May 31, 2024

Brainsway Ltd.
℅ Ahava Stein
Regulatory Consultant
A. Stein - Regulatory Affairs Consulting Ltd.
18 Hata`as Str., Suite 21
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Israel

Re: K222196
Trade/Device Name: Deep TMS System
Regulation Number: 21 CFR 882.5805
Regulation Name: Repetitive transcranial magnetic stimulation system
Regulatory Class: Class II
Product Code: OBP
Dated: May 27, 2024
Received: May 28, 2024

Dear Ahava Stein:

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,

Doe W. Kumsa -S

for Pamela Scott, MS
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: 07/31/2026
See PRA Statement below.

510(k) Number *(if known)*
K222196

Device Name
BrainsWay Deep TMS™ System

Indications for Use *(Describe)*
The BrainsWay Deep TMS™ System is indicated for the treatment of depressive episodes and for decreasing anxiety symptoms for those who may exhibit comorbid anxiety symptoms in adult patients suffering from Major Depressive Disorder (MDD) and who failed to achieve satisfactory improvement from previous antidepressant medication treatment 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)

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information unless it displays a currently valid OMB number."

510(K) SUMMARY

BRAINSWAY DEEP TMS™ SYSTEM

510(k) Number K222196

Applicant Name:
Company Name: BrainsWay Ltd
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Date Prepared: July 14, 2022

Trade Name: BrainsWay Deep TMS™ System

Common Name: Transcranial Magnetic Stimulation System

Classification Name: CFR Classification section 882.5805; (Product Code OBP)

Classification: Class II Medical Device

Predicate Device:

The subject device is a substantially equivalent to the BrainsWay Deep TMS™ Systems (Model 102 and 104) ("predicate device") cleared in 510(k) K210201.

Device	Manufacturer	510(k) No.
BrainsWay Deep TMS™ System	BrainsWay Ltd.	K210201

Device Description:

The BrainsWay Deep TMS™ System enables direct non-invasive activation of deep brain structures. Transcranial magnetic stimulation (TMS) is a non-invasive technique used to apply brief magnetic pulses to the brain. The pulses are administered by passing high currents through an electromagnetic coil placed adjacent to a patient's scalp. The pulses induce an electric field in the underlying brain tissue. When the induced field is above a certain threshold and is directed in an appropriate orientation relative to the brain's neuronal pathways, localized axonal depolarizations are produced, thus activating neurons in the targeted brain structure.

The BrainsWay Deep TMS™ System is composed of the following main components:

1. Cart
    a) TMS Neurostimulator
    b) Cooling System
    c) Positioning Device
2. Helmet
    a) Aiming Apparatus (i.e., ruler/grid)
    b) Electromagnetic Coil (H Coil)
    c) Cap

The BrainsWay Deep TMS™ System is identical to the previously cleared BrainsWay Deep TMS™ Systems.

The purpose of this 510(k) submission is to enable modifications to the device labeling (Instructions for Use), based on clinical data from a randomized clinical study and from Real-World Data (RWD), to support the extension of the adult population to include adult subjects ≥22 and ≤86 years of age, suffering from MDD.

Intended Use/Indication for Use:

The BrainsWay Deep TMS™ System is indicated for the treatment of depressive episodes and for decreasing anxiety symptoms for those who may exhibit comorbid anxiety symptoms in adult patients suffering from Major Depressive Disorder (MDD) and who failed to achieve satisfactory improvement from previous antidepressant medication treatment in the current episode.

