September 1, 2022

Magnus Medical, Inc.
Susan Noriega
VP Regulatory Affairs
1350 Old Bayshore Highway, Suite 600
Burlingame, CA 94010

Re: K220177
Trade/Device Name: Magnus Neuromodulation System (MNS) with SAINT Technology, Model Number 1001K
Regulation Number: 21 CFR 882.5805
Regulation Name: Repetitive Transcranial Magnetic Stimulation System
Regulatory Class: Class II
Product Code: OBP
Dated: August 2, 2022
Received: August 2, 2022

Dear Susan Noriega:

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

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 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,

for Pamela Scott
Assistant Director
DHT5B: Division of Neuromodulation
and Physical Medicine Devices
OHT5: Office of Neurological
and Physical Medicine Devices
Office of Product Evaluation and Quality
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: 06/30/2023
*See PRA Statement below.*

510(k) Number *(if known)*
[not yet assigned] K220177

Device Name
Magnus Neuromodulation System (MNS) with SAINT® Technology

Indications for Use *(Describe)*
The Magnus Neuromodulation System with SAINT Technology is indicated for the treatment of Major Depressive Disorder (MDD) in adult patients who have failed to achieve 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)

**CONTINUE ON A SEPARATE PAGE IF NEEDED.**

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**510(k) Summary Provided in Accordance with 21 CFR §807.92(c)**

magnusmedical

| | |
|---|---|
| Date Summary Prepared: | August 30, 2022 |
| 510(k) Number: | K220177 |
| 510(k) Owner: | Magnus Medical, Inc.<br>1350 Old Bayshore Highway, Suite 600<br>Burlingame CA 94010 USA<br>(415) 690-7358 |
| Submitter and Official Contact: | Susan Noriega<br>Magnus Medical, Inc.<br>1350 Old Bayshore Highway, Suite 600<br>Burlingame CA 94010 USA<br>susan@magnusmed.com<br>(650) 793-1966 |
| Trade Name: | Magnus Neuromodulation System (MNS) with SAINT Technology |
| Common Name: | Transcranial Magnetic Stimulation Device |
| Classification Name: | Repetitive Transcranial Magnetic Stimulator for Treatment of Major Depressive Disorder |
| Primary Classification Regulation: | 21 CFR §882.5805 |
| Primary Product Code: | OBP |
| Secondary Classification and Code: | 21 CFR §882.1870/GWF<br>21 CFR §882.4560/HAW |
| Substantially Equivalent Device: | Nexstim Navigated Brain Therapy (NBT) System 2<br>Nexstim Plc<br>Helsinki, Finland<br>Premarket Notification K182700<br>Cleared on March 22, 2019 |
| Device Description: | The Magnus Neuromodulation System (MNS) with SAINT Technology is a non-invasive repetitive transcranial magnetic stimulation (rTMS) system that delivers individualized and navigationally directed repetitive magnetic pulses to the left dorsolateral prefrontal cortex (L- |

| | |
|---|---|
| | DLPFC) to treat Major Depressive Disorder (MDD) in adult patients who have failed to achieve satisfactory improvement from prior antidepressant medication in the current episode.<br><br>The MNS with SAINT Technology is available for prescription use only and is intended for use by trained medical professionals in either an inpatient or outpatient setting.<br><br>The Magnus Neuromodulation System consists of hardware devices (stimulator with treatment coil and neuronavigation system) intended to deliver SAINT Technology; that is, rTMS (as intermittent theta burst stimulation (iTBS)) to a target area within the L-DLPFC along with proprietary software informed by structural and functional MRI and designed to identify the individualized target within the L-DLPFC for stimulation. Also included in the system are a coil and monitor for motor threshold determination, which is used to inform patient-specific stimulation settings. SAINT Technology is the combination of using the specific individualized target for treatment along with a proprietary accelerated treatment protocol that condenses treatment to five days. The Magnus Neuromodulation System is designed to support successful delivery of SAINT Technology. |
| Intended Use: | The Magnus Neuromodulation System with SAINT Technology is intended for the delivery of SAINT neuromodulation therapy to treat major depressive disorder (MDD) in adult patients who have failed to achieve satisfactory improvement from prior antidepressant medication in the current episode. |
| Technology Comparison: | The Magnus Neuromodulation System with SAINT Technology has the same intended use and technological characteristics as the predicate device. |
| Compatible Hardware: | The Magnus Neuromodulation System is a complete set of mutually compatible hardware components that have been specifically selected and evaluated to safely and effectively deliver SAINT Technology in conjunction with the Magnus Cloud Software. The following includes the set of hardware components included with the Magnus Neuromodulation System: |

