



September 16, 2019

Subtle Medical, Inc.
% Mr. Jared Seehafer
Regulatory Consultant
Enzyme Corporation
360 Langton Street, Suite 100
SAN FRANCISCO CA 94103

Re: K191688

Trade/Device Name: SubtleMR
Regulation Number: 21 CFR 892.2050
Regulation Name: Picture archiving and communications system
Regulatory Class: Class II
Product Code: LLZ
Dated: July 15, 2019
Received: July 17, 2019

Dear Mr. 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,

For

Thalia T. Mills, Ph.D.
Director
Division of Radiological Health
OHT7: Office of In Vitro Diagnostics
and 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: 06/30/2020

See PRA Statement below.

510(k) Number (if known)

K191688

Device Name

SubtleMR

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 and knee MRI, or increase image sharpness for non-contrast enhanced 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.

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
PRASStaff@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."

5 510(k) Summary

K191688

Table 5-1. Subject Device Overview.

Submitter's Name:	Subtle Medical, Inc.
Address:	883 Santa Cruz Ave, Suite 205 Menlo Park, CA 94025
Contact Person:	Jared Seehafer
Title:	Regulatory Consultant
Telephone Number:	415-857-9554
Fax Number:	415-367-1279
Email:	jared@enzyme.com
Date Summary Prepared:	24-JUN-2019
Device Proprietary Name:	SubtleMR
Model Number:	V 1.0.0
Common Name:	SubtleMR
Regulation Number:	21 CFR 892.2050
Regulation Name:	System, Image Processing, Radiological
Product Code:	LLZ
Device Class:	Class II
Predicate Device	Trade name: ZOOM Manufacturer: Zetta Medical Technologies, LLC. 1313 Ensell Road Lake Zurich, IL 60047 Regulation Number: 21 CFR 892.2050 Regulation Name: System, Image Processing, Radiological Device Class: Class II Product Code: LLZ 510(k) Number: K172768 510(k) Clearance Date: April 24, 2018

5.1 Device Description

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 increasing the image sharpness. The algorithm's specific parameters vary depending on the choice of image enhancement: noise reduction or image sharpness increase, 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.

5.2 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 and knee MRI, or increase image sharpness for non-contrast enhanced head MRI.

5.3 Summary of Technological Characteristics Comparison

Table 5-2 shows the similarities and differences between the technological characteristics of the two products. The key difference is software algorithm. Testing demonstrates that the differences do not raise new questions of safety or effectiveness.

Table 5-2. Summary of Technological Characteristics Comparison.

Topic	Predicate Device	Subject Device
Physical Characteristics	Software package that operates on off-the-shelf hardware	Same
Computer	PC Compatible	Linux Compatible
DICOM Standard Compliance	The software processes DICOM compliant image data	Same
Operating System	Windows	Linux
Modalities	MRI	Same
User Interface	The software is designed for use on a radiology workstation.	None – enhanced images are viewed on existing PACS workstations

Topic	Predicate Device	Subject Device
Image Enhancement Algorithm Description	ZOOM image enhancement software implements a noise reduction algorithm using wavelets and image guided filtering. Original images are decomposed into different wavelet sub bands and noise in each band is a soft threshold. De-noised images are reconstructed from soft thresholded images using inverse wavelet transform.	SubtleMR software implements an image enhancement algorithm using convolutional neural network based filtering. Original images are enhanced by running through a cascade of filter banks, where thresholding and scaling operations are applied. Separate neural network based filters are obtained for noise reduction and sharpness increase. The parameters of the filters were obtained through an image-guided optimization process.
Workflow	The software, which is installed on a remote computer, receives DICOM images from MRI host computer, automatically processes the received images and sends the enhanced images to a PACS server. Enhanced images exist in conjunction to the original images.	The software operates on DICOM files on the file system, enhances the images, and stores the enhanced images on the file system. The receipt of original DICOM image files and delivery of enhanced images as DICOM files depends on other software systems. Enhanced images co-exist with the original images.

5.3 Performance Data

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 an increase of image sharpness.

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 (ii) the visibility of small structures in the test datasets before and after SubtleMR is on average less than or equal to 0.5 Likert scale points. This test passed.

For the sharpness increase 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.

5.4 Substantial Equivalence Conclusion

SubtleMR is an image enhancement software which has similar intended use and indications for use statement as the predicate device. The two devices have similar technological characteristics: both algorithms use image based nonlinear filtering and reconstruction, and both methods have optimized parameters to ensure robustness of the algorithm. This 510(k) submission includes information on the SubtleMR technological characteristics, as well as performance data and verification and validation activities demonstrating that SubtleMR is as safe and effective as the predicate, and does not raise different questions of safety and effectiveness.