Siemens Healthcare GmbH
℅ Kira Kuzmenchuk
Regulatory Affairs Specialist
Siemens Medical Solutions USA, Inc.
40 Liberty Blvd., Mail Code 65-1
MALVERN PA 19355

April 15, 2022

Re: K213706
Trade/Device Name: AI-Rad Companion Brain MR
Regulation Number: 21 CFR 892.2050
Regulation Name: Medical image management and processing system
Regulatory Class: Class II
Product Code: QIH
Dated: March 11, 2022
Received: March 15, 2022

Dear Kira Kuzmenchuk:

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: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*

K213706

Device Name
AI-RAD Companion Brain MR

Indications for Use *(Describe)*

AI-Rad Companion Brain MR is a post-processing image analysis software that assists clinicians in viewing, analyzing, and evaluating MR brain images.

AI-Rad Companion Brain MR provides the following functionalities:

- Automated segmentation and quantitative analysis of individual brain structures and white matter hyperintensities
- Quantitative comparison of brain structure with normative data from a healthy population
- Presentation of results of reporting that includes all numerical values as well as visualization of these results

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
FOR
AI-Rad Companion Brain MR

Submitted by:
Siemens Medical Solutions USA, Inc.
40 Liberty Boulevard
Malvern, PA 19355
Date Prepared: November 22, 2021

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of Safe Medical Devices Act of 1990 and 21 CFR §807.92.

1. Submitter

Importer/Distributor

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Malvern, PA 19355
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3. Device Name and Classification

Product Name:	AI-Rad Companion Brain MR
Trade Name:	AI-Rad Companion Brain MR
Classification Name:	Medical Image Management and Processing System

Classification Panel:	Radiology
CFR Section:	21 CFR §892.2050
Device Class:	Class II
Product Code:	QIH

4. Predicate Device

Product Name:	AI-Rad Companion Brain MR
Propriety Trade Name:	AI-Rad Companion Brain MR
510(k) Number:	K193290
Clearance Date:	June 17, 2020
Classification Name:	Picture Archiving and Communication System
Classification Panel:	Radiology
CFR Section:	21 CFR §892.2050
Secondary CFR Section:	21 CFR §892.1000
Device Class:	Class II
Primary Product Code:	LLZ
Secondary Product Code:	LNH
Recall Information:	N/A

5. Indications for Use

AI-Rad Companion Brain MR is a post-processing image analysis software that assists clinicians in viewing, analyzing and evaluating MR brain images.

AI-Rad Companion Brain MR provides the following functionalities:

- Automatic segmentation and quantitative analysis of individual brain structures and white matter hyperintensities
- Quantitative comparison of each brain structure with normative data from a healthy population
- Presentation of results for reporting that includes all numerical values as well as visualization of these results.

6. Device Description

AI-Rad Companion Brain MR VA40 is an enhancement to the predicate, AI-Rad Companion Brain MR VA20 **(**K193290**)**. Just as in the predicate, AI-Rad Companion Brain MR addresses the automatic quantification and visual assessment of the volumetric properties of various brain structures based on T1 MPRAGE datasets. In AI-Rad Companion Brain MR VA40, the quantification and visual assessment extends to white matter hyperintensities on the basis of T1 MPRAGE and T2 weighted FLAIR datasets. These datasets are acquired as part of a typical head MR acquisition. The results are directly archived in PACS as this is the standard location for reading by radiologist. From a predefined list of 30 structures (e.g. Hippocampus, Left Frontal

Grey Matter, etc.), volumetric properties are calculated as absolute and normalized volumes with respect to the total intercranial volume. The normalized values for a given patient are compared against age-matched mean and standard deviations obtained from a population of healthy reference subjects.

The white matter hyperintensities can be visualized as a 3D overlay map and the quantification in count and volume as per 4 brain regions in the report.

