icometrix NV
℅ Dirk Smeets
VP Clinical Applications
Kolonel Begaultlaan 1b/12
3012 Leuven, Vlaams-Brabant
BELGIUM

December 13, 2019

Re: K192130
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 10, 2019
Received: October 15, 2019

Dear Dirk Smeets:

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: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*

K192130

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.

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.

The burden time for this collection of information is estimated to average 79 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

K192130

icometrix
IMAGING BIOMARKER EXPERTS

Section 6. 510(k) Summary (icobrain 5.0)

icometrix NV - Kolonel Begaultlaan 1b box 12 - 3012 Leuven - Belgium
info@icometrix.com - www.icometrix.com - T +32 16 369 000
IBAN: BE02 7360 2208 4540 - BIC KRED BE BB - BTW/VAT BE 0833.377.379

6.1 Submitter

Name:	ico**metrix** NV
Address:	Kolonel Begaultlaan 1b / 12 3012 Leuven BELGIUM
Contact Person:	Dirk Smeets
Telephone number:	+32 16 369 000
Fax Number:	N.A.
E-mail:	dirk.smeets@icometrix.com
Date Prepared:	18 Jul 2019

6.2 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

6.3 Predicate Device

Device	ico**brain**
510(k) Number	K181939
Manufacturer	ico**metrix** NV
Common Name:	Medical Image Processing Software
Classification Name:	System, Image processing, Radiological
Number	892.2050
Product Code	LLZ
Classification Panel:	Radiology

6.4 Device Description

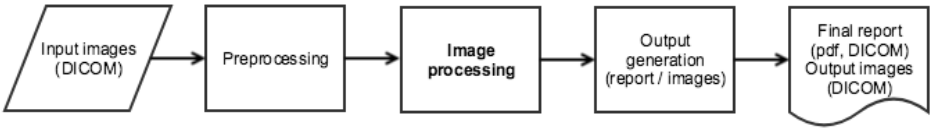
ico**brain** is intended for automatic labeling, visualization and volumetric quantification of segmentable brain structures from a set of MR or NCCT images. This software is intended to automate the current manual process of identifying, labeling and quantifying the volume of segmentable brain structures 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.

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 (current ico**brain** software - K181939). During the pre-processing, 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.

MR outputs

Report 1:

- unnormalized volume and volume changes (total, new, enlarging and shrinking) of FLAIR white matter hyperintensities, in different regions (peri-ventricular, juxta-cortical, infra-tentorial, deep white matter).
- unnormalized volume and volume changes (total, new, enlarging and shrinking) of T1 white matter hyperintensities and hypointensities.
- normalized volume and volume changes of the whole brain (sum of white and gray matter),
- normalized volume and volume changes of gray matter

Report 2:

- normalized volume and volume changes of the frontal, temporal and parietal lobe
- normalized volume and volume changes of the hippocampi
- unnormalized volume and volume changes of FLAIR white matter hyperintensities

Report 3:

- unnormalized volume and volume changes (total, new, enlarging and shrinking) of FLAIR white matter hyperintensities, in different regions (sub-cortical, corpus callosum, brainstem)
- normalized volume and volume changes of the cortical gray matter
- normalized volume and volume changes of the hippocampi

Report 4:

- unnormalized volume and volume changes (total, new, enlarging and shrinking) of juxtacortical FLAIR white matter hyperintensities
- normalized volume and volume changes of the left and right hippocampi
- asymmetry index between the left and right hippocampi

The whole brain, gray matter, cortical gray matter, frontal lobe, temporal lobe, parietal lobe and hippocampal volumes are normalized for head size by comparing to a healthy population using a statistical model. Asymmetry index between the left and right hippocampi is also compared to a healthy population. The reported FLAIR or T1 white matter hyperintensities or hypointensities volumes are not normalized since they are not comparable to a reference population.

