July 17, 2024

Microstructure Imaging, Inc.
℅ Michelle Rubin-Onur
Regulatory Consultant
Enzyme Corporation
611 Gateway Blvd, Suite 120
South San Francisco, California 94080

Re: K241121
Trade/Device Name: MICSI-RMT
Regulation Number: 21 CFR 892.2050
Regulation Name: Medical image management and processing system
Regulatory Class: Class II
Product Code: LLZ
Dated: April 23, 2024
Received: April 23, 2024

Dear Michelle Rubin-Onur:

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 (the 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 available 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.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

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 Part 803) for devices or postmarketing safety reporting (21 CFR Part 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 Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 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
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: 07/31/2026
*See PRA Statement below.*

Submission Number *(if known)*

K241121

Device Name

MICSI-RMT

Indications for Use *(Describe)*

MICSI-RMT 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 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.***

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MICSI

## 510(k) Summary

**Contact Details** **21 CFR 807.92(a)(1)**

| | |
|---|---|
| Applicant Name | Microstructure Imaging, Inc. |
| Applicant Address | 370 Jay St, 7th Floor<br>Brooklyn NY 11201 United States |
| Applicant Contact | Gregory Lemberskiy, PhD |
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| Correspondent Address | 611 Gateway Blvd, Suite 120<br>South San Francisco CA 94080 United States |
| Correspondent Contact Telephone | (415) 579-1152 |
| Correspondent Contact | Michelle Rubin-Onur, PhD |
| Correspondent Contact Email | mrubinonur@enzyme.com |
| Date | July 16, 2024 |

**Device Name** **21 CFR 807.92(a)(2)**

| | |
|---|---|
| Device Trade Name | MICSI-RMT |
| Common Name | Medical image management and processing system |
| Classification Name | System, Image Processing, Radiological |
| Regulation Number | 892.2050 |
| Product Code(s) | LLZ |

**Legally Marketed Predicate Device** **21 CFR 807.92(a)(3)**

| Predicate # | Predicate Trade Name | Product Code |
|---|---|---|
| K191688 | SubtleMR | LLZ |

**Device Description Summary** **21 CFR 807.92(a)(4)**

MICSI-RMT Denoising (MICSI-RMT) is a Software as a Medical Device (SaMD) intended to enhance magnetic resonance imaging (MRI) images by reducing the image noise for head MRI images. The software can analyze both functional (fMRI) MRI and diffusion (dMRI) images. The device is intended to be used by radiologists in an imaging center, clinic, or hospital. The device is compatible with DICOM 3.0 standard.

The subject device has no user interface. The DICOM images obtained from a compatible MRI machine are streamed from the scanner to the designated DICOM destination, e.g., picture archiving and communication system (PACS), then to a DICOM router and processor (Mercure). It is within this router and processor where the subject device denoises the images. For fMRI images, parametric maps will be generated using pre-existing hospital software. For dMRI images, the subject device uses DTI to perform parameter estimation after denoising. Once the processing is complete, the device outputs are then routed to the target PACS (which can be the same one as before or a new DICOM destination) where the intended user can view the new images and the original images. Image processing time varies as it is dependent on the central processing unit (CPU), input image size, and the number of input images. When multiple jobs have been submitted to MICSI-RMT, they are queued and processed sequentially based on the order received.

**Intended Use/Indications for Use** **21 CFR 807.92(a)(5)**

MICSI-RMT 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 MRI.

**Indications for Use Comparison** **21 CFR 807.92(a)(5)**

The subject device has the same intended use as the predicate device; both devices are intended to enhance MRI images by reducing noise for MRI images of the head.

**Technological Comparison** **21 CFR 807.92(a)(6)**

The subject device has the same intended use environment and user and similar technological characteristics (e.g., Linux compatibility, use of MRI images, and processing of DICOM compliant image data) as the predicate device. One key difference is that the algorithm in the subject device is based on principal component analysis whereas the predicate uses a convolutional neural network-based algorithm. MICSI-RMT has undergone software and performance to ensure that any differences in technological characteristics do not raise different questions of safety and effectiveness and demonstrate substantial equivalence.

**Non-Clinical and/or Clinical Tests Summary & Conclusions** **21 CFR 807.92(b)**

Software verification was completed, and documentation was provided as recommended by the Guidance for Industry and FDA Staff *Content of Premarket Submissions for Device Software Functions (issued June 14, 2023)* for a basic level device.

To validate the performance of the MICSI-RMT software, MICSI conducted a HIPAA-compliant, retrospective IRB approved rater study. The study evaluated two qualitative and three quantitative metrics between the MICSI-RMT processed and standard of care (SOC) processed images.

The qualitative metrics evaluated were image quality and artifact presence. Image quality and artifact presence have an impact on the distinctiveness and contrast of small structures in the brain.

For image quality, a group of expert neuroradiologist raters, blinded to the processing technique used, rated the denoised MRI images on a Likert scale for overall image quality. These scores were aggregated to determine the mean Likert score for each image. The predetermined acceptance criterion was set at a mean Likert score greater than 3. Expert neuroradiologists defined a score of 3 or greater as the ability to visualize small structures in brain white matter, adequate contrast to distinguish adjacent tissue types, and for fMRI, that activation relevant to language tasks was anatomically appropriate. For each test dataset, the MICSI-RMT enhanced images were rated at a Likert score of 3 or greater, indicating that this test passed.

For artifact presence, the predetermined acceptance criterion was set at a mean Likert score greater than 3. The criteria used to determine the score for this test included artificial signal blurring, noise that could occlude anatomy of interest, and for fMRI, the presence of false positive activation. For each test dataset, the MICSI-RMT enhanced images were rated at a Likert score of 3 or greater, indicating that this test passed.

The three quantitative metrics evaluated were signal-to-noise ratio (SNR) change, fMRI activation map change, and dMRI STD change. The quality of image signal is important, as it enables fine white matter structures to be traceable along their full lengths, facilitating the evaluation of complex topographic-anatomical relationships in both normal and pathological conditions.

For SNR change, source diffusion and fMRI images that were enhanced by MICSI-RMT resulted in a greater than or equal to 5% change as compared to the original images over a region of interest spanning all white matter voxels.

For fMRI activation maps, the test dataset focused on Broca's and Wernicke's regions, where subcortical activation is expected in response to language based stimuli and found that median z-score improved from 3.01 to 3.64 in Broca's region and from 2.80 to 3.41 in Wernicke's region. Higher activation levels correspond to stronger confidence in the detection of neural activity, which can lead to a reduction in false positives and improved reliability of activation maps.

For dMRI STD, which was a measure of the reduction in the standard deviation of mean diffusivity (MD) and fractional anisotropy (FA) defined over the posterior limb of the internal capsule, an anatomically homogenous region of white matter, we anticipated a change in STD with MICSI-RMT processed parametric maps. A reduction in STD indicated that the MICSI-RMT parametric maps had greater precision. MD images enhanced with MICSI-RMT had an STD reduction from 0.16 to 0.075, and FA images had an STD reduction from 0.09 to 0.069, demonstrating that the image enhancement process leads to more precise parametric maps.

All three quantitative tests met their predetermined acceptance criteria.

Overall, the retrospective study found that MICSI-RMT processing results in enhanced high quality denoised images that have a greater or equal to 5% change in SNR and more clearly defined activation levels in fMRI activation maps. Based on these results, MICSI-RMT performance was determined to be substantially equivalent to the predicate device.