March 17, 2023

GrayMatters Health Ltd.
% Allison Komiyama, PhD
Principal Consultant
RQM+
2251 San Diego Ave, Suite B-257
San Diego, California 92110

Re: K222101
Trade/Device Name: Prism
Regulation Number: 21 CFR 882.5050
Regulation Name: Biofeedback device
Regulatory Class: Class II
Product Code: HCC
Dated: February 13, 2023
Received: February 14, 2023

Dear Dr. Komiyama:

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,

Pamela D. Scott -S

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)*
K222101

Device Name
Prism

Indications for Use *(Describe)*
Prism is a neurofeedback software device intended for relaxation and stress reduction through the use of EEG biofeedback. The device is indicated as an adjunctive treatment of symptoms associated with posttraumatic stress disorder (PTSD), to be used under the direction of a healthcare professional, together with other pharmacological and/or non-pharmacological interventions.

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
PRAStaff@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
K222101

DATE PREPARED
March 16, 2023

MANUFACTURER AND 510(k) OWNER
GrayMatters
82 Ha' Atzmaut Street, Haifa, Israel
Telephone: +972 54 234 77770
Official Contact: Adar Shani, VP Clinical and Regulatory affairs

REPRESENTATIVE/CONSULTANT
Allison C. Komiyama, Ph.D., RAC
Pierre Bounaud, Ph.D.
Matthieu Kirkland, M.S.
RQM+
Telephone: +1 (412) 816-8253
Email: akomiyama@rqmplus.com

DEVICE INFORMATION

Proprietary Name/Trade Name:	Prism
Common Name:	Device, Biofeedback
Regulation Number:	21 CFR 882.5050
Class:	Class 2
Product Code:	HCC
Premarket Review:	Neurological and Physical Medicine Devices (OHT5) Neuromodulation and Physical Medicine Devices (DHT5B)
Review Panel:	Neurology

PREDICATE DEVICE IDENTIFICATION
Prism is substantially equivalent to the following predicates:

510(k) Number	*Predicate Device Name / Manufacturer*	*Predicate*
K122879	EEGer4 / EEG Software LLC.	Primary Predicate
K180173	Freespira / Palo Alto Health Sciences, Inc.	Secondary Predicate

The predicate devices have not been subject to a design related recall.

DEVICE DESCRIPTION
Prism is a software as medical device, to be prescribed for treatment of patients with PTSD by clinicians as adjunct to standard of care. Prism is a software device running on a laptop that uses EEG signal input from an EEG device (g.Nautilos PRO (K171669)).

Prism therapy consists of 15, 30-minute sessions and optional periodic refresher sessions. During a session, the patient is connected to 8 or more EEG channels and views an interactive audio/visual interface.

INDICATIONS FOR USE

Prism is a neurofeedback software device intended for relaxation and stress reduction through the use of EEG biofeedback.

The device is indicated as an adjunctive treatment of symptoms associated with posttraumatic stress disorder (PTSD), to be used under the direction of a healthcare professional, together with other pharmacological and/or non-pharmacological interventions.

COMPARISON OF SUBSTANTIAL EQUIVALENCE

GrayMatters believes that Prism is substantially equivalent to the predicate devices based on the information summarized here:

The subject device has the same intended use and similar indications for use as the predicate devices. Both the subject and predicate devices utilize biofeedback technology based on visual and/or auditory signals to help patients regulate and voluntarily control their physiological parameters.

The subject device has the same technological characteristics as compared to the primary predicate device and the same intended use. Both the subject device and the primary predicate cleared in K122879 have the same principle of operation and train patients to find strategies to regulate their physiological parameters. The subject device and the primary predicate utilize the same energy input and output. Namely, both the subject device and primary predicate provide biofeedback training to patients supported by EEG data collected from an EEG device. Both devices use, measure, and process EEG signals to produce frequency band energy indications for biofeedback purposes.

Both the subject device and predicate devices do not provide any diagnostic conclusions nor provide any classification, diagnosis, or clinical interpretation of data. Finally, the subject device does not incorporate any changes in method of operation, material or design that could affect safety or effectiveness.

These technological characteristics have undergone testing to ensure the device is as safe and effective as the primary predicate. Based on the testing performed (i.e., software verification and validation, and clinical testing), it can be concluded that the subject device does not raise different questions of safety or effectiveness.