As an update to the previously cleared device, the following modifications have been made:

1. Modified Intended Use Statement
2. Addition of white matter hyperintensities overlay map, count and volume as per 4 brain regions
3. Enhanced DICOM Structured Report (DICOM SR)
4. Updated deployment structure

7. Substantially Equivalent (SE) and Technological Characteristics

The intended use of the predicate device and the subject device are equivalent. The main difference is that AI-Rad Companion Brain MR VA40 adds the additional analysis of white matter hyperintensities compared to the predicate, AI-Rad Companion Brain MR VA20.

The subject device, AI-Rad Companion Brain MR VA40 is substantially equivalent with regard to the intended use and technical characteristics compared to the predicate device, AI-Rad Companion Brain MR VA20 (K193290), with respect to the software features, functionalities, and core algorithms. The additional features, enhancements and improvements provided in AI-Rad Companion Brain MR VA40 increase the usability and reduce the complexity of the imaging workflow for the clinical user. The white matter hyperintensity algorithm within AI-Rad Companion Brain MR VA40 is equivalent to the algorithm in icobrain (K192130). Icobrain serves as a reference device within this submission and a dedicated comparison of technological characteristics is provided.

The risk analysis and non-clinical data support that both devices perform equivalently and do not raise different questions of the safety and effectiveness.

	Subject Device: AI-Rad Companion Brain MR VA40	**Predicate Device: AI-Rad Companion Brain MR VA20 (**K193290**)**	**Reference Device: icobrain (**K192130**)**
Indications for Use	AI-Rad Companion Brain MR is a post-processing image analysis software that assists clinicians in viewing, analyzing, and evaluating MR brain images.	AI-Rad Companion Brain MR is a post-processing image analysis software that assists clinicians in viewing, analyzing, and evaluating MR brain images.	icobrain is intended for automatic labeling, visualization and volumetric quantification of segmentable brain structures

	AI-Rad Companion Brain MR provides the following functionalities: • Automatic segmentation and quantitative analysis of individual brain structures and white matter hyperintensities • Quantitative comparison of each brain structure with normative data from a healthy population • Presentation of results for reporting that includes all numerical values as well as visualization of these results	AI-Rad Companion Brain MR provides the following functionalities: • Automatic segmentation and quantitative analysis of individual brain structures • Quantitative comparison of each brain structure with normative data from a healthy population • Presentation of results for reporting that includes all numerical values as well as visualization of these results	from a set of MR or NCCT images. This software is intended to automate the current manual process of identifying, labeling and quantifying the volume of segmentable brain structures identified on MR or NCCT images. icobrain consists of two distinct image processing pipelines: icobrain cross and icobrain long. icobrain cross is intended to provide volumes from MR or NCCT images acquired at a single time point. icobrain long is intended to provide changes in volumes between two MR images that were acquired on the same scanner, with the same image acquisition protocol and with same contrast at two different timepoints. The results of icobrain cross cannot be compared with the results of icobrain long.
Brain Morphometry Segmentation	Pre-processing functionality for automatic segmentation	Pre-processing functionality for automatic segmentation	Image processing for automatic segmentation and

	and volumetry of MPRAGE data.	and volumetry of MPRAGE data.	volumetry of MPRAGE data.
Brain Morphometry Quantification	Calculation of label maps (display of brain segmentation) and partially combined label maps (fused with the processed MPRAGE data).	Calculation of label maps (display of brain segmentation) and partially combined label maps (fused with the processed MPRAGE data).	Normalized and unnormalized volume and volume changes of different brain structures.
Brain Morphometry: *Deviation Map*	Calculation of deviation map (representation of brain status in relation to reference data) and partially combined deviation maps (fused with the processed MPRAGE data) User customizable color labels for the overlay map.	Calculation of deviation map (representation of brain status in relation to reference data) and partially combined deviation maps (fused with the processed MPRAGE data) User customizable color labels for the overlay map.	Not available
Brain White Matter Hyperintensities Segmentation	Pre-processing functionality for automatic segmentation and volumetry of MPRAGE and FLAIR data.	Not available	Image processing for automatic segmentation and volumetry of FLAIR data.
Brain White Matter Hyperintensities Quantification	Calculation of white matter hyperintensities count and volume as per 4 brain regions.	Not available	Unnormalized volume and volume changes of FLAIR white matter hyperintensities as per 4 brain regions
Brain White Matter Hyperintensities Map	Calculation of white matter hyperintensities map fused with the processed FLAIR data User customizable color labels for the overlay map.	Not available	Calculation of white matter hyperintensities map overlaid with the FLAIR data
Distribution & Archiving	Creation of an image series for a morphometry	Creation of an image series for a	Automatic transfer of generated image

