icometrix NV
Jan Verheyden
VP
Kolonel Begaultlaan 1b/12
Leuven, 3012
BELGIUM

November 6, 2018

Re: K181939
Trade/Device Name: icobrain
Regulation Number: 21 CFR 892.2050
Regulation Name: Picture Archiving And Communications System
Regulatory Class: Class II
Product Code: LLZ
Dated: October 3, 2018
Received: October 3, 2018

Dear Jan Verheyden:

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/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm); 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 http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). 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 (http://www.fda.gov/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

Robert A. Ochs, Ph.D.
Director
Division of Radiological Health
Office of In Vitro Diagnostics
and Radiological Health
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)*
K181939

Device Name
icobrain

Indications for Use *(Describe)*
icobrain 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.

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.

Doc. 1348731 99.21 (/display/MSMET/CT_Section+5.+510%28k%29+Summary), 2018-10-09 14:56 UTC

5.1 Submitter

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Address:	Kolonel Begaultlaan 1b/12 3012 Leuven Belgium
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E-mail:	jan.verheyden@icometrix.com
Date Prepared:	10 Sep 2018

5.2 Device

Device Trade Name:	ico**brain**
Common Name	Medical Image Processing Software
Classification Name	System, Image processing, Radiological
Number	892.2050
Product Code:	LLZ
Classification Panel:	Radiology

5.3 Predicate Device

Device	ico**brain**
510(k) Number	K180326
Manufacturer	ico**metrix** NV

5.4 Intended Use

ico**brain** 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.

ico**brain** consists of two distinct image processing pipelines: ico**brain** cross and ico**brain** long.

- ico**brain** cross is intended to provide volumes from MR or NCCT images acquired at a single time point.
- ico**brain** 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 ico**brain** cross cannot be compared with the results of ico**brain** long.

5.5 Device Description

The following flowchart illustrates the overall architecture of ico**brain.**

The input images can be MR images (current ico**brain** software - K161148 and K180326) or CT images. During the pre-processing, the modality and/or sequence of each scan is detected and each scan is converted from DICOM format to NIFTI format. The image processing then performs the actual segmentation and calculates the measurements of the brain structures and abnormalities. Finally, the computed measurements are summarized into an electronic report and (some) segmentations are overlaid on the input images, generating output images in DICOM format.

Since the processing of MR images remains unchanged compared to the currently approved ico**brain** software (see K161148 and K180326), the remainder of this file will focus on the design of the software that processes CT images. We refer to the overall architecture focused on (pre)processing CT images as the CT pipeline.

outputs of CT pipeline

Report 1:

- normalized volume of the whole brain (sum of white and grey matter)
- normalized volume of the lateral ventricles

This report is useful to be applied in (potential) dementia patients.

Report 2:

- measurement of the midline shift, i.e. the shift of the brain past its center line.
- normalized volume of basal cisterns (suprasellar, quadrigeminal, prepontine)
- volume (total, highest) of hyperdensities

This report is useful to be applied in (potential) TBI patients.

5.6 Comparison with predicate device

Likewise our clinical product ico**brain** 3.0 (K180326), ico**brain** 4.0 intends for automatic labeling, visualization and volumetric quantification of segmentable brain structures based on 3-dimensional medical images. The devices both take 3D images of the brain as input and generate an electronic report with similar quantitative information.The main difference is that icobrain 4.0 will use CT images in addition to MR images to start from. The table below compares the device to market with the proposed predicate device. The main differences are underlined.

	Predicate device	**Device to market**
Device Trade Name	ico**brain**	ico**brain**
Version	3.0	4.0
Common Name	Medical Image Processing Software	Medical Image Processing Software
510(k) Number	K180326	
Manufacturer	ico**metrix** NV Kolonel Begaultlaan 1b / 12 3012 Leuven BELGIUM	ico**metrix** NV Kolonel Begaultlaan 1b / 12 3012 Leuven BELGIUM
Regulation Number	21 CFR 892.2050	21 CFR 892.2050
Device Classification Name	System, Image processing, Radiological	System, Image processing, Radiological
Product Code	LLZ	LLZ
Regulatory Class	II	II
Classification Panel	Radiology	Radiology
Function	Automatically identifying and quantifying the volumes of brain segmentable structures, automatic labeling and visualization.	Automatically identifying and quantifying the volumes of brain segmentable structures, automatic labeling and visualization.

