuroStar TMS System, has the following similarities to the predicate TMS device (NeuroStar TMS Therapy System, K061053/K083538/K130233):

- Principles of operation
- Design for delivery of Transcranial Magnetic Stimulation (TMS)
    - Output stimulation parameters (pulse width, frequency, train duration, inter-train interval, etc.)
- Materials

The proposed change for the NeuroStar TMS Therapy System in this submission is a modification to the current FDA-cleared Indication for Use to expand the indicated population in major depression to adult patients who have failed to benefit from one or more prior antidepressant medications in the current episode. The proposed change is supported by information submitted in this premarket notification and with the following rationale:

1. **Device is substantially equivalent to the FDA-cleared NeuroStar TMS Therapy System**: The NeuroStar TMS Therapy System that is the subject of the premarket notification is the same device cleared by the FDA under 510(k)s K061053, K083538 and K130233.
2. **Device new clinical data supports the revised Intended Use:** New clinical data from a randomized, controlled trial (OPT-TMS RCT) demonstrate the safety and efficacy of the NeuroStar TMS Therapy System in the treatment of patients with major depression as described in the revised Intended Use.

Changes to the device labeling are to include the revised Intended Use and new clinical data. No other changes are made to the device or labeling. Therefore, the NeuroStar TMS Therapy System with the change proposed in the premarket notification is substantially equivalent to the predicate device.

Clinical Performance:

Randomized Controlled Trial OPT-TMS

The OPT-TMS randomized controlled trial (RCT) (ClinicalTrials.gov Identifier NCT00149838) was conducted to evaluate the safety and efficacy of NeuroStar TMS Therapy in adult patients (N=197) with moderate to severe major depressive disorder and who failed to benefit from 1-4 adequate antidepressant medication trials as defined using the Antidepressant Treatment History Form (ATHF) (George, et al., 2010).

After determination of protocol eligibility and medication washout, patients participated in a multi-site, parallel group, double-blind, sham-controlled, randomized comparison of active NeuroStar TMS Therapy and sham treatment for a fixed trial period of 3 weeks. At the end of this period, patients who showed a criterion level of improvement were eligible to continue with their blinded, randomized assignment for up to 3 additional weeks, based on twice weekly determinations of clinical progress in a duration-adaptive phase.

Treatment was according to the standard treatment protocol described in the NeuroStar TMS Therapy System labeling. In addition to standard blinding methods, an "active" sham coil was used for blinding against TMS-related stimulation adverse effects. A post-study survey was conducted at the conclusion of the study to assess study blinding which indicated that blinding was effectively maintained.

Enrolled patients were aged 18-70, and experiencing a DSM-IV defined major depressive episode with moderate to severe depression as determined by a baseline HAMD24 $\geq$20 with a 5 year limit on the duration of the current depressive episode. Patients had a moderate to severe level of current treatment resistance, with at least 1 but no more than 4 ATHF level 3 (i.e., minimum labeled dose, 4 weeks duration) treatment attempts without clinical benefit, or had intolerance to 3 or more antidepressant medications. Excluded were patients who were unlikely to show response according to the TMS literature (presence of psychosis, comorbid and prominent anxiety disorder or substance abuse), and those patients for whom TMS treatment might be unsafe (e.g. those with prior head trauma, seizures, suicidal intent). Because this was an antidepressant medication-free study conducted in outpatients only, patients who could not tolerate being tapered from medications were excluded.

Demographic and clinical features of the enrolled population were not statistically significantly different between the active TMS and sham TMS treatment groups and were similar for patients studied in randomized controlled trial Study 101 (O'Reardon, et al., 2007). Roughly half of the population was female and the average age was 47 years. Patients had moderate to severe major depression by symptom measures. Current episode treatment resistance averaged 1.6 failed research-quality adequate treatment trials (verified by ATHF criteria), which translates

approximately to 3 to 6 clinical antidepressant medication attempts in the current episode. During their lifetime, patients had failed 3.3 research-adequate treatment trials (approximately 9 clinical attempts).