Performance Standards:

The BrainsWay Deep TMS™ System complies with the following FDA recognized consensus standards:

- EC 60601-1 Medical Electrical Equipment - Part 1: General requirements for basic safety and essential performance (Ed 3.1, 2005 + CORR.1:2006 + CORR.2:2007 + A1:2012 AND 2006 + AC:2010 + A1:2013)

- IEC 60601-1-2 Medical Electrical Equipment - Part 1-2: General requirements for basic safety and essential performance - Collateral standard: Electromagnetic Disturbances - Requirements and test (Ed 4 2014)
- IEC 62304 Medical Devices Software life-cycle processes (2006 + A1:2015)
- ISO 10993-5 Biological evaluation of medical devices - Part 5: Tests for in vitro cytotoxicity (199)
- ISO 10993-10 Biological evaluation of medical devices - Part 10: Tests for irritation and delayed-type hypersensitivity (2002)
- ISO 14971 Medical devices - Application of risk management to medical devices (2nd Ed. 2007, (R) 2016)

Non-Clinical (Bench) Performance Data:

Tests were conducted on the BrainsWay Deep TMS™ System. The tests were performed according to the FDA Guidance Document *Class II Special Controls Guidance Document: Repetitive Transcranial Magnetic Stimulation (rTMS) Systems*. These tests included Output Waveform, Electrical Field Spatial Distribution, and Magnetic Field Strength Gradient Testing. The results of the performance tests demonstrated that the BrainsWay Deep TMS™ System is substantially equivalent to the predicate device.

Animal Performance Data / Histology Data:

Not Applicable

Clinical Performance Data:

Data from a double-blind, randomized, sham-controlled trial (Kaster 2018 Study) and from RWD provide valid scientific evidence that is relevant, reliable, and accurate to support the safety and effectiveness of the expanded patient population.

In the Kaster 2018 Study, Deep TMS was associated with a meaningful remission rate (64%) (Table 1), which is higher than that reported for the Deep TMS group in the MDD Multicenter Study (30.4%) submitted in support of the cleared 510(k) K122288 for the BrainsWay Deep TMS™ System. The reported NNT for remission (2.2) in the elderly MDD patient population was better than that reported in the MDD Multicenter Study (6.85) for the overall adult MDD patient population.

Furthermore, Deep TMS was associated with a meaningful response rate (64.0%) (Table 2), which is also higher than that reported for the Deep TMS group in the MDD Multicenter Study (37.0%) submitted in support of the cleared 510(k) K122288 for the BrainsWay Deep TMS™ System. Similarly, the reported NNT for response (2.4) in the elderly MDD patient population was better than that reported in the MDD Multicenter Study (7.05) for the overall adult MDD patient population.

Table 1: Remission Rate based on HDRS-21 (ITT)

		Active Deep TMS Treatment		Sham Deep TMS Treatment	
		% (n/N)	Two-sided 95% CI	% (n/N)	Two-sided 95% CI
ITT	After 4 Weeks of Treatment	64.0% (16/25)	[42.5%; 82.0%]	18.5% (5/27)	[6.3%; 38.1%]

Table 2: Response Rate based on HDRS-21 (ITT)

		Active Deep TMS Treatment		Sham Deep TMS Treatment	
		% (n/N)	Two-sided 95% CI	% (n/N)	Two-sided 95% CI
ITT	After 4 Weeks of Treatment	64.0% (16/25)	[42.5%; 82.0]	22.2% (6/27)	[8.6%; 42.3%]

The difference between the active and sham Deep TMS treatment groups, in the change from baseline in HDRS-21 scores at 4 weeks of treatment (i.e., after 20 treatment sessions) was 5.35 points. This difference was found to be statistically significantly different (p=0.0025). Here too, the difference between the treatment groups for the elderly MDD patient population is higher than the difference between the treatment groups in the general MDD patient population, as reported in the MDD Multicenter Study as 2.23 points.

The elderly (≥ 60 years old) MDD participants randomized to active Deep TMS experienced a remission rate and response rate that was significantly greater than that observed in the sham group, based on both versions of the HDRS scale. The change from baseline in HDRS-21 scores after 4 weeks of treatment was also statistically significantly better in the active Deep TMS treatment group than in the sham treatment group.

RWD from adult MDD patients (≥ 60 years old) was provided to further support the safety and effectiveness of the Deep TMS treatment in this patient population. The reliability, accuracy, and relevancy of the RWD was demonstrated.