The similar indications for use, mode of operation (i.e., biofeedback device), and performance characteristics for the proposed Prism are assessed to be substantially equivalent to the predicate devices under product code HCC.

SUMMARY OF NON-CLINICAL TESTING

Software Verification: The software development and testing were executed according to FDA's Guidance for the *Content of Premarket Submissions for Software Contained in Medical Devices* and according to IEC 62304 *Medical device software — Software life cycle processes.*

The results of these tests indicate that Prism is substantially equivalent to the predicate device.

SUMMARY OF CLINICAL TESTING

GrayMatters Health performed a prospective, single arm study, open label, unblinded study to assess of the Safety and Effectiveness of Prism, as an Adjunct to Standard of Care, in Subjects with Posttraumatic Stress Disorder (PTSD). The purpose of the study was to assess the safety and effectiveness of fifteen (15) EEG-Neurofeedback training sessions using the Prism software in reducing PTSD-related symptoms. Fifteen neurofeedback sessions were delivered twice per week, on non-consecutive days, over 8 consecutive weeks. Subjects (ages 22 to 65) had been diagnosed with PTSD from 1 year to 20 years after index trauma, (i.e., patients with Chronic PTSD). Diagnosis of PTSD was established according to the DSM-5 criteria and CAPS-5. The study was conducted at 4 outside the United States (OUS) sites in Israel and one US site.

The following activities were performed as part of the Baseline Assessment:

- Clinician assessments performed and documented by the investigator or qualified and trained designee: CAPS-5, CGI-S
- Subjects instructed to complete all questionnaires on the ePRO system: PCL-5, ERQ, PHQ-9

During the study, the subjects were provided with a short pre-training session during the baseline assessment visit or combined with the 1st Prism EEG-NF training to become familiar with the system operation prior to the actual Prism EEG-NF training sessions.

Device

Prism software processes EEG signals to provide visual feedback to the patient to aid the patient in learning to control the EEG activity. The EEG signal was provided by the g.Nautilus PRO EEG device.

Primary Performance Measures

The primary measure of this study was to assess the proportion of subjects who demonstrate a 6-point reduction in the Clinician Administered PTSD Scale (CAPS-5) score from Baseline to the 3 months follow-up visit.

Safety Performance Measures

The safety objectives of this study were to assess the safety of Prism Neurofeedback training by evaluating the incidence, severity, and frequency of adverse events.

Secondary Performance Measures

1. Assess the proportion of subjects who demonstrate a 10-point reduction or more in the PTSD Checklist for DSM-5 (PCL-5).
2. Assess the change from Baseline to the 3 months follow-up in the following scores:
    a. Clinician Administered PTSD Scale (CAPS–5)
    b. PTSD Checklist for DSM-5 (PCL-5)
    c. Emotion Regulation Questionnaire (ERQ)
    d. Patient Health Questionnaire (PHQ-9)
    e. Clinical Global Impression (CGI)

Analysis Set

There were 101 subjects screened for the study with 79 included in the full analysis dataset, 66 included in the efficacy analysis set, and 63 in the per protocol analysis set. The mean time from traumatic event in these subjects was 10 years and ranged between 1 and 20 years with the mean time from first PTSD symptoms being 8.8 years. The majority of the US and OUS patients reported military related PTSD symptoms.

Primary Endpoint

The response rate, i.e., the percent of subjects (50%) with at least 6 points improvement in CAPS-5 from baseline to the 3 months follow up visit (primary effectiveness endpoint) as well as at 8 weeks (exploratory endpoint) was deemed to have been successfully met.

Efficacy Analysis Set (EF)	**Response (reduction ≥)**				
	6 points	**10 points**	**13 points**	**16 points**	**21 points**
8 weeks	69.70%	50.00%	45.45%	33.33%	22.73%
3 months follow-up	66.67%	54.55%	50.00%	40.91%	27.27%

Safety Conclusions

The serious adverse event (SAE) rate was 2.53% (2/79). None of the SAEs were considered related to the software or to the EEG device. While 50.6% (40/79) of the subjects experienced adverse events (AE's), the majority were mild AEs (headache, fatigue) and recovered right after the training sessions with no further intervention. The pre-specified safety goals of this study were met, and the safety profile was found to be acceptable.

