January 13, 2023

Olea Medical
% John J. Smith
Partner
Hogan Lovells US LLP
Columbia Square
555 Thirteenth Street, NW
WASHINGTON DC 20004

Re: K223502
Trade/Device Name: MR Diffusion Perfusion Mismatch V1.0
Regulation Number: 21 CFR 892.2050
Regulation Name: Medical image management and processing system
Regulatory Class: Class II
Product Code: LLZ
Dated: November 21, 2022
Received: November 21, 2022

Dear John Smith:

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.
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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)*
K223502

Device Name

MR Diffusion Perfusion Mismatch V1.0

MR Diffusion Perfusion Mismatch V1.0 is an automatic calculation tool indicated for use in radiology. The device is an image processing software allowing computation of parametric maps from (1) MR Diffusion-weighted imaging (DWI) and (2) MR Perfusion-weighted imaging (PWI) and extraction of volumes of interest based on numerical thresholds applied to the aforementioned maps. Computation of mismatch between extracted volumes is automatically provided.

The device is intended to assist trained radiologists and surgeons in the imaging assessment workflow by extraction and communication of metrics from MR Diffusion-weighted imaging (DWI) and MR Perfusion-weighted imaging (PWI).

The results of MR Diffusion Perfusion Mismatch V1.0 are intended to be used in conjunction with other patient information and, based on professional judgment, to assist the clinician in the medical imaging assessment. Trained radiologists and surgeons are responsible for viewing the full set of native images per the standard of care.

The device does not alter the original medical image. MR Diffusion Perfusion Mismatch V1.0 is not intended to be used as a standalone diagnostic device and shall not be used to take decisions with diagnosis or therapeutic purposes. Patient management decisions should not solely be based on MR Diffusion Perfusion Mismatch V1.0 results.

MR Diffusion Perfusion Mismatch V1.0 can be integrated and deployed through technical platforms, responsible for transferring, storing, converting formats, notifying of detected image variations and display of DICOM imaging data.

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

Olea Medical's MR Diffusion Perfusion Mismatch V1.0

Submitter

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Date Prepared: January 9, 2023

Name of Device: MR Diffusion Perfusion Mismatch V1.0

Common or Usual Name: Picture archiving and communication system (PACS)

Regulation Name: Medical Image Management and Processing System

Regulatory Class: 21 CFR 892.2050

Product Code: LLZ

Predicate Device: Olea Sphere V3.0 (K152602)

Indications for Use

MR Diffusion Perfusion Mismatch V1.0 is an automatic calculation tool indicated for use in radiology. The device is an image processing software allowing computation of parametric maps from (1) MR Diffusion-weighted imaging (DWI) and (2) MR Perfusion-weighted imaging (PWI) and extraction of volumes of interest based on numerical thresholds applied to the aforementioned maps. Computation of mismatch between extracted volumes is automatically provided.

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Device Description

Introduction

The MR Diffusion Perfusion Mismatch V1.0 application can be used to automatically compute qualitative as well as quantitative perfusion maps based on the dynamic (first-pass) effect of a contrast agent (CA). The perfusion application assumes that the input data describes a well-defined and transient signal response following rapid administration of a contrast agent.

Olea Medical proposes MR Diffusion Perfusion Mismatch V1.0 as an image processing application, Picture Archiving Communications System (PACS) software module that is intended for use in a technical environment which incorporates a Medical Image Communications Device as its technical platform.

MR Diffusion Perfusion Mismatch V1.0 interaction with the technical platform

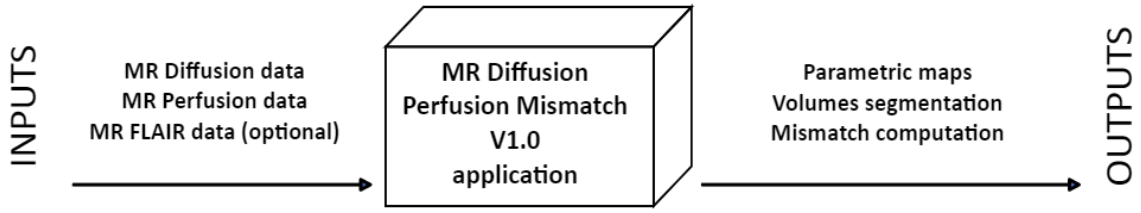
To be used, the docker needs a technical base, which is provided by a Medical Image Communications Device (MICD). The technical platform allows the docker to:

- receive the inputs
- provide the outputs
- visualize the outputs as the docker has no interface.