The real-world data (RWD) was derived from electronic health records of 1,198 patients (>22 years old) from 20 sites over the US, who received BrainsWay treatment for MDD over a span of 10 years from 2012 to 2022. A total of 152 subjects were included in the ITT patient population analysis, who met the main study eligibility criteria and included subjects ≥ 69 years of age and had a primary diagnosis of MDD, with moderate or greater depression, defined as a PHQ-9 score ≥ 10 or an HDRS-21 score ≥14. The mean patient age was 73.6 years (range 69-86), 65% were female, 66% from the southeast US region and 34% from other regions of the US, the vast majority (97%) were from suburban/suburban dense areas and approximately 50% were treated by providers with >10 years or < 10 years of experience.

The RWD based on only HDRS-21 scores or HDRS-21 and PHQ-9 scores, obtained for the elderly MDD patient population (≥ 69 years of age), has shown remission and response rates that are comparable to and consistent with those reported in the Kaster 2018 Study. The RWD remission and response rate are as good as or better than the remission and response rates reported in the MDD Multicenter Study. The RWD change from baseline in HDRS-21 scores was similar to the Kaster 2018 Study for a similar elderly MDD patient population and better than the change from baseline HDRS-21 scores in the MDD Multicenter Study. The RWD CGI-S remission rate is comparable to the

MDD Multicenter Study CGI-S remission rate. The RWD CGI-S response rate is significantly greater than the CGI-S response rate in the MDD Multicenter Study. The change from baseline in CGI-S scores are significantly better than the MDD Multicenter Study CGI-S results.

There did not appear to be large differences when comparing the safety and efficacy of the RWD by U.S. geographical location of the sites or urban-rural regions or when comparing safety of the RWD by provider experience. When comparing the efficacy of the RWD by provider experience, a slightly higher remission rate was seen in subjects treated by providers with more experience, as may be expected. Furthermore, in the review of data it was noted that the response rate was much higher in the RWD population of older patients than in the younger age group. A literature review of RCTs using TMS for treating MDD subjects in the expanded age range was conducted, which yielded 17 relevant studies (see Table 3 below). This literature review included studies with a wide variety of elderly age ranges and indicated heterogeneity with response rates ranging from 30-74%. Another study[1], although not a RCT but a retrospective analysis of 378 MDD patients aged 18-80 treated with Brainsway Deep TMS device, found response and remission rates increased with age and were stronger in female patients.

Table 3- Results of a formal literature search of rTMS in late-life depression

Ref	Study	Study type	N	Nactive	Age range	Scale	Response [%]	Remission [%]
1	Kaster 2018	RCT	52	25	60-80	HDRS	44%	40%
2	Blumberger 2022	RCT	172	87 bilateral, 85 TBS	>60	MADRS	Bilateral: 32.9% TBS: 44.3%	Bilateral: 32.9% TBS: 35.4%
3	Trevizol 2019	RCT	43	20-bilateral, 11-unilateral HF	60-85	HDRS	Bilateral: 45% Unilateral: 0%	Bilateral: 40% Unilateral: 0%
4	Zhang 2023 Meta-analysis	Meta-analysis	637	338	60-	HDRS	52.7%	18%
5	Jorge 2008	RCT	92	Exp 1: 15 Exp 2: 33	50-	HDRS	Exp 1: 33.3% Exp 2: 39.4%	Exp 1: 13.3% Exp 2: 27.3%
6	Cristancho 2023	RCT	17	8	60-85	MADRS	37.5%	NA
7	Manes 2001	RCT	20	10	>50	HDRS	30%	NA
8	Mosimann 2004	RCT	24	15	40-90	HDRS	6.7%	NA
9	Leblhuber 2019	RCT	29	19	Mean=72.4	HAMD-7	NA	NA
10	Desbeaumes Jodoin 2019	Retrospective	≥60: 19 <60: 54	19	60-89	MADRS	≥60: 73.7% <60: 35.2%	≥60: 63.2% <60: 33.3%
11	Milev 2009	Open study	49	49	58-89	HDRS	18.4%	8.2%
12	Almheiri 2023	Retrospective	≥60: 78 <60: 427	78	>60		≥60: 33% <60: 30%	≥60: 36% <60: 36%
13	Fabre 2004	Open study	11	11	56-77	HDRS	45.5%	NA
14	Conelea 2017	Retrospective	≥60: 75 <60: 156	75	60-84	IDS-SR PHQ-9	IDS-SR: ≥60: 45.3% <60: 44.9% PHQ-9: ≥60: 58.7% <60: 55.4%	IDS-SR: ≥60: 26.7% <60: 25% PHQ-9: ≥60: 33.3% <60: 25.6%
15	Quinn 2023	Open study	25	25	50-79	IDS-C-30	52%	20%
16	Cristancho 2020	Open study	13	13	61-73	MADRS	33.3%	33.3%
17	Vidya 2023	RCT	31	16	50-79	HDRS	50%	56.3%