| Item | Qty | Magnus Part # | Supplier Name/Model | Supplier Part # | 510(k) Clearance |
|---|---|---|---|---|---|
| Stimulator | 1 | 1002 | MagVenture/X100 | 9016E0711 | K173620 |
| Treatment Coil | 1 | 1003 | MagVenture/Cool-B65 | 9016E0491 | K171967 |
| Motor Threshold Coil | 1 | 1004 | MagVenture/C-B60 | 9016E0673 | K171967 |
| Coil Arm | 1 | 1005 | MagVenture/Super Flexible Arm | 9016B0181 | K173620 |
| Stimulator Cart | 1 | 1006 | MagVenture/Trolley with Holding Arrangements | 9016B0383 | K173620 |
| Isolation Transformer | 1 | 1007 | MagVenture/Isolation Transformer | 9016D0031 | K173620 |
| Cooling System | 1 | 1008 | MagVenture/Coil Cooler Unit | 9016B0151 | K173620 |
| Evoked Response Monitor | 1 | 1009 | MagVenture/MEP Monitor | 9016C0711 | K162873 |
| Neuronavigation System with accessories (cart and PC) | 1 | 1010 | Brain Science Tools (Soterix)/Neural Navigator | HD-SWN (nav) HD-SWTA (cart) HD-SWAPC (pc) | K191422 |

MagVenture devices and accessories are supplied by Tonica Elektronik / MagVenture
Brain Science Tools Neural Navigator is supplied by Soterix Medical

All hardware components were utilized in non-clinical bench performance testing as included in their respective 510(k) clearances. Stimulator, Treatment Coil, Motor Threshold Coil, Coil Arm, Stimulator Cart, Isolation Transformer, Cooling System, and Evoked Response Monitor hardware components were additionally utilized in clinical performance testing.

Table 1: Technology Comparison for the Magnus Neuromodulation System vs. the Predicate Device

| | ***Predicate Device*** | ***Proposed Device*** | ***Notes*** |
|---|---|---|---|
| ***Characteristic*** | ***Nexstim NBT System 2 K182700*** | ***Magnus Neuromodulation System with SAINT Technology*** | |
| ***Intended Use*** | The Nexstim Navigated Brain Therapy (NBT) System 2 is intended for the treatment of major depressive disorder in adult patients who have failed to achieve satisfactory improvement from prior | The Magnus Neuromodulation System (MNS) with SAINT Technology is intended for the delivery of SAINT neuromodulation therapy to treat major depressive disorder (MDD) in adult | No difference |

| | ***Predicate Device*** | ***Proposed Device*** | ***Notes*** |
|---|---|---|---|
| | antidepressant medication in the current episode. | patients who have failed to achieve satisfactory improvement from prior antidepressant medication in the current episode. | |
| ***Main System Hardware*** | ● TMS Stimulator<br>● Motor Threshold and Treatment Coil<br>● Tracking System for coil positioning<br>● Evoked response monitor for motor threshold determination<br>● Cooling Unit | ● TMS Stimulator<br>● Treatment Coil<br>● Tracking System for coil positioning<br>● Evoked response monitor for motor threshold determination<br>● Cooling Unit<br>● Motor Threshold Coil | The predicate device combines motor threshold measurement and stimulation treatment in one coil while the Magnus System utilizes two separate dedicated purpose coils. |
| ***Treatment Target Identification*** | Proprietary software utilizing structural MRI to assist in locating the target area within the L-DLPFC for depression therapy. | Proprietary software utilizing structural and functional MRI data to locate the target area within the L-DLPFC for depression therapy. | The Magnus System uses functional MRI connectivity data in addition to structural MRI data to inform the individual treatment target localization software. Both Magnus and predicate methods aid in localization of appropriate target areas within the L-DLPFC for stimulation and both methods provide more individual specificity than the historically used external anatomical landmarks. |
| ***Treatment Coil Positioning*** | Real time visualization of the treatment target relative to the treatment coil position via a tracking system (neuronavigation system) | Real time visualization of the treatment target relative to the treatment coil position via a tracking system (neuronavigation system) | No difference |
| ***Motor Threshold Determination*** | Visual inspection of finger movement + EMG | Visual inspection of finger movement + EMG | No difference |
| ***Treatment Intensity Determination*** | Motor threshold and electrical field model is used to adjust stimulation intensity | Motor threshold and depth-correction is used to adjust stimulation intensity | Nexstim and Magnus both primarily rely on MT to determine treatment intensity. Nexstim also uses a proprietary electrical field model to orient the rotation of the coil, while Magnus uses a depth correction to adjust for differences in distance between motor cortex and frontal cortex at the target. |
| ***Stimulation Protocol*** | 10 Hz and iTBS | iTBS | The Magnus Neuromodulation System with SAINT Technology uses only iTBS; the 10 Hz protocol is not needed for the Magnus System |