	report. Automatic transfer of generated maps and morphometry report to a PACS system.	morphometry report. Automatic transfer of generated maps and morphometry report to a PACS system.	series and report to a PACS system.
User Interface Confirmation	Confirmation UI with basic visualization functionality	Confirmation UI with basic visualization functionality	Not available.
User Interface Configuration	Configuration UI	Configuration UI	Not available
Architecture	Cloud solution and Edge components deployed on customer premise.	Cloud only solution with no components deployed on customer premise.	Cloud only solution with no components deployed on customer premise.
DICOM SR	DICOM structured report representation of a natural language report	Basic morphometry report	DICOM structured report

Table 1: Comparison table for AI-Rad Companion Brain MR VA40, predicate device AI-Rad Companion Brain MR VA20 (K193290) and reference device icobrain (K192130)

Siemens Healthineers has determined that icobrain (K192130) has similar technological and performance characteristics with respect to the segmentation and quantification of white matter hyperintense lesions. Icobrain produces reports that identify unnormalized volumes and volume changes of FLAIR white matter hyperintensities of four different regions (juxtacortical, periventricular, infratentorial, deep white matter) using equivalent methodology used in the subject device, AI-Rad Companion Brain MR VA40.

The conclusions from all verification and validation data suggest that these enhancements are equivalent with respect to safety and effectiveness of the predicate device. These modifications do not change the intended use of the product. Siemens is of the opinion that AI-Rad Companion Brain MR VA40 is substantially equivalent to the currently marketed device, AI-Rad Companion Brain MR VA20 (K193290).

8. Nonclinical Tests

Non-clinical tests were conducted to test the functionality of AI-Rad Companion Brain MR. Software validation and bench testing have been conducted to assess the performance claims as well as the claim of substantial equivalence to the predicate device.

AI-Rad Companion has been tested to meet the requirements of conformity to multiple industry standards. Non-clinical performance testing demonstrates that AI-Rad Companion Brain MR complies with the FDA guidance document, “Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices” (May 11, 2005) as well as with the following voluntary FDA recognized Consensus Standards listed in **Section 9.**

Verification and Validation

Software documentation for a Moderate Level of Concern software, per FDA's Guidance Document "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices" issued on May 11, 2005, is also included as part of this submission. The performance data demonstrates continued conformance with special controls for medical devices containing software. Non-clinical tests were conducted on the subject device during product development.

Software "bench" testing in the form of Unit, System and Integration tests were performed to evaluate the performance and functionality of the new features and software updates. All testable requirements in the Requirement Specifications and the Risk Analysis have been successfully verified and traced in accordance with the Siemens Healthineers DH product development (lifecycle) process. Human factor usability validation is addressed in system testing and usability validation test records. Software verification and regression testing have been performed successfully to meet their previously determined acceptance criteria as stated in the test plans.

Siemens Healthineers adheres to the cybersecurity requirements as defined the FDA Guidance "Content of Premarket Submissions for Management for Cybersecurity in Medical Devices," issued October 2, 2014 by implementing a process of preventing unauthorized access, modifications, misuse or denial of use, or the unauthorized use of information that is stored, accessed, or transferred from a medical device to an external recipient.

9. Performance Software Validation

To validate the AI-Rad Companion Brain MR software from clinical perspective, the white matter hyperintensities segmentation and analysis algorithm underwent a scientific evaluation. The results of clinical data-based software validation for the subject device AI-Rad Companion Brain demonstrated equivalent performance in comparison to the reference device. A complete scientific evaluation report is provided in support of the device modifications. The brain morphometry algorithm, unchanged from the predicate, did not undergo a new scientific evaluation.