[1] Kryatova MS, Seiner SJ, Brown JC, Siddiqi SH. Older age associated with better antidepressant response to H1-coil transcranial magnetic stimulation in female patients. J Affect Disord 2024:S0165-0327(24)00176-9. doi: 10.1016/j.jad.2024.01.160. Online ahead of print.

Overall safety of the BrainsWay Deep TMS System in both the Kaster 2018 Study and the RWD demonstrated adverse effects that were similar and typical of TMS treatment. There were no reports of new or unanticipated adverse events.

The results of the Kaster 2018 Study and the RWD provide sufficient supportive data to expand the use of the BrainsWay Deep TMS System to adult MDD patients ≥69 years old.

Furthermore, effect sizes from the elderly MDD patient population from the Kaster 2018 Study and from the RWD demonstrate a clinically meaningful improvement in anxiety symptoms in MDD for the BrainsWay Deep TMS System, in the elderly (≥69 years old) MDD patient population.

The current Indication for Use statement, including treatment of MDD and reducing anxiety symptoms in the overall adult MDD patient population (i.e., ≥22 years) is supported by the clinical data provided in this 510(k) submission.

Substantial Equivalence:

The subject BrainsWay Deep TMS™ Systems (Models 102 and 104) have the same intended use and indications for use as the predicate BrainsWay Deep TMS™ Systems cleared in 510(k) K210201. The subject devices and the cleared BrainsWay Deep TMS™ Systems are similar in terms of their intended prescription use only, suitable for adult population, indicated for the same anatomical sites, according to the same indications for use and to be used in the same hospital and/or clinic settings.

The subject BrainsWay Deep TMS™ Systems have the same mechanism of operation and use the same underlying technology as the predicate BrainsWay Deep TMS™ Systems. The performance characteristics, including the Output Waveform, Electrical and Magnetic Field Distribution are substantially equivalent to the previously cleared BrainsWay Deep TMS™ Systems. The subject devices, as the cleared devices, introduce similar safety features and comply with same relevant consensus standards, including electrical and mechanical safety, EMC (electromagnetic compatibility), and software validation.

The subject BrainsWay Deep TMS™ Systems are composed of the same device components as the previously cleared, predicate BrainsWay Deep TMS™ Systems (Model 102 and Model 104).

This 510(k) contains clinical data to support the safety and efficacy of the subject BrainsWay Deep TMS™ Systems for the treatment of MDD in the adult elderly population. The clinical data demonstrates that the BrainsWay Deep TMS™ Systems are substantially equivalence to the performance of the predicate BrainsWay Deep TMS™ Systems for the treatment of MDD. No new questions of safety and efficacy have arisen due to the treatment in this additional patient population.

Conclusions:

Consequently, it can be concluded that the subject BrainsWay Deep TMS™ Systems (Models 102 and 104) are substantially equivalent to the predicate BrainsWay Deep TMS™ Systems (Models 102 and 104), cleared under 510(k) K210201 and therefore, the modified BrainsWay Deep TMS™ System can be legally marketed in the USA.