| | *Predicate Device* | *Proposed Device* | *Notes* |
|---|---|---|---|
| ***Area of Brain Stimulated*** | L-DLPFC | L-DLPFC | No difference |

Treatment Protocol Comparison: The Magnus Neuromodulation System with SAINT Technology utilizes the same type of treatment (intermittent theta burst stimulation/iTBS) as the predicate device but with more pulses (90,000 vs. 18,000) delivered over a shorter period of time (five days vs. six weeks) thus allowing for a more rapid response and more flexibility in terms of where treatment can be delivered; the more compressed schedule makes acute inpatient treatment more feasible.

Table 2: Treatment Protocol Comparison of SAINT Technology iTBS vs. Predicate iTBS

| ***Treatment Parameter*** | ***Nexstim NBT System 2 K182700 (predicate device)*** | ***Magnus Neuromodulation System with SAINT Technology (proposed device)*** | ***Notes*** |
|---|---|---|---|
| ***Stimulation Dose*** | 600 pulses per session/day, 12,000-18,000 pulses total | 1,800 pulses per session, 18,000 pulses per day, 90,000 pulses total | The number of pulses and timing of sessions are optimized for effectiveness and compressed treatment schedule with no impact on safety. |
| ***Magnetic Field Intensity*** | 120% Motor Threshold | 90% Motor Threshold | iTBS administered at amplitudes less than 100% of motor threshold may be safer and more focal, and may be more effective than iTBS at amplitudes greater than 100% motor threshold. |
| ***Pulse Frequency*** | 50 Hz | 50 Hz | No difference |
| ***Pulses per burst*** | 3 | 3 | No difference |
| ***Burst Frequency*** | 5 Hz | 5 Hz | No difference |
| ***Stimulus Train Duration*** | 2 seconds | 2 seconds | No difference |
| ***Inter-train Interval*** | 8 seconds | 8 seconds | No difference |
| ***Magnetic Pulses per Session*** | 600 | 1800 | The number of pulses and timing of sessions are optimized for effectiveness and compressed treatment schedule with no impact on safety. |
| ***Treatment Session Duration*** | 3.3 minutes | 10 minutes | |
| ***Treatment Sessions per Day*** | 1 | 10 | |
| ***Treatment Sessions per Week*** | 5 | 50 | |

| ***Treatment Parameter*** | ***Nexstim NBT System 2 K182700 (predicate device)*** | ***Magnus Neuromodulation System with SAINT Technology (proposed device)*** | ***Notes*** |
|---|---|---|---|
| ***Total Treatment Minutes*** | 99 | 500 | |
| ***Total Treatment Sessions*** | 30 | 50 | |
| ***Total Treatment Pulses*** | 18,000 | 90,000 | |
| ***Treatment Duration*** | 6 weeks | 5 days | Shorter total treatment duration than the predicate is possible because of an optimized and compressed treatment schedule. |

Summary of Performance Data:

Sterilization and Shelf Life: The Magnus Neuromodulation System with SAINT Technology is not provided as a sterile device and is not intended for sterilization by the user.

