November 24, 2021

metaMe Health, Inc.
Nandini Murthy
Regulatory Consultant
222 W. Merchandise Mart Plaza - Suite 1230
Chicago, IL 60654

Re: K211463
Trade/Device Name: Regulora™
Regulation Number: 21 CFR§ 876.5960
Regulation Name: Computerized Behavioral Therapy Device For Treating Symptoms
Regulatory Class: II
Product Code: QMY
Dated: October 25, 2021
Received: October 26, 2021

Dear Nandini Murthy:

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,

Shanil P. Haugen, Ph.D.
Assistant Director
DHT3A: Division of Renal, Gastrointestinal,
Obesity and Transplant Devices
OHT3: Office of GastroRenal, ObGyn,
General Hospital and Urology 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)*
K211463

Device Name
Regulora™

Indications for Use *(Describe)*

Regulora™ is a prescription-only digital therapeutic device intended to provide behavioral therapy through gut-directed hypnotherapy for adults 22 years of age and older who have been diagnosed with Irritable Bowel Syndrome (IBS). Regulora is indicated as a 3-month treatment for patients with abdominal pain due to IBS and is intended to be used together with other IBS treatments.

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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Section 5 – 510(k) Summary
-Regulora-

Title: *Regulora*™

Submitter:
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Date Prepared: October 24, 2021

Device Trade Name: *Regulora*™

Device Common Name: Prescription Digital Therapeutic Device

Classification Panel: Gastroenterology/Urology

Classification Regulation: 21 CFR 876.5960, Class II Medical Device (Product Code: QMY)

Classification Name: Computerized behavioral therapy device for treating symptoms

Predicate Device: Parallel, DEN200029

Device Description

Regulora™ is prescription-only digital therapeutic software indicated for use in the treatment of abdominal pain due to Irritable Bowel Syndrome (IBS). The *Regulora* program is Software as a Medical Device (SaMD) that resides on and is accessed through the user's mobile device and can be executed at home. *Regulora* digitizes scripted therapist-administered GDH behavior therapy and provides 7 unique treatment sessions, each lasting ~30 minutes, every other week over 12 weeks. The treatment sessions are designed to first induce deep physical and autonomic relaxation which is followed by metaphorical storytelling and a combination of

direct and indirect suggestions targeted at somatic control mechanisms. *Regulora* also provides for IBS symptom tracking, which patients can share with their doctor in the management of their IBS.

Indications for Use

Regulora™ is a prescription-only digital therapeutic device intended to provide behavioral therapy through gut-directed-hypnotherapy for adults 22 years of age and older who have been diagnosed with Irritable Bowel Syndrome (IBS). Regulora is indicated as a 3-month treatment for patients with abdominal pain due to IBS and is intended to be used together with other IBS treatments.

Rationale for Substantial Equivalence

Regulora™ shares the same intended use and technical characteristics of Parallel. Both are prescription digital therapeutics, both are computerized behavior therapy, both are intended to treat gastrointestinal conditions, and both comply with the special controls for product code QMY. Below is a table summarizing the comparison of the devices:

Specifications / Devices	*Regulora*™	Parallel (Predicate Device)
FDA Clearance	K211463	DEN200029
Regulation	21 CFR 876.5960 QMY	21 CFR 876.5960 QMY
Intended Use	A computerized behavioral therapy device for treating symptoms of gastrointestinal conditions is a prescription device intended to provide a computerized version of condition-specific therapy as an adjunct to standard of care treatments to patients with gastrointestinal conditions.	A computerized behavioral therapy device for treating symptoms of gastrointestinal conditions is a prescription device intended to provide a computerized version of condition-specific therapy as an adjunct to standard of care treatments to patients with gastrointestinal conditions.
Indications for Use	Regulora is a prescription-only digital therapeutic device intended to provide behavioral therapy through gut-directed hypnotherapy for adults 22 years of age and older who have been diagnosed with Irritable Bowel Syndrome (IBS). Regulora is indicated as a 3 month treatment for patients with abdominal pain due to IBS and is intended to be used together with other IBS treatments.	Parallel is a prescription-only digital therapeutic device intended to provide cognitive behavioral therapy for adults aged 22 years of age and older who have been diagnosed with Irritable Bowel Syndrome (IBS). Parallel is indicated as a 3 month treatment for patients with IBS. Parallel treats IBS by reducing the severity of symptoms and is intended to be used together with other IBS treatments.