CT outputs

Report 1:

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

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

Report 2:

- unnormalized measurement of the midline shift, i.e. the shift of the brain past its center line
- unnormalized volumes of NCCT hyperdensities (epidural, subdural, intraparenchymal and their total); and largest hyperdensity component
- normalized volumes of the left and right lateral ventricles, and of the fourth ventricle
- normalized volumes of basal cisterns (suprasellar, quadrigeminal, prepontine & ambient)
- asymmetry index between the left and right lateral ventricle

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

The whole brain, ventricles and cisterns volumes are normalized for head size by comparing to a healthy population using a statistical model. The reported CT hyperdensities volumes are not normalized since they are not comparable to a reference population.

6.5 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.

*This intended use of the modified device is **equal** to the intended use of the previously cleared predicate device [K181939].*

6.6 Device modifications

ico**brain** 5.0 is an update of the ico**brain** 4.0 (the predicate device). The modifications of the device mostly include new measurements of brain segmentable structures, new output reports, new output images, and new output format.

New measurements:

- normalized volume and volume changes of the the left and right hippocampi,
- unnormalized volumes of NCCT hyperdensities in different regions (epidural, subdural, intraparenchymal and their total); and largest hyperdensity component,
- normalized volumes of the left and right lateral ventricles, and of the fourth ventricle.

These new measurements, together with the original measurements, are now included in the previously available report types, as well as a new report type for MR input.

New output images include:

- the segmentation of NCCT hyperdensities, color-coded for the region and overlaid on the input NCCT image,
- the segmentation of the left and right lateral ventricles, and of the fourth ventricle, overlaid on the input NCCT image.

New output formats:

- DICOM structured report representation of a natural language report
- DICOM encapsulated PDF representation of a natural language report

6.7 Performance testing

Quality and safety

ico**brain** has been designed, developed and tested in accordance with the following product and process standards:

- ISO 14971:2007 Medical devices - Application of risk management to medical devices
- IEC 62304:2006 Medical device software - Software life-cycle processes

- IEC 62366:2014 Medical devices - Application of usability engineering to medical devices
- ISO 12052:2006 Digital imaging and communication in medicine (DICOM)
- CFR 21 part 820 Quality System Regulation for Medical Devices
- ISO 13485:2016 Medical devices - Quality management systems

The changes made in ico**brain** compared to the original device do not affect the safety of the device. This conclusion is based on:

- Failure mode and effects analysis on the added functionality.
- Risk category classification of new software components.

Product performance

To demonstrate the performance of ico**brain**, the measured volumes and volume changes of the segmentable brain structures are validated for accuracy and reproducibility. The subjects upon whom the device was tested include healthy subjects, Alzheimer's disease patients, multiple sclerosis patients, traumatic brain injury patients, depression patients.

In the accuracy experiments, the volumes / volume changes are compared to simulated and/or manually labeled ground truth volumes / volume changes; in the reproducibility experiments, the volumes / volume changes are compared on test-retest image data sets. A literature review has been performed to set relevant acceptance criteria for each type of experiment. The acceptance criteria were based on the 90^{th} percentile of the absolute differences in comparison to the validation threshold. All experiments passed the acceptance criteria.

The experiments encompassed 463 MR and 618 CT subject datasets in total. Averaged over all MR experiments, the Pearson correlation coefficient between the compared measurements was 0.91 and the intraclass correlation coefficient was 0.90. Averaged over all CT experiments, the Pearson correlation coefficient between the compared measurements was 0.94 and the intraclass correlation coefficient was 0.93.

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

6.8 Conclusions

Because of the identical intended use same and technological characteristics, ico**brain** 5.0 is substantially equivalent to a device (ico**brain** 4.0) that has been approved in the United States. The performance testing demonstrates that ico**brain** 5.0 is as safe and effective as 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 Dirk Smeets, Vice President Clinical Applications of ico **metrix**, based on the present data and information.

Signature	Date
	26 Jul 2019