May 11, 2023

Subtle Medical Inc.
% Jared Seehafer
Regulatory Consultant
Enzyme Corporation
611 Gateway Blvd #120
SOUTH SAN FRANCISCO CA 94080

Re: K223623
Trade/Device Name: SubtleMR (2.3.x)
Regulation Number: 21 CFR 892.2050
Regulation Name: Medical image management and processing system
Regulatory Class: Class II
Product Code: LLZ
Dated: November 22, 2022
Received: April 13, 2023

Dear Jared Seehafer:

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,

Daniel M. Krainak, Ph.D.
Assistant Director
Magnetic Resonance and Nuclear Medicine Team
DHT8C: Division of Radiological Imaging
and Radiation Therapy Devices
OHT8: Office of Radiological Health
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.

Submission Number *(if known)*

K223623

Device Name

SubtleMR (2.3.x)

Indications for Use *(Describe)*

SubtleMR is an image processing software that can be used for image enhancement in MRI images. It can be used to reduce image noise for head, spine, neck, abdomen, pelvis, prostate, breast, and musculoskeletal MRI, or increase image sharpness for head MRI.

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

Table 1. Contact Details & Device Name

Date Summary Prepared:	2023-05-08
Contact Details	
Applicant Name:	Subtle Medical, Inc.
Applicant Address:	883 Santa Cruz Ave, Suite 205 Menlo Park, CA 94025 United States
Applicant Contact:	Mr. Ajit Shankaranarayanan
Applicant Contact Telephone:	(650) 397-8709
Applicant Contact Email:	ajit@subtlemedical.com
Correspondent Name:	Enzyme Corporation
Correspondent Address:	611 Gateway Blvd, Ste 120 South San Francisco, CA 94080 United States
Correspondent Contact:	Mr. Jared Seehafer
Correspondent Contact Telephone:	(415) 638-9554
Correspondent Contact Email:	jared@enzyme.com
Device Name	
Device Trade Name:	SubtleMR (2.3.x)
Common Name:	Medical image management and processing system
Classification Name:	System, Image Processing, Radiological
Regulation Number:	21 CFR 892.2050
Product Code:	LLZ
Device Class:	Class II
Legally Marketed Predicate Device:	Predicate #: K203182 Predicate Trade Name: SubtleMR Predicate Manufacturer: Subtle Medical, Inc.

Device Description Summary

SubtleMR is Software as a Medical Device (SaMD) consisting of a software algorithm that enhances images taken by MRI scanners. As it only processes images for the end user, the device has no user interface. It is intended to be used by radiologists in an imaging center, clinic, or hospital. The software can be used with MR images acquired as part of MRI exams on 1.2 Tesla, 1.5 Tesla or 3 Tesla scanners. The device's inputs are standard of care MRI images. The outputs are images with enhanced image quality.

The software uses a convolutional neural network-based algorithm to improve image quality by reducing noise or enhancing the image sharpness. The algorithm's specific parameters vary depending on the choice of image enhancement: noise reduction or sharpness enhancement, while the network designs are similar. For each choice, there is a fixed set of parameters and the algorithm is working as a fixed nonlinear filter. The choice of image enhancement is made by the end user via the DICOM Series Description, command line argument, or environment variable.

Intended Use / Indications for Use

SubtleMR is an image processing software that can be used for image enhancement in MRI images. It can be used to reduce image noise for head, spine, neck, abdomen, pelvis, prostate, breast, and musculoskeletal MRI, or increase image sharpness for head MRI.

Intended Use / Indications for Use Comparison

The intended use and indications for use of the subject device are identical to those of the predicate device.

Technological Comparison

The technological characteristics of the subject device are identical to those of the predicate device with two exceptions.

With respect to workflow, in the predicate device, the software operates on DICOM files on the file system, enhances the images, and stores the enhanced images on the file system. The subject device maintains this functionality, and in addition is capable of processing images communicated over ISMRM Raw Data Format (ISMRMRD).

With respect to the design of the device's neural networks, the properties of the predicate and subject device were as follows:

Predicate: The application consists of two models: sharpness enhancement (SRE) and denoising (DNE).
Subject: Same

Predicate: The SRE model is an EDSR neural network model. The DNE model is an EDSR neural network model.
Subject: The SRE model is an EDSR neural network model. The DNE model is an PGDnet neural network model.

Predicate: Model was built using the Tensorflow/Keras machine learning framework.
Subject: Model was built using the PyTorch machine learning framework.

Predicate: Uses composite L1 and SSIM loss function.
Subject: Uses composite L1, SSIM, perceptual, and high frequency loss function. Also, a weighting is used in the loss function to mitigate the pixel-level mis-alignment issue between the training data pairs.

The subject device was validated with test methods identical to those used to test the predicate device, and changes in technological characteristics do not present new questions of safety and effectiveness.

Non-Clinical and/or Clinical Tests Summary & Conclusions

Subtle Medical conducted the following performance testing:

- Software verification and validation testing
- Study that utilized retrospective clinical data to demonstrate the software enhanced image quality in MR images via a reduction of noise or sharpness enhancement.

Test methods were identical to those of the predicate device.

The main performance study, utilizing retrospective clinical data, was divided into two tests.

For the noise reduction performance test, acceptance criteria were that signal-to-noise ratio (SNR) of a selected region of interest (ROI) in each test dataset is on average improved by greater than or equal to 5% after SubtleMR enhancement compared to the original images, and the visibility of small structures in the test datasets after SubtleMR was rated on average non-inferior to that before SubtleMR based on a Likert reader study. This test passed.

For the sharpness enhancement performance test, acceptance criteria were that the thickness of anatomic structure and the sharpness of structure boundaries are improved after SubtleMR enhancement in at least 90% of the test datasets. This test passed.

Based upon the results of this testing, the SubtleMR performance was determined to be substantially equivalent to the predicate device.