System	Prescription Digital Therapeutic mobile application designed to deliver Behavioral Therapy through Gut-Directed-Hypnotherapy (GDH) via a mobile app that is downloaded onto a patient's mobile device	Prescription Digital Therapeutic web application designed to deliver Cognitive Behavioral Therapy (CBT) via the patient's desktop or laptop computer's web browser with therapist involvement
Platform	iOS / Android mobile devices	Microsoft Windows / MacOS laptop or desktop computers
Patient Population	Adults, 22 years of age or older diagnosed with IBS	Adults, 22 years of age or older diagnosed with IBS
Adjunctive Usage	Intended to provide Behavioral Therapy through Gut-Directed-Hypnotherapy (GDH) as an adjunct to other IBS treatments	Intended to provide Cognitive Behavioral Therapy (CBT) as an adjunct to other IBS treatments
Treatment Duration	3 months	3 months

The *Regulora* Software as a Medical Devices (SaMD) was developed under a 21 CFR part 820 quality management system, in accordance with the IEC 62304 standard for medical device software lifecycle management, and within an ISO 14971 risk management framework. Regulora was further reviewed according to the FDA Guidance document, "Guidance for the Content of Premarket Submissions for Software Contained in Medical Device" and the software was found to have a moderate level of concern. FDA review of the design, development, verification, and validation documentation provided in support of *Regulora* was found to be acceptable. Additionally, metaMe complies with the special controls for product code QMY, Computerized behavioral therapy device for treating symptoms of gastrointestinal conditions, pertaining to clinical data, software development documentation, useability assessment, and labeling of this prescription device.

Compatible Devices

Regulora is compatible with smartphones, tablets, and other mobile devices that are connected to the internet. Specifically:

iOS devices

- Operating System: iOS 12.4 or later
- Processor: 1.4 GHz minimum
- Memory (RAM): 1 GB minimum
- Examples of minimally compatible models: iPhone 6 or later; iPad Air 2 and iPad Mini 4 or later

Android devices

- Operating System: Android 8 or later
- Processor: 1.8 GHz minimum

- Memory (RAM): 2 GB minimum
- Examples of minimally compatible models: Samsung Galaxy S8, LG G5, Motorola Moto G7 or later

Network Connection and Speed

- Wi-Fi network or cellular data network
- Minimum 2 Mbps (megabits per second; for example 4G)
- Recommended 5 Mbps or greater (for example LTE, 5G or Wi-Fi)

Performance Testing – Bench:

In addition to the software verification testing, metaMe emphasizes performance bench testing to measure the performance characteristics of Regulora. Performance tests include:

- Uptime Testing - to ensure Regulora is accessible to and functional for patients
- Stress Testing - to ensure platform will support all prescribed patients at any given time
- Operating System Testing – to ensure Regulora is supported by the most recent iOS and Android operating system releases
- Cybersecurity considerations were addressed both via design specifications and bench testing.

Performance Testing – Clinical:

In the EASITx clinical trial (Efficacy and Safety of IBS Digital GDH Treatment, EASITx - NCT04133519), evaluable adult subjects with IBS (n=362) were randomized 1:1 to receive either 12 weeks of *Regulora* digital remotely-administered GDH behavioral therapy (n=181) or digital remotely-administered muscle relaxation therapy (MR) as a control (n=181). The primary endpoint was abdominal pain, the IBS symptom that most often prompts clinical consultation [3]. The EASITx primary outcome compared a 4-week pre-treatment period to a 4-week off-treatment period that began after completion of the *Regulora* program. During this off-treatment period (the primary outcome), 30.4% of subjects in the *Regulora* group and 27.1% of the subjects in the control group experienced at least a clinically meaningful 30% reduction in abdominal pain intensity scores[1] ($p = 0.5352$), not achieving statistical significance. However, during the on-treatment period (weeks 1-12), two separate analyses of the primary endpoint of abdominal pain achieved clinically significant separation from the EASITx control arm. During the final 4 weeks of treatment, a pre-specified endpoint, 30.9% of subjects in the GDH (Regulora) group and 21.5% of the subjects in the control group experienced at least a clinically meaningful 30% reduction in abdominal pain intensity scores. Throughout the on-treatment period (weeks 1-12), 29.3% of subjects in the Regulora group and 18.8% of the subjects in the MR group experienced at least a clinically meaningful 30% reduction in abdominal pain intensity scores. Thus, as with the predicate device (Parallel) [1,2], *Regulora* demonstrates clinically meaningful results within the intended use population.

