Qure.ai Technologies
℅ Pooja Rao
Head, Research and Development
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Mumbai, Maharashtra 400063
INDIA

July 30, 2021

Re: K211222
Trade/Device Name: qER-Quant
Regulation Number: 21 CFR 892.2050
Regulation Name: Medical image management and processing systems
Regulatory Class: Class II
Product Code: QIH
Dated: June 30, 2021
Received: July 1, 2021

Dear Pooja Rao:

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)*
K211222

Device Name
qER-Quant

Indications for Use *(Describe)*
The qER-Quant device is intended for automatic labeling, visualization and quantification of segmentable brain structures from a set of Non-Contrast head CT (NCCT) images. The software is intended to automate the current manual process of identifying, labeling and quantifying the volume of segmentable brain structures identified on NCCT images.
qER-Quant provides volumes from NCCT images acquired at a single time point and provides a table with comparative analysis for two or more images that were acquired on the same scanner with the same image acquisition protocol for the same individual at multiple time points.
The qER-Quant software is indicated for use in the analysis of the following structures: Intracranial Hyperdensities, Lateral Ventricles and Midline Shift.

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 K211222

Qure.ai's qER-Quant

1.1 Submitter

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Contact Person: Pooja Rao

Date Prepared: April 20, 2021

1.2 Device

Name of Device:	qER-Quant
Common or Usual Name:	Automated Radiological Image Processing Software
Classification Name:	Medical image management and processing system
Regulatory Class:	Class II
Regulation Number:	21 CFR 892.2050
Product Code:	QIH

1.3 Predicate Device

Name of Device:	Icobrain
Manufacturer:	Icometrix NV
510(k) Number:	K181939

Intended Use / Indications for Use:

The qER-Quant device is intended for automatic labeling, visualization and quantification of segmentable brain structures from a set of Non-Contrast head CT (NCCT) images. The software is

intended to automate the current manual process of identifying, labeling and quantifying the volume of segmentable brain structures identified on NCCT images.

qER-Quant provides volumes from NCCT images acquired at a single time point and provides a table with comparative analysis for two or more images that were acquired on the same scanner with the same image acquisition protocol for the same individual at multiple time points.

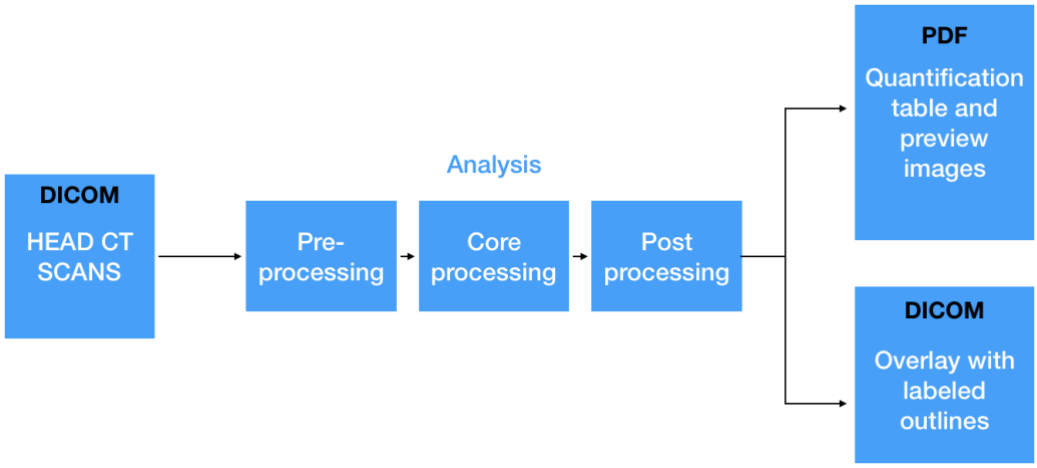
The qER-Quant software is indicated for use in the analysis of the following structures: Intracranial Hyperdensities, Lateral Ventricles and Midline Shift.

1.4 Device Description

qER-Quant is a standalone software device that processes non-contrast head CT scans to outline and quantify the structures described in the intended use. The qER-Quant software interacts with the user's picture archiving and communication system (PACS) to receive scans and returns the results to the same destination.

The analysis module of the qER-Quant software contains of a set of pre-trained convolutional neural networks (CNNs), that form the core processing component shown in Figure 1. This core processing component is coupled with a pre-processing module to prepare input digital imaging and communications in medicine (DICOMs) for processing by the CNNs and a post-processing module to convert the output into visual and tabular output for users.

Figure 1: Schematic showing qER-Quant design and workflow



CT scans are sent to qER-Quant by means of transmission functions within the user's PACS system. Upon completion of processing, the qER-Quant device returns results to the user's PACS or other user-specified radiology software system or database.

The inputs to qER-Quant are non-contrast head CT scans in DICOM format. The plain axial series of the input DICOM file is used for processing. The qER-Quant device produces PDF and DICOM format outputs that enable users to view the quantification results in visual and table form.

PDF format output consists of a table with volumes of the quantified structure and selected preview images showing representative CT scan slices. If more than one CT scans from the same subject and the same scanner is available, qER-Quant performs a comparison between the scans, and returns a longitudinal comparison with a graphic illustrating the changes in absolute volume and size of the quantified structures over time.