Performance testing for AI-Rad Companion Brain MR WMH was performed on Siemens Healthineers test data from 89 subjects, which included Multiple Sclerosis patients (MS), Alzheimer's patients (AD), cognitive impaired (CI) and healthy controls (HC). Testing data has balanced distribution with respect to gender and age of the patient according to target patient population and field strength of the MR scanner used. Accuracy was validated by comparing the results of the subject device to manual annotated ground truth from three radiologists. Three sets of white matter hyper-intensity ground truth were annotated manually by a disjoint group of annotator, reviewer, and clinical expert, with each expert randomly assigned per case to minimize annotation bias. Reproducibility studies were conducted to demonstrate the robustness of the WMH segmented by our device with respect to instrumental and patient noise.

Acceptance Criteria:

Validation Type	Acceptance Criteria
Volumetric Segmentation Accuracy	PCC 95% Confidence Interval includes 0.91
	ICC 95% Confidence Interval includes 0.95
Voxel-wise Segmentation Accuracy	Mean Dice score >= 0.58
WMH Lesion-wise Segmentation Accuracy	Mean F1-score >= 0.57
Reproducibility	Lower Bound of the 95% Bootstrap CI Dice >= 0.63

Summary Performance data, Standard Deviations & CIs:

	Volumetric Segmentation		Voxel-wise Segmentation	WMH Lesion-wise Segmentation	Reproducibility
	PCC	ICC	Dice	F1-score	Dice
AVG	0.98	0.97	0.60	0.60	0.79
STD	n.a.	n.a.	0.18	0.14	0.11
95% CI	[0.97,0.99]	[0.96,0.98]	[0.53,0.63]	[0.57,0.64]	[0.77,0.81]

Testing Data Information:

	Reproducibility Cohort	Testing Cohort
# Subjects	25	64
# Studies	100	64
# of Females	12	35
# of Males	13	29
Age Range	23-55	19-83

Medical Indication	MS – all	MS – 36 Cognitive Impairment – 17 Other neurological disease – 5 Cognitive Normal – 5 Unknown – 1
Scan Protocol	3D T1w MPRAGE 3D T2w FLAIR	T1w MPRAGE T2w FLAIR
Field Strength	3T	1.5T: 30 3.0T: 34
Manufacturer	Siemens	Siemens
Data Origin	Cleveland (US): 16 Baltimore (US): 9	New York (US): 25 ADNI (US): 12 Lausanne (CH): 8 CLEMENS (CH): 10 Montpellier (FR): 9

Standard Annotation Process:

For each dataset, three sets of white matter hyperintensity ground truth are annotated manually. Each set is annotated by a disjoin group of annotator, reviewer, and clinical expert with the expert randomly assigned per case to minimize annotation bias. For each test dataset, the three initial annotations are annotated by three different in-house annotators. Then, each initial annotation is reviewed by the in-house reviewer. Afterwards, each initial annotation is reviewed by the referred clinical expert. The clinical expert reviews and corrects the initial annotation of the WMH according to the annotation protocol.

Testing & Training Data Independence:

The training data used for the training of the White matter hyperintensity algorithm is independent of the data used to test the white matter hyperintensity algorithm.

10. Clinical Tests

No clinical tests were conducted to test the performance and functionality of the modifications introduced within AI-Rad Companion Brain MR. Verification and validation of the enhancements and improvements have been performed and these modifications have been validated for their intended use. The data from these activities were used to support the subject device and the substantial equivalence argument. No animal testing has been performed on the subject device.

11. Safety and Effectiveness

The device labeling contains instructions for use and any necessary cautions and warnings to ensure safe and effective use of the device.

Risk management is ensured via ISO 14971:2019 compliance to identify and provide mitigation of potential hazards in a risk analysis early in the design phase and continuously throughout the development of the product. These risks are controlled via measures realized during software development, testing and product labeling.

Furthermore, the device is intended for healthcare professionals familiar with the post processing of magnetic resonance images.