[1] The pain and stool responder definitions of a 30% improvement from baseline for Regulora follows the *FDA Guidance for Industry, Irritable Bowel Syndrome — Clinical Evaluation of Drugs for Treatment, May 2012.*

In addition to the between-group analyses described above, subjects assigned to *Regulora* experienced clinically meaningful within-group improvement from baseline in IBS symptoms following 12 weeks of treatment, although these measures did not show statistically significant separation from control and therefore the associated endpoints were not met. As measured with clinically validated independent instruments over a 4-week post-treatment period, 44.9% of subjects experienced at least a 30% improvement in the proportion of stools with normal consistency. Half of subjects (50.3%) were either a pain or stool responder, while a 47% responder rate was reported in the predicate device. In the IBS-D subgroup (N=56), 48.2% of participants experienced at least a 50% reduction in days with loose or watery stools, while in the IBS-C subgroup, 39.7% of participants experienced at least 1 increased bowel movement per week. Additionally, 64.0% reported Adequate Relief and 67.7% of subjects reported overall satisfaction with the Regulora treatment.

There were no treatment-related serious adverse events. Non-serious adverse events with a reasonable possible relation to treatment included headache (0.5%, n=1), fatigue (0.5%, n=1), abdominal pain (0.5%, n=1), and constipation (0.5%, n=1).

The clinical data also showed that study subjects could use the program in the intended use environment by downloading, installing, and using Regulora on their mobile device at home.

Special Controls

metaMe complies with the special controls for product code QMY, Computerized behavioral therapy device for treating symptoms of gastrointestinal conditions, pertaining to clinical data, software development documentation, useability assessment, and labeling of this prescription device.

- Clinical data were provided that describe a model of therapy for the indicated gastrointestinal conditions.
- The model was further validated in a clinical trial of Regulora with validated clinical endpoints, demonstrating clinically meaningful results within the intended use population.
- All adverse events resulting from the clinical trial were evaluated.
- The Software was described in detail in the software requirements specification (SRS) and software design specification (SDS). Software verification, validation, and hazard analysis was performed. Software documentation demonstrated that the device effectively implements the behavioral therapy model.
- Usability assessment demonstrated that the intended user can correctly use the device.

- Labeling includes instructions for use, with images that demonstrate how to interact with the device along with a list of the minimum operating system requirements that support the software of the device, a warning that the device is not intended for use in lieu of a standard therapeutic intervention or represent a substitution for the patient's medication, a warning to seek medical care if a patient has feelings or thoughts of harming themselves or others; and a summary of the clinical testing with the device.

Conclusion

Regulora meets the threshold of substantial equivalence to the predicate device. From a design and clinical perspective, Regulora and Parallel (predicate device) have the same technological characteristics and share the same intended use. Both are prescription digital therapeutics, both are computerized behavior therapy, and both are intended to treat one or more gastrointestinal conditions. Software design, development, and verification along with bench and clinical performance testing validates Regulora for its intended use. Regulora meets the Special Controls as defined in 21 CFR 876.5960 (QMY) for clinical data, software design lifecycle documentation, patient usability, and device labeling. Regulora demonstrates clinically meaningful results within the intended use population.

Reference List

1. Everitt H, Landau S, Little P, et al. Therapist telephone-delivered CBT and web-based CBT compared with treatment as usual in refractory irritable bowel syndrome: the ACTIB three-arm RCT. *Health Technol Assess*. 2019;23(17):1-154. doi:10.3310/hta23170

2. Everitt H, Landau S, Little P, et al; ACTIB trial team. Assessing Cognitive behavioural therapy in irritable bowel (ACTIB): protocol for a randomised controlled trial of clinical-effectiveness and cost-effectiveness of therapist delivered cognitive behavioural therapy and web-based self-management in irritable bowel syndrome in adults. *BMJ Open*. 2015;5(7):e008622. doi:10.1136/bmjopen-2015-008622.

3. Hungin AP, Chang L, Locke GR, Dennis EH, Barghout V. Irritable bowel syndrome in the United States: prevalence, symptom patterns and impact. Aliment Pharmacol Ther. 2005 Jun 1;21(11):1365-75. doi: 10.1111/j.1365-2036.2005.02463.x. PMID: 15932367.