DICOM format output consists of a complete additional series with labeled overlays indicating the location and extent of the quantified structures.

1.5 Comparison with Predicate Device

Like the predicate device, qER-Quant is intended for automatic labeling, visualization and quantification of segmentable brain structures. The devices both take DICOM format 3D images of the brain as input and generate an electronic report in PDF and DICOM formats with similar quantitative information. The primary difference is that qER-Quant operates only on NCCT scans, while the predicate device operates on both MRI and NCCT scans. The table below compares qER-Quant with the predicate device, and lists the similarities and differences between them. The minor differences do not raise any new questions of safety or effectiveness.

Table 1: Comparison between qER-Quant and the Predicate Device

	qER-Quant Device Subject Device	Predicate Device
Device Name	qER-Quant	Icobrain
510(k) Number	K211222	K181939
Regulation	21 CFR 892.2050	21 CFR 892.2050
Product Code	QIH	LLZ
Regulation Description	Medical image management and processing system	Picture archiving and communications system
Device type	Automated Radiological Image Processing Software	Radiological Image Processing System
Manufacturer	Qure.ai Technologies	icometrix NV
Overview of Similarities between qER-Quant and the Predicate Device		

	qER-Quant Device Subject Device	Predicate Device
Intended Use/ Indications for Use	The qER-Quant device is intended for automatic labeling, visualization and quantification of segmentable brain structures from a set of Non-Contrast head CT (NCCT) images. The software is intended to automate the current manual process of identifying, labeling and quantifying the volume of segmentable brain structures identified on NCCT images. qER-Quant provides volumes from NCCT images acquired at a single time point and provides a table with comparative analysis for two or more images that were acquired on the same scanner with the same image acquisition protocol for the same individual at multiple time points. The qER-Quant software is indicated for use in the analysis of the following structures: Abnormal Intracranial Hyperdensities, Lateral Ventricles and Midline Shift.	The Icobrain device is intended for automatic labeling, visualization and volumetric quantification of segmentable brain structures 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.
Technological Characteristics	- Software package - Operates on off-the-shelf hardware (multiple vendors) - DICOM compatible - Segmentation by deep learning (supervised voxel classification with Convolutional Neural Networks)	- Software package - Operates on off-the-shelf hardware (multiple vendors) - DICOM compatible - Segmentation by classical machine learning and deep learning (supervised voxel classification with Convolutional Neural Networks)
Output	Multiple electronic reports with volumetric information of brain structures and midline shift AND Annotated DICOM Images	Multiple electronic reports with volumetric information of brain structures and midline shift AND Annotated DICOM Images
Reference Standard for Performance testing	<u>Accuracy</u> Manually labeled images for all structures <u>Reproducibility</u>	<u>Accuracy</u> Manually labelled or simulated ground truth for MRI images Manually labeled images (lesions and midline shift) and images labeled by previously cleared Icobrain MRI software for CT images (lateral ventricles and whole brain) <u>Reproducibility</u>

	qER-Quant Device Subject Device	Predicate Device
	Test-retest images	MRI measurement changes compared on test-retest images; simulation study used for CT measurements
Comparison of Differences between qER-Quant and the predicate device		
Input Images	Non-contrast CT from a single or multiple time points	T1-weighted and fluid-attenuated inversion recovery (FLAIR) MR images from a single or multiple time points and/or Non-contrast CT from a single time point
Target structures analyzed on NCCT scans	Intracranial hyperdensities, lateral ventricles and midline shift	Intracranial hyperdensities, lateral ventricles, basal cisterns and midline shift

1.6 Testing

Software

Software verification and validation testing were conducted and documentation was provided as recommended by FDA's Guidance for Industry and FDA Staff, "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices." The software for this device has a Moderate level of concern.

Performance Testing

Qure.ai performed standalone consisted of a set of head CT scans with the outlines of the target structures manually labeled by experts. Volume or shift measurement accuracy and segmentation accuracy were reported for the target structures. Reproducibility testing was performed using 20% of these CT scans, labeled similarly, with accuracy measured using similar metrics. For all target structures, the standalone performance exceeded the preset acceptance criteria. The table below shows a summary of the results of performance testing.

Table 2: Results of performance testing

	Absolute error versus ground truth (volume in ml or shift in mm)		Dice Score
Structure (Number of Scans)	Mean (Standard Deviation)	Median (10th - 90th percentile)	Mean (95% confidence interval)
Intracranial Hyperdensity (183)	6.56 (7.33) ml	3.98 (0.52 - 17.35) ml	0.75 (0.72 - 0.78)
Midline Shift (188)	1.37 (1.23) mm	1.15 (0.23 - 2.59) mm	Not applicable

Left Lateral Ventricle (210)	2.09 (1.88) ml	1.60 (0.29 - 4.24) ml	0.79 (0.78 - 0.81)
Right Lateral Ventricle (210)	2.18 (1.72) ml	1.88 (0.40 - 4.53) ml	0.75 (0.73 - 0.77)

qER-Quant also passed software validation and system verification checks.

1.7 Conclusion

The comparison in Table 1 and the software and performance testing presented above demonstrate that the qER-Quant device is substantially equivalent to the predicate device.