The shelf life and/or useful life of the hardware components are as indicated in their respective labeling and instructions for use. Software components will have updates managed as appropriate by Magnus Medical or its suppliers and therefore do not have a defined useful life at this time.

Biocompatibility: Patient contact materials that are part of the Magnus Neuromodulation System were tested and are compliant with ISO 10993-1, *Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process*.

Software: Software for the Magnus Neuromodulation System with SAINT Technology was designed and developed in accordance with current FDA guidance and industry standards including IEC 62304, *Medical Device Software – Software lifecycle processes* and ISO 14971, *Application of risk management to medical devices*.

Hardware: The hardware components of the Magnus Neuromodulation System have undergone all applicable electrical safety, electromagnetic compatibility, performance, and usability testing required.

Clinical: Clinical testing was performed to provide assurance of safety and effectiveness of the Magnus Neuromodulation System with SAINT Technology. The system was evaluated in four clinical studies, three open-label and one randomized and sham controlled. Data from these studies are summarized in the following tables:

Table 3: Summary of Clinical Studies Performed with SAINT Technology

| Title of Study | Number of Participants | Summary of Results |
|---|---|---|
| High-dose Spaced theta-burst TMS as a Rapid-acting Antidepressant in Highly Refractory Depression[1] | 6 | 5/6 (83.3%) responded (≥50% decrease in Hamilton Depression Rating Scale (HDRS-17) and 4/6 remitted (HDRS≤7) with no serious adverse events. |
| Stanford Accelerated Intelligent Neuromodulation Therapy for Treatment Resistant Depression[2] | 21 | 19/21 (90.5%) of participants met remission criteria (score <11 on the Montgomery-Asberg Depression Rating Scale [MADRS]) with no serious adverse events or negative cognitive side effects. |
| Stanford Neuromodulation Therapy (SNT): A Double-Blind Randomized Controlled Trial[3] | 29 (14 active, 15 sham) | 12/14 (85.7%) in the active treatment group met response criteria (≥50% reduction in MADRS) and 11/14 (78.6%) met remission criteria (MADRS ≤10) vs 4/15 (27%) in the sham group met response criteria and 2/15 (13.3%) remitted. The study was terminated early based on clear superiority of active treatment vs. sham at the planned interim analysis. No serious adverse events were reported. |
| An Open Label Pilot Trial to Assess the Feasibility of Using the Magnus Neuromodulation System (MNS) with Magnus Intelligent Neuromodulation Therapy (MINT[4]) as a Maintenance Treatment for Depression | 14 | 13/14 (92.8%) of subjects responded (≥50% reduction in MADRS) and 11/14 (78.6%) met remission criteria (MADRS ≤10) after the initial 5 days of treatment. No serious adverse events have been reported. |

Data from four clinical trials using SAINT Technology have demonstrated similar clinical outcomes with equivalent results as compared to the predicate device.

Demographic and effectiveness data are presented separately for the each of the four SAINT studies and compared to the published iTBS data[5] in Table 4. Patient demographics in terms of severity of depression and resistance to depression are comparable for the SAINT and THREE-D

[1] Williams NR, Sudheimer KD, Bentzley BS, et al., High-dose spaced theta-burst TMS as a rapid-acting antidepressant in highly refractory depression. Brain 2018;141:1-5.

[2] Cole EJ, Stimpson KH, Bentzley BS, at al., Stanford Accelerated Intelligent Neuromodulation Therapy for Treatment Resistant Depression. Am J Psychiatry 2020;177:716-726.

[3] Cole EJ, Phillips AL, Bentzley BS, et al. Am J Psychiatry. 2021 Oct 29:appiajp202120101429. doi: 10.1176/appi.ajp.2021.20101429. Epub ahead of print. PMID: 34711062.

[4] Note that MINT, SNT, and SAINT all refer to the same combination of target identification and treatment delivery that is SAINT Technology.

[5] Blumberger DM et al. Effectiveness of theta burst vs. high-frequency repetitive transcranial magnetic stimulation in patients with depression (THREE-D): a randomized non-inferiority trial. Lancet 2018;391:1683-92.

populations and the outcomes for SAINT trials, both open-label and randomized controlled trials, demonstrate equivalent effectiveness as compared to the results from the THREE-D trial without introduction of any new safety concerns.

