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

February 26, 2021

Re: K203182
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: November 28, 2020
Received: December 1, 2020

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,

Michael D. O'Hara 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)*
K203182

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, 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.**

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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# 510(k) Summary

K203182

**Table 1. Subject Device Overview.**

| | |
|---|---|
| **Submitter's Name:** | Subtle Medical, Inc. |
| **Address:** | 883 Santa Cruz Ave, Suite 205<br>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:** | 18-FEB-2021 |
| **Device Proprietary Name:** | SubtleMR |
| **Model Number:** | V 2.0.0 |
| **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: SubtleMR<br>Manufacturer: Subtle Medical, Inc.<br>Regulation Number: 21 CFR 892.2050<br>Regulation Name: System, Image Processing, Radiological<br>Device Class: Class II<br>Product Code: LLZ<br>510(k) Number: K191688<br>510(k) Clearance Date: September 16, 2019 |

# 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 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.

# 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, abdomen, pelvis, prostate, breast and musculoskeletal MRI, or increase image sharpness for head MRI.

# 3 Purpose of Submission

The purpose of this 510(k) is to provide premarket notification for an expansion in the indications for use of SubtleMR to include: a) additional anatomical locations for which SubtleMR can reduce image noise and b) that SubtleMR can increase image sharpness in both contrast-enhanced and non-contrast-enhanced head MRI.

# 4 Summary of Technological Characteristics Comparison

Table 2 shows the similarities and differences between the technological characteristics of the two products.

**Table 2. Summary of Technological Characteristics Comparison.**

| Topic | Predicate Device | Subject Device |
|---|---|---|
| Physical Characteristics | Software package that operates on off-the-shelf hardware | Same |
| Computer | Linux Compatible | Same |
| DICOM Standard Compliance | The software processes DICOM compliant image data | Same |

| Topic | Predicate Device | Subject Device |
|---|---|---|
| Operating System | Linux | Same |
| Modalities | MRI | Same |
| User Interface | None | Same |
| Image Enhancement Algorithm Description | 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 enhancement. The parameters of the filters were obtained through an image-guided optimization process. | Same |
| Workflow | 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. | Same |
| Target Anatomical Locations | Head, spine, neck, and knee MRI | Head, spine, neck, abdomen, pelvis, prostate, breast and musculoskeletal MRI |

## *5 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 sharpness enhancement.

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 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.

## *6 Substantial Equivalence Conclusion*

The predicate for the subject device is its legally marketed prior revision (K191688). The two devices have the same intended use and similar indications for use. The two devices have nearly identical technological characteristics, the lone exception being the subject device's expanded target anatomical locations relative to the predicate device. The subject device was verified and validated using the same test methods and acceptance criteria as the predicate device and does not introduce any additional risk relative to its predicate. Therefore, this difference in technological characteristics does not raise different questions of safety and effectiveness. Consequently, SubtleMR is substantially equivalent to the predicate device.