The primary outcome measure was the clinically significant categorical outcome of remission, defined as HAMD24 total score ≤3 or 2 consecutive ratings of a HAMD24 total score <10 between 3-6 weeks according to the pre-specified duration adaptive design. There was a statistically significant advantage of NeuroStar TMS Therapy on remission rate as compared to sham control (P=0.0173) in the ITT sample (N=197) **(Table 1)**. There were 13.4% remitters in the TMS arm and 5.0% in the sham arm; the adjusted odds ratio was 4.05 (95% confidence interval (CI), 1.28-12.83).

Table 1. OPT-TMS Randomized Controlled Trial Primary Outcome (ITT, N=197)

Measure HAMD24	Active TMS N=97	Sham TMS N=100	P-Value (Favoring Active TMS)	Adjusted odds ratio (95% CI)[§]
Remission	13.4%	5.0%	0.0173	4.05 (1.28-12.83)

[§] Odds ratios was adjusted for site (categorical), age (continuous), duration of current depressive episode, and medication resistance (low vs. high).

Remission occurred as early as week 3, with additional patients achieving remission across weeks 4-5. None of the pre-specified covariates (including the severity of pre-treatment antidepressant resistance) used in the logistic regression model had a statistically significant effect on the outcome in the pre-specified analysis model, thereby establishing efficacy across the ATHF 1-4 study population.

The baseline to endpoint change score outcome using the HAMD24 also favored active TMS to sham treatment (p=0.0588). Baseline to endpoint outcomes for patients treated with active TMS were statistically significant as compared to sham treatment as measured using the MADRS (P=0.0136), CGI-S (P=0.0181) and the patient-rated IDS-SR (P=0.0008). For the categorical endpoints, higher rates of remission were observed for patients receiving active TMS as compared to sham treatment as measured using the MADRS (P=0.0170) and the patient-rated IDS-SR (P=0.1199), and for response (50% improvement from baseline) for all three outcome measures (HAMD24, P=0.0104; MADRS, P=0.0063; IDS-SR, P=0.0145). Response and remission rates were consistent in clinical magnitude on all three outcome measures (i.e., HAMD24, MADRS, and IDS-SR).

The results for the continuous outcome measures are shown in **Table 2** with 95% confidence intervals for the treatment difference, and estimates of the standardized effect size. Standard effect sizes range from 0.43 to 0.67, indicating a moderate to large treatment effect for NeuroStar TMS Therapy in a study population with major depression with a broad spectrum of antidepressant medication treatment resistance (ATHF 1-4) in the current episode.

Table 2. OPT TMS RCT: Continuous Outcomes Measures (ITT, N=197)

Outcome Measure	Treatment Group	Baseline		End of Acute Phase		Treatment Effect (95% CI)	Standardized Effect Size	P-Value
		Mean (SD)	N	Mean (SD)	N			
HAMD24	Active	26.4 (4.9)	97	21.8 (9.2)	85	-2.11 (-4.30, 0.08)	-0.43	0.0588
HAMD24	Sham	26.6 (4.9)	100	23.5 (7.4)	93			
MADRS	Active	29.6 (6.9)	97	24.8 (11.5)	85	-3.41 (-6.12, -0.71)	-0.51	0.0136
MADRS	Sham	29.9 (6.5)	100	27.9 (9.0)	93			
CGI-S	Active	4.6 (0.7)	95	4.0 (1.2)	84	-0.36 (-0.65, -0.06)	-0.52	0.0181
CGI-S	Sham	4.6 (0.7)	100	4.3 (0.9)	92			
IDS-SR	Active	41.1 (9.1)	91	32.7 (15.3)	80	-6.46 (-10.19, -2.74)	-0.67	0.0008
IDS-SR	Sham	40.5 (10.1)	96	37.1 (14.0)	90			

Safety of the NeuroStar TMS Therapy System was assessed at each study visit by review of spontaneously reported adverse events and separate reporting of all serious adverse events. All adverse events are included in **Table 3**, regardless of the relationship to the assigned treatment condition determined by the investigator.