Table 4: Summary of Demographic and Effectiveness Data for Clinical Studies Performed with SAINT Technology Compared to the Predicate iTBS (THREE-D)

| | **Study #1** | **Study #2** | **Study #3** | **Study #4** | **THREE-D*** |
|---|---|---|---|---|---|
| # of Subjects | 6 | 22 (21 per protocol) | 29 (15 active/14 sham) | 14 | 209 active |
| **Baseline Characteristics** | | | | | |
| Age (mean) | 56 | 45 | 49/52 | 52 | 42 |
| *Age (range)* | 38-69 | 19-78 | 27-73 | 23-82 | 18-65 |
| *Gender (% female)* | 67% | 57% | 34% | 50% | 59% |
| Maudsley Staging Method Score (mean) | 14 | 10 | 9/9 | 9.5 | 6.3 |
| # having prior TMS | 6 | 7 (only 1 previously remitted) | 0 | - | 0 |
| # having prior ECT | 6 | 0 | 0 | - | 16 |
| # having prior VNS | 1 | 0 | 0 | - | 0 |
| MADRS at baseline (mean) | 40.3 | 34.86 | 31/35 | 32 | - |
| HDRS at baseline (mean) | 16 (6-item) 28.8 (17-item) | 13.9 (6-item) 25.9 (17-item) | 14/15 (6-item) 24/26 (17-item) | 12.5 (6-item) | 23.7 (17-item) |
| Type of Study | Single arm, Open label | Single arm Open label | Randomized, blinded | Single arm Open label | Randomized, Open label |
| Treatment Arms | Single, active | Single, active | 2 arms – active (n=14) vs. sham (n=15) | Single, active | 2 arms – 10 Hz rTMS (n=205) vs. iTBS (n=209) |
| Treatment | 5 days SAINT iTBS | 5 days SAINT iTBS | 5 days SAINT iTBS vs. 5 days sham SAINT | 5 days SAINT iTBS | 4-6 weeks 10 Hz rTMS vs. 6 weeks iTBS |
| **Outcome** | | | | | |
| Response (MADRS reduction ≥50%) | 83.3% (assessed at end of 5 days of treatment) | 90.5% (assessed at end of 5 days of treatment) | 85.7% active vs. 26.7% sham (assessed during the month after treatment) | 92.8% (assessed during the week after treatment) | - |
| Remission (MADRS ≤10) | 83.3% (assessed at end of 5 days of treatment) | 90.5% (assessed at end of 5 days of treatment for the 21 per protocol subjects) | 78.6% active vs. 13.3% sham (assessed during the month after treatment) | 78.6% (assessed during the week after treatment) | - |
| Response (HDRS reduction ≥50%) | 83.3% (assessed at end | 86.4 % (HDRS-17) | - | 71.4% (HDRS-6) | 49% (HDRS-17) |

| | Study #1 | Study #2 | Study #3 | Study #4 | THREE-D* |
|---|---|---|---|---|---|
| | of 5 days of treatment) | 81.8% (HDRS-6) | | | |
| Remission (HDRS-17 ≤7 or HDRS-6 ≤4) | 66.7% (assessed at end of 5 days of treatment) | 77.3% (HDRS-17)<br>81.8% (HDRS-6) | - | 57.1% (HDRS-6) | 32% (HDRS-17) |
| Serious Adverse Events | 0 | 0 | 0 | 0 | 3 (1%) |
| Comments | The single non-responding subject was later determined to have a primary diagnosis of OCD | 23 subjects recruited, 1 ineligible, 1 withdrew on treatment day 1 because of anxiety | The trial was terminated at the planned interim analysis due to the superiority of the active treatment | This trial is ongoing | |

*The predicate device, Nexstim Navigated Brain Therapy (NBT) System 2, relied on the THREE-D Clinical Study data for clearance, via its own predicate (K173620).

Note: The clinical performance data for the Magnus Neuromodulation System (MNS) with SAINT Technology were obtained from a total of 70 patients enrolled in four clinical trials (one randomized double-blind, sham-controlled study and three open-label studies) conducted in close geographical proximity. As a result of studies being performed at a single site, generalizability to the broader United States population has not been evaluated.