The technical base can support several applications encapsuled in a docker such as MR Diffusion Perfusion Mismatch V1.0.

MR Diffusion Perfusion Mismatch V1.0 principle of operations and technological characteristics

MR Diffusion Perfusion Mismatch V1.0 image processing application is designed as a docker installed on a technical platform (i.e., a Medical Image Communications Device), as depicted below.



MR Diffusion Perfusion Mismatch V1.0 inputs/outputs

MR Diffusion Perfusion Mismatch V1.0 is a docker totally independent from the technical platform in which it is integrated:

- Input DICOM images are received by the technical platform;
- Relevant series are automatically identified among the images received in the platform by reading the relevant DICOM tags and are provided to the application;
- The arrival of identified series will launch MR Diffusion Perfusion Mismatch V1.0;

- The MR Diffusion Perfusion Mismatch V1.0 processes the identified series;
- The generated results are automatically pushed to the technical platform;
- The results can be visualized with any DICOM viewer comprising but not limited to the technical platform or exported to dedicated file location.

Substantial Equivalence

Substantial equivalence comparison table

MR Diffusion Perfusion Mismatch V1.0	Olea Sphere® V3.0 (K152602)
Parametric maps	YES
Volumes segmentation	YES
Mismatch computation	YES

MR Diffusion Perfusion Mismatch V1.0 represents a subset of the predicate Olea Sphere V3.0. Comparative performance testing was conducted using the comparable Diffusion, Perfusion and Analysis modules in Olea Sphere V3.0.

Both MR Diffusion Perfusion Mismatch V1.0 and Olea Sphere® V3.0 are user-defined software analysis tools used for the analysis of MR studies. Both devices are intended for use in hospitals and imaging centers. Importantly, neither software product is used for diagnosis. Patient management decisions should not be based solely on the results of either software. Therefore, the intended use of the software is the same.

Both the MR Diffusion Perfusion Mismatch V1.0 and Olea Sphere V3.0 have similar technological characteristics as they both:

- provide processing capabilities for the analysis of MR series;
- are designed to be able to process MR series;
- are able to provide same outputs;
- are able to automatically compute the mismatch between extracted volumes.

The three minor differences between the two devices are:

1. MR Diffusion Perfusion Mismatch V1.0 represents a subset of Olea Sphere V3.0. Accordingly, the indications for use of the subject device, MR Diffusion Perfusion Mismatch V1.0, is considered substantially equivalent to Diffusion, Perfusion and Analysis modules of the predicate, Olea Sphere V3.0. Olea Sphere® V3.0 provides other processing capabilities both on MR and CT, whereas the MR Diffusion Perfusion Mismatch V1.0 only analyzes MR images.
2. Olea Sphere V3.0 is equipped with a visualization interface, whereas MR Diffusion Perfusion Mismatch V1.0 needs to communicate with the technical platform to visualize the outputs.
3. The following are differences in the algorithms applied prior to maps computation:
    - MR Diffusion Perfusion Mismatch V1.0 uses a motion correction algorithm based on a 3D rigid method, while Olea Sphere® V3.0 uses a 2D rigid motion correction algorithm. This difference does not impact the calculation method of the outputs.
    - MR Diffusion Perfusion Mismatch V1.0 uses a Diffusion Brain Extraction Tool (BET) and a Perfusion Background Segmentation step based on AI algorithms. This difference does not impact the calculation method of the outputs.

In sum, these minor differences do not raise new questions of safety or effectiveness of the subject device.

Performance Data

Olea Medical has conducted extensive validation testing of the MR Diffusion Perfusion Mismatch V1.0. Internal verification and validation testing confirm that the product specifications are met and supports substantial equivalence of the intended use and technological characteristics to the predicate device.

MR Diffusion Perfusion Mismatch V1.0 has been validated to ensure that the system meets all performance specifications necessary to operate according to its intended use and in a manner substantially equivalent to the predicate device.

