



March 8, 2018

icomatrix NV  
% Dirk Smeets  
VP Clinical Applications  
Kolonel Begaultlaan 1b /12  
Leuven, 3012  
BELGIUM

Re: K180326

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: February 2, 2018  
Received: February 6, 2018

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. 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); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820);

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 the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

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](mailto:DICE@fda.hhs.gov)) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

A handwritten signature in black ink that reads "Robert A. Ochs". The signature is written in a cursive style. In the background, there is a large, light blue watermark of the letters "FDA".

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

**Indications for Use**

510(k) Number (if known)

K180326

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 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.

icobrain consists of two distinct image processing pipelines: icobrain cross and icobrain long.

icobrain cross is intended to provide volumes from images acquired at a single timepoint

icobrain 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 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.**

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## I Submitter

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Date Prepared:	 01 Feb 2018

## 2 Device

Device Trade Name:	icob <b>rain</b>
Common Name:	Medical Image Processing Software
Classification Name:	System, Image processing, Radiological
Number	892.2050
Product Code:	LLZ
Classification Panel:	Radiology

### 3 Predicate Device

Device	icobrain
510(k) Number	K161148
Manufacturer	icomatrix NV
Common Name:	Medical Image Processing Software
Classification Name:	System, Image processing, Radiological
Number	892.2050
Product Code	LLZ
Classification Panel:	Radiology

### 4 Device Description

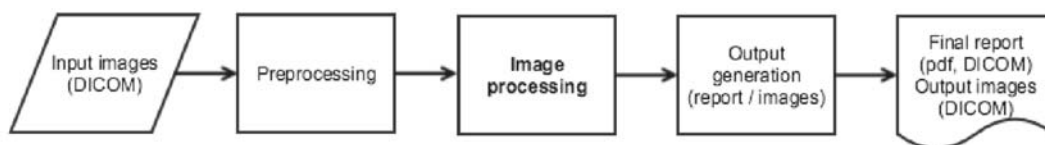
icobrain is intended for automatic labeling, visualization and volumetric quantification of segmentable brain structures from a set of MR images. This software is intended to automate the current manual process of identifying, labeling and quantifying the volume of segmentable brain structures identified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

icobrain consists of two distinct image processing pipelines: icobrain cross and icobrain long.

- icobrain cross is intended to provide volumes from images acquired at a single timepoint
- icobrain 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 icobrain cross cannot be compared with the results of icobrain long.

The following flowchart illustrates the overall architecture of icobrain.



As input, icobrain uses T1-weighted and a fluid-attenuated inversion recovery (FLAIR) DICOM MR images from a single or from multiple time points. In case of multiple time points, i.e. multiple MRI scans from the same subject, for each time point one FLAIR and one T1 image are used as input. During the pre-processing, the scan type (T1, FLAIR) is detected for every input image before it is converted from DICOM format to NIFTI format. The image processing then performs the actual segmentation and

calculates the volumes of the brain structures. In case MRI scans from the same subject on multiple time points are available, the changes in volume of the brain structures are calculated as well. Finally, the computed volumes and volume changes (in case of multiple time points) are summarized into an electronic report and (some) segmentations are overlaid on the input images.

The software displays the following volumetric measures in three reports

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 grey matter),
- normalized volume and volume changes of grey 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

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. The reported FLAIR or T1 white matter hyperintensities or hypointensities volumes are not normalized since they are not comparable to a reference population.

## 5 Intended use

**icobrain** 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.

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

- icobrain cross is intended to provide volumes from images acquired at a single timepoint
- icobrain 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 icobrain cross cannot be compared with the results of icobrain long.

*This intended use of the modified device is **equal** to the intended use of the previously cleared predicate device [K161148].*

## 6 Device modifications

**icobrain** 3.0 is an update of the **icobrain** 1.3 (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 (json).

New measurements:

- 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, sub-cortical, corpus callosum, brainstem),
- unnormalized volume and volume changes (total, new, enlarging and shrinking) of T1 white matter hyperintensities and hypointensities,
- normalized volume and volume changes of the frontal, temporal and parietal lobe,
- normalized volume and volume changes of the hippocampi,
- normalized volume and volume changes of the cortical gray matter,
- normalized volume and volume changes of the hippocampi.

These new measurements, together with the original measurements, are now structured in three different report types.

New output images include:

- the segmentation of FLAIR WM hyperintensities, color-coded for the region and overlaid on the input FLAIR images,
- the segmentation of new and enlarging FLAIR WM hyperintensities, overlaid on the input FLAIR images,
- the segmentation of frontal, temporal and parietal lobe and the hippocampi, overlaid on the input T1 images.

## 7 Performance testing

### Quality and safety

**icobrain** 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 **icobrain** 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 **icobrain**, 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. All experiments passed the acceptance criteria.

The experiments encompassed 463 subject datasets in total. Averaged over all experiments, the Pearson correlation coefficient between the compared measurements was 0.91 and the intraclass correlation coefficient was 0.89.



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

## 8 Conclusions

Because of the identical intended use same and technological characteristics, icobrain 3.0 is substantially equivalent to a device (icobrain 1.3) that has been approved in the United States. The performance testing demonstrates that icobrain 3.0 is as safe and effective as the predicate device.

Declarations:	<ul style="list-style-type: none"><li>• This summary includes only information that is also covered in the body of the 510(k).</li><li>• This summary does not contain any puffery or unsubstantiated labeling claims.</li><li>• This summary does not contain any raw data, i.e., contains only summary data.</li><li>• This summary does not contain any trade secret or confidential commercial information.</li><li>• This summary does not contain any patient identification information.</li></ul>
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This document is reviewed and approved by Dirk Smeets, Vice President Clinical Applications of icometrix, based on the present data and information.

Signature 	Date  08 Mar 2018
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