Study Conclusion

The primary endpoint of this study was responder rate based on a quantitative improvement as measured using the Clinician Administered PTSD Scale (CAPS-5). Using this scale, "Response" was defined as a reduction of 6 or more points. The primary effectiveness hypothesis was that from baseline to the 3 months follow-up, at least 50% of study participants will experience a response to the treatment (defined as a 6-point reduction in CAPS-5 score from baseline). From baseline to the 3-month follow-up, 54.55% of study participants experienced a reduction in the CAPS-5 of 10 points or more and 50% of study participants experienced a reduction of 13 points or more

The totality of the clinical data collected in the study demonstrates that Prism is substantially equivalent to the predicate device in terms of safety and effectiveness.

CONCLUSION

Based on the testing performed, including software verification and validation and clinical testing, it can be concluded that the subject device does not raise different questions of safety or effectiveness compared to the predicate devices. The similar indications for use, technological characteristics, and performance characteristics for the proposed Prism are assessed to be substantially equivalent to the predicate devices.

	Subject Device	***Primary Predicate Device***	***Secondary Predicate Device***	***Statement of Equivalence***
	GrayMatters Health Ltd. Prism for PTSD	EEG Software LLC EEGer4 K122879	Palo Alto Health Sciences, Inc. Freespira K180173	
Intended Use	Utilize biofeedback technology based on visual and/or auditory signals to help patients regulate and voluntarily control their physiological parameters	Utilize biofeedback technology based on visual and/or auditory signals to help patients regulate and voluntarily control their physiological parameters	Utilize biofeedback technology based on visual and/or auditory signals to help patients regulate and voluntarily control their physiological parameters	Identical to the predicate devices.
Indications for Use	Prism is a neurofeedback software device intended for relaxation and stress reduction through the use of EEG biofeedback. The device is indicated as an adjunctive treatment of symptoms associated with posttraumatic stress disorder (PTSD), to be used under the direction of a healthcare professional, together with other pharmacological and/or non-pharmacological interventions.	This device is to be used for general relaxation training when used with supported amplifier/encoders.	Freespira is intended for use as a relaxation treatment for the reduction of stress by leading the user through guided and monitored breathing exercises. The device is indicated as an adjunctive treatment of symptoms associated with panic disorder (PD) and/or post-traumatic stress disorder (PTSD), to be used under the direction of a healthcare professional, together with other pharmacological and/or non-pharmacological interventions.	Substantially equivalent to the predicate devices. No impact on safety and effectiveness.
Product Codes / Regulation Number	HCC / 21 CFR 882.5050	HCC / 21 CFR 882.5050	HCC / 21 CFR 882.5050 CCK / 21 CFR 868.1400	Identical to the predicate devices. No impact on safety and effectiveness.
Class	Class 2	Class 2	Class 2	Identical to the predicate devices. No impact on safety and effectiveness.
Regulation Description	Device, Biofeedback	Device, Biofeedback	Device, Biofeedback	Identical to the predicate devices. No impact on safety and effectiveness.
Principle of Operation	This system trains patients to find mental strategies to regulate their physiological parameters (e.g., brain activity level) to reduce symptoms associated with PTSD	This system trains patients to find mental strategies to regulate their general relaxation	This system trains patients to control and normalize their physiological parameters (e.g., breathing patterns) to reduce symptoms associated with PTSD	Substantially equivalent to the predicate devices. No impact on safety and effectiveness.
Intended User	Healthcare professional	Healthcare professional	Patient	Identical to the primary predicate device. No impact on safety and effectiveness.

Assessment Mode for Biofeedback	This is a software-only component that receives EEG signals from the g.Nautilus PRO EEG and processes those signals to visual and audio feedback that are used for biofeedback training.	This software-only component of an EEG biofeedback system accepts EEG data from an external FDA-approved amplifier/encoder and provides biofeedback information.	Respiratory information using capnography	Identical to the primary predicate device. No impact on safety and effectiveness.
Supported Devices	FDA-cleared medical-grade wearable EEG headset to record brain activity in medical and clinical environments.	FDA-cleared medical-grade wearable EEG headsets to record brain activity in medical and clinical environments.	N/A	Identical to the primary predicate device. No impact on safety and effectiveness.
Number of EEG Channels	8 - 16	4	N/A	Substantially equivalent to the primary predicate device. No impact on safety and effectiveness.
Sampling Rate	250 Hz	256 Hz	N/A	Substantially equivalent to the primary predicate device. No impact on safety and effectiveness.
Bandwidth	0 – 60 Hz	0 – 50 Hz	N/A	Substantially equivalent to the primary predicate device. No impact on safety and effectiveness.