Intended use	ico**brain** is intended for automatic labeling, visualization and volumetric quantification of segmentable brain structures from a set of MR 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 images. ico**brain** consists of two distinct image processing pipelines: ico**brain** cross and ico**brain** long. • ico**brain** cross is intended to provide volumes from images acquired at a single timepoint. • ico**brain** long is intended to provide changes in volumes between two 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 ico**brain** cross cannot be compared with the results of ico**brain** long.	ico**brain** 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. ico**brain** consists of two distinct image processing pipelines: ico**brain** cross and ico**brain** long. • ico**brain** cross is intended to provide volumes from MR or NCCT images acquired at a single time point. • ico**brain** 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 ico**brain** cross cannot be compared with the results of ico**brain** long.

Technical characteristics	• Software package
	• Operates on off-the-shelf hardware (multiple vendors)
	• DICOM compatible
	• segmentation by classical machine learning (unsupervised voxel classication with Gaussian Mixture Models)
	• Input: T1-weighted and fluid-attenuated inversion recovery (FLAIR) MR images from a single or multiple time points
	• Output:
	  • multiple electronic reports with volumetric information of brain structures
	  • annotated DICOM images
		• Software package
		• Operates on off-the-shelf hardware (multiple vendors)
		• DICOM compatible
		• segmentation by classical machine learning and deep learning (in our case supervised voxel classication with Convolutional Neural Networks)
		• Input:
		  • T1-weighted and fluid-attenuated inversion recovery (FLAIR) MR images from a single or multiple time points
		  • non-contrast CT from a single time point
		• Output:
		  • multiple electronic reports with volumetric information of brain structures and midline shift
		  • annotated DICOM images

Performance measurement testing	**Accuracy**
	• brain segmentable structure volumes / volume changes compared to simulated and/or manually labeled ground truth
	
	Reproducibility
	• brain segmentable structure volumes / volume changes compared on test-retest images
		Accuracy
		• MR measurements
		  • brain segmentable structure volumes / volume changes compared to simulated and/or manually labeled ground truth
		• CT measurements
		  • lesions and midline shift: compared to manually labeled ground truth
		  • lateral ventricles and whole brain: MR images segmented by cleared ico**brain** 3.0 software taken as ground truth
		
		Reproducibility
		• MR measurements
		  • brain segmentable structure volumes / volume changes compared on test-retest images
		• CT measurements
		  • simulation study

Environment of use	ico**brain** is used by trained professionals in hospitals, imaging centers or in image processing labs.	ico**brain** is used by trained professionals in hospitals, imaging centers or in image processing labs.
Testing	• Product Risk Assessment • Software verification tests • Software validation tests	• Product Risk Assessment • Software verification tests • Software validation tests

5.7 Performance testing

To demonstrate the performance of the CT pipeline of ico**brain** 4.0, the measurements are validated for accuracy and reproducibility. The subjects upon whom the CT software was tested include TBI patients and potential dementia patients.

In the accuracy experiments, the lesions, basal cisterns, lateral ventricles and midline shift are compared

to manually segmented ground truth, while the lateral ventricles and whole brain volumes are compared to MR images segmented by the cleared ico**brain** 3.0 software. Reproducibility was also tested on CT images produced in the same scanning session. Literature review has been performed to set relevant acceptance criteria for each type of experiment. All experiments passed the acceptance criteria.

The experiments encompassed **544** subject datasets in total. Averaged over all experiments, the Pearson correlation coefficient between the compared measurements was **0.95** and the intraclass correlation coefficient was **0.94**.

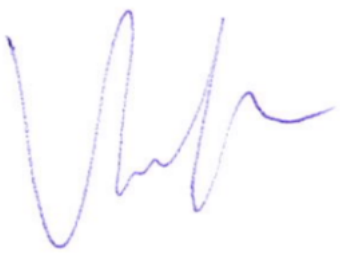
Besides the verification experiments, validation tests demonstrate the system as a whole provides all the capabilities necessary to operate according to its intended use.

5.8 Conclusions

The performance testing presented above establishes that the ico**brain** is safe and effective for its intended use. The comparison above demonstrates that the ico**brain** device is substantially equivalent to the predicate device.

Declarations:	• This summary includes only information that is also covered in the body of the 510(k). • This summary does not contain any puffery or unsubstantiated labeling claims. • This summary does not contain any raw data, i.e., contains only summary data. • This summary does not contain any trade secret or confidential commercial information. • This summary does not contain any patient identification information.

This document is reviewed and approved by Jan Verheyden, Vice President Traumatic Brain Injury of ico **metrix**, based on the present data and information.

Signature	Date
	01 Oct 2018