The following performance evaluations were conducted:

- Product risk assessment;
- Software modules verification tests;
- Software validation test;
- Comparative clinical image study

Based on the clinical performance as documented in a comparative clinical image study, the MR Diffusion Perfusion Mismatch V1.0 has a safety and effectiveness profile that is similar to the predicate device. Testing results are summarized below:

- **Parametric maps result comparison**: ADC, CBF, CBV, MTT and tMIP parametric maps computed with MR Diffusion Perfusion Mismatch V1.0 and Olea Sphere® V3.0 were statistically equivalent with Pearson and Spearman correlation coefficients greater than 0.8, while TTP and Tmax temporal maps did not meet the acceptance criteria. Indeed, TTP and Tmax values are more prone to differences induced by slight variations because these parameters depend on the acquisition grid. However, the qualitative assessment allowed an US board-certified neuroradiologist to conclude that all parametric maps were substantially equivalent.

- **Volume_1**: Bland-Altman analysis showed that the average estimated bias (average of differences) was close to zero (-0.33 ml), with 95% of the measurement differences ranging between -1.83 ml and +1.16 ml. These values were considered as acceptable, since they are within the range of inter-software variability reported in the literature for threshold-based volume segmentations. Moreover, they were also considered as acceptable according to an US board-certified neuroradiologist.

  Mean DICE index (similarity coefficient) was excellent and equal to 0.96 between MR Diffusion Perfusion Mismatch V1.0 and Olea Sphere® V3.0 Volume_1 segmentations. Moreover, the absolute mean of the differences was close to zero (0.63 ml). Scatterplot linear regression (excellent correlation with R2 = 0.99) and boxplots supported these findings. Finally, the appraisal performed by an US board-certified neuroradiologist led to the conclusion that Volume_1 was visually equivalent for all 30 cases.

- **Volume_2**: Bland-Altman analysis showed that the average estimated bias (average of differences) was small (-3.74 ml), with 95% of the measurement differences ranging between -33.59 ml and +26.10 ml. These values were considered as acceptable, since they are within the range of inter-software variability reported in the literature for threshold-based volume

segmentations. Moreover, they were also considered as acceptable according to an US board-certified neuroradiologist.

The variability of Volume_2 between both devices was reflected by a 0.75 mean DICE index. Moreover, the absolute mean of the differences remained low (11.77 ml), which is acceptable according to an US board-certified neuroradiologist, and the scatterplot linear regression showed an excellent correlation (R2 = 0.95). Moreover, the visual inspection performed by an US board-certified neuroradiologist led to the conclusion that Volume_2 was equivalent for all 30 cases.

- **Mismatch Ratio**: Bland-Altman analysis showed that the average estimated bias was close to zero (0.88) with 95% of the measurement differences ranging between -11.01 and +12.77, which is an acceptable range according to an US board-certified neuroradiologist. The absolute mean of the differences was 1.87, which is acceptable according to an US board-certified neuroradiologist.

- **Mismatch Volume**: Bland-Altman analysis showed that the average estimated bias was -3.09 ml, with 95% of the measurement differences ranging between -32.82 ml and +26.64 ml, which is an acceptable range according to an US board-certified neuroradiologist. The absolute mean of the differences was 11.81 ml, which is acceptable according to an US board-certified neuroradiologist.

- **Relative Mismatch**: Bland-Altman analysis showed that the average estimated bias was -6.57 %, with 95% of the measurement differences ranging between -57.28 % and +44.15 %, which is an acceptable range according to an US board-certified neuroradiologist. The absolute mean of the differences was 13.21 %, which is acceptable according to an US board-certified neuroradiologist.

Conclusions

MR Diffusion Perfusion Mismatch V1.0 is substantially equivalent to the predicate device, Olea Sphere® V3.0. The MR Diffusion Perfusion Mismatch V1.0 has the same intended use and similar indications for use, technological characteristics, and principles of operation as its predicate device.

In addition, the minor technological differences between the MR Diffusion Perfusion Mismatch V1.0 and its predicate devices raise no new questions of safety or effectiveness. Performance data demonstrate that the MR Diffusion Perfusion Mismatch V1.0 is as safe and effective as the Olea Sphere® V3.0. Thus, the MR Diffusion Perfusion Mismatch V1.0 is substantially equivalent.