Table 3. OPT-TMS RCT: Spontaneous Adverse Events (N=197, ITT)

Adverse Event	NeuroStar TMS N=97 N(%)	Sham TMS N=100 N(%)
Headache	31 (32.0)	23 (23.0)
Discomfort at the site of stimulation	17 (17.5)	10 (10.0)
Insomnia	7 (7.2)	10 (10.0)
Worsening of depression or anxiety	6 (6.2)	8 (8.0)
Gastrointestinal	6 (6.2)	3 (3.0)
Fatigue	5 (5.2)	4 (4.0)
Muscle aches	4 (4.1)	4 (4.0)
Vertigo	2 (2.1)	2 (2.0)
Skin pain	1 (1.0)	1 (1.0)
Facial muscle twitching	0	1 (1.0)
Other	20 (20.6)	14 (14.0)

Adverse events were coded to link similar terms to the same events using the most common terms reported in studies of TMS. The code term of "Other" was used for any event that did not match to the code terms specified. The most frequently reported events were headache and application site pain. These events were more frequently reported in the active TMS group but were not significantly different between treatment arms.

Treatment with NeuroStar TMS Therapy was well tolerated. There were no deaths or seizures during this study. The all-cause discontinuation was 16.3% (N=31). Of these, 19.6% (N=18) were allocated to the NeuroStar TMS treatment group, while 13.3% (N=13) were allocated to

sham TMS. No patients reported an adverse event as the primary reason for study discontinuation.

There were two serious adverse events, both without long-term sequelae: one patient in the active TMS group had syncope that the investigator deemed unlikely related to the treatment and one patient in the sham group experienced paranoid ideation, possibly related to the study. One serious adverse event occurred before treatment: a patient's depression worsened, likely owing to medication discontinuation in the washout phase, and this patient was not randomized.

Substantial Equivalence Statement:

The NeuroStar TMS Therapy System that is the subject of this premarket 510(k) notification is the same (substantially equivalent) device cleared by the FDA under premarket notifications K061053, K083538 and K130233. New clinical data from the OPT-TMS randomized, controlled trial demonstrate the safety and efficacy of the NeuroStar TMS Therapy System in the treatment of adult patients with major depression who have failed to receive satisfactory improvement from prior antidepressant medication in the current episode.

[1]The NeuroStar® and NeuroStar TMS Therapy® are registered trademarks of Neuronetics, Inc. TMS Therapy™ and NeuroStar TrakStar™ are trademarks of Neuronetics, Inc.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center - WO66-G609
Silver Spring, MD 20993-0002

March 28, 2014

Neuronetics, Inc.
c/o Judy P. Ways, Ph.D.
Vice President, Regulatory Affairs and Quality Assurance
31 General Warren Boulevard
Malvern, PA 19355

Re: K133408
Trade/Device Name: NeuroStar TMS Therapy System
Regulation Number: 21 CFR 882.5805
Regulation Name: Repetitive Transcranial Magnetic Stimulation System
Regulatory Class: Class II
Product Code: OBP
Dated: February 26, 2014
Received: February 27, 2014

Dear Dr. Ways:

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 Small Manufacturers, International and Consumer Assistance 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 Small Manufacturers, International and Consumer Assistance 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

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 on last page.

510(k) Number *(if known)*
K133408

Device Name
NeuroStar TMS Therapy System

Indications for Use *(Describe)*
The NeuroStar TMS Therapy System is indicated for the treatment of Major Depressive Disorder in adult patients who have failed to receive satisfactory improvement from prior antidepressant medication in the current episode.

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)*

Carlos L. Pena -S

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

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

March 28, 2014

Orthoscan, Inc.
% Mr. Adam Menzies
VP Product Development
8212 E Evans Road
SCOTTSDALE AZ 85260

Re: K133174
Trade/Device Name: Orthoscan FD Mini C-Arm
Regulation Number: 21 CFR 892.1650
Regulation Name: Image-intensified fluoroscopic x-ray system
Regulatory Class: II
Product Code: OXO, MQB
Dated: February 25, 2014
Received: February 26, 2014

Dear Mr. Menzies:

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 Small Manufacturers, International and Consumer Assistance 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.

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Sincerely yours,

for

Janine M. Morris
Director, Division of Radiological Health
Office of In Vitro Diagnostics
and Radiological Health
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)*
K133174

Device Name
OrthoScan FD Mini C-arm

Indications for Use *(Describe)*
The OrthoScan FD Mini C-arm is designed to provide the physician with general fluoroscopic visualization of the patient's extremities including, but not limited to, surgical orthopedic procedures and critical emergency care procedures in hospital, emergency care, critical care, or physician office environments.

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)

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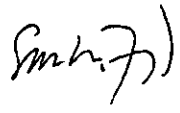

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