Note: The Magnus Neuromodulation System (MNS) with SAINT Technology has been evaluated at four weeks post treatment in all four clinical trials. Effectiveness has not been established beyond the timepoints evaluated in the four clinical studies.

Note: Blinding Assessment Study #3
The adequacy of blinding utilized in the investigation was assessed by asking participants to guess their treatment allocation and to report their confidence in their guess (on a scale of 1 to 5) on the last day of treatment. This guess and confidence level were translated to a guess metric that ranged from 0 (participant had full confidence that he or she received the sham treatment) to 1 (participant had full confidence he or she received the active treatment). Twenty-three (23) participants provided guesses as to which treatment they received, and 19 indicated their confidence in their guess. One-way t tests indicated no significant differences from chance (chance guess metric=0.50) in the sham (mean guess metric=0.39, p=0.56) and active (mean guess metric=0.43, p=0.52) treatment groups. Because not all participants indicated their confidence in their guess, binomial tests were also used to determine whether the number of correct guesses exceeded chance. Binomial tests indicated no significant differences from chance in proportion of correct guesses in the sham (6 of 10 correct, p=0.38) and active (7 of 13 correct, p=0.50) treatment groups. Finally, linear regression analysis detected no relationship between the guess metric and the change in depression severity as indicated by magnitude of proportional change in MADRS scores (r=0.11, p=0.66). Since only 19 of 29 participants completed both parts of the blinding assessment, uncertainty remains as to the adequacy of the blinding for the remainder of the study population.

Adverse events from the Study #3 active treatment arm and the open label study (Study #4) of SAINT are listed in Table 5 below along with the adverse events reported in the THREE-D iTBS Study. (Note that Study #1 and Study #2 are not shown in the table, because these university-based studies did not formally tabulate non-serious adverse events; zero serious adverse events were observed in either study.) All the adverse events reported for SAINT are similar to those

reported for THREE-D iTBS in type and incidence with the exception that fatigue is reported more frequently with SAINT, likely because of the increased time spent in the clinic for the five days of SAINT treatment. Notably, rates of fatigue were the same for active and sham SAINT groups.

Table 5: Adverse Events: SAINT compared to THREE-D iTBS

| **Event** | **Number participants reporting event (%)[6]** | | |
|---|---|---|---|
| | SAINT n=14 (active arm from Study #3) | SAINT n=14 (Study #4) | iTBS (THREE-D) n=209 |
| Headache | 8 (57%) | 6 (43%) | 136 (65%) |
| Nausea | - | - | 14 (7%) |
| Dizziness | - | 1 (7%) | 18 (9%) |
| Unrelated medical problem | - | 5 (36%) | 46 (22%) |
| Fatigue | 8 (57%) | 5 (36%) | 16 (8%) |
| Insomnia | - | 5 (36%) | 10 (5%) |
| Anxiety or agitation | 4 (29%) | 2 (14%) | 9 (4%) |
| Back or neck pain/discomfort | 7 (50%) | 3 (21%) | 6 (3%) |
| Unrelated accidents | - | 1 (7%) | 3 (1%) |
| Vomiting | - | - | 1 (<1%) |
| Tinnitus | - | 2 (14%) | 3 (1%) |
| Migraine aura | - | - | 4 (2%) |
| Abnormal sensations | - | - | 4 (2%) |
| Pain/discomfort at treatment site | 5 (36%) | 4 (29%) | - |
| Other head/neck area pain | 3 (21%) | 3 (21%) | - |
| Any serious adverse events | 0 | 0 | 3 (1%) |

In summary, the clinical study results indicate that iTBS delivered using the Magnus Neuromodulation System with SAINT Technology is safe, effective, and substantially equivalent to iTBS delivered using the predicate device, the Nexstim NBT System 2 (K182700), and without introduction of any new risks or safety concerns.

Conclusion: The Magnus Neuromodulation System (MNS) with SAINT Technology has equivalent hardware components, the same general principle for target identification, the same intended use, and the same technological features as the predicate device. The Magnus Neuromodulation System (MNS) with SAINT Technology does not raise any new issues of safety and effectiveness and is substantially equivalent to the predicate device.

[6] Shown here are outcomes from the active SAINT arm (Study #3), active SAINT (Study #4), and the iTBS arm from the THREE-D study.