BrainNow Medical Technology Limited
℅ You Yijie
General Manager
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CHINA

January 15, 2021

Re: K202847
Trade/Device Name: AccuBrain
Regulation Number: 21 CFR 892.2050
Regulation Name: Picture archiving and communications system
Regulatory Class: Class II
Product Code: LLZ
Dated: September 11, 2020
Received: December 11, 2020

Dear You Yijie:

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)*
K202847

Device Name
AccuBrain

Indications for Use *(Describe)*
AccuBrain is a fully automated post-processing software that provides automatic labeling, visualization and volumetric quantification of hippocampus from a set of MRIs and returns an analysis report.

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

"510(k) Summary" as required by 21 CFR Part 807.92.

1. Submitter's Information

Establishment Registration Information

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Date to prepare: 9/11/2020

2. Device Information

Device Name: AccuBrain
Common Name: Neuroimage Analysis Software
Model: AccuBrain_Intl
Software version: V1.0.0.200703
Classification Name: System, Image Processing, Radiological
Regulation Number: 21 CFR 892.2050
Regulation Description: Picture archiving and communications system
Product Code: LLZ
Classification Panel: Radiology
Regulation Class: II

3. Predicate Device Information

Item	Primary Predicate(A)	Predicate or Reference Device (B)
510(k) submitter/holder	CorTechs Labs, Inc	Brainreader Aps
510(K) Number	K170981	K140828
Device name	NeuroQuant	NeuroReader Medical Image Processing Software
Common name	Medical Image Processing Software	Neuroreader

Regulation Description	Picture archiving and communications system	Picture archiving and communication system
Review panel	Radiology	Radiology
Product code	LLZ	LLZ, LNH
Regulation Class	Class II	Class II
Regulation Number	21 CFR 892.2050	21 CFR 892.2050

4. Device Description

AccuBrain is a fully automated post-processing software that provides automatic labeling, visualization and volumetric quantification of hippocampus from a set of T1W MRIs and returns an analysis report. The resulting output is a morphometric report in PDF format. The software is suitable for use in both clinical trial research and routine patient care as a support tool for clinicians in assessment of structural MRIs.

AccuBrain provides morphometric measurements based on 3D T1 MRI series. The output of the software includes volumes of hippocampus.

The AccuBrain processing architecture includes an automated internal pipeline that performs artifact correction, segmentation, hippocampus quantification, volume calculation and report generation.

Additionally, automated safety measures include automated quality control functions, such as DICOM check, age check and image resolution check and image quality check.

5. Principle of operation

AccuBrain automatically segmented the subject's hippocampi using the uploaded T1W MRIs in a multi-atlas-based segmentation manner. The quantification and visualization of hippocampal segmentation results were output in the form of a morphometric analysis report.

The hippocampal segmentation procedure is described as follows. 1) Pre-processing to increase the image quality, including noise reduction, bias field correction, and intensity normalization to normalize intensity level of MRIs from different scanners. For noise reduction method, we used non-local mean filtering method [1]. Bias correction method used in AccuBrain is N4 bias correction [2]. Intensity Normalization method used in AccuBrain is histogram matching [3]. 2) Atlas selection. The atlas pool, consisting of 300 brain MRIs together with their segmentation labels, were previously obtained from different individuals using different scanners and have highly variable appearances. Each atlas contains both brain MRI and the prior encoded radiologist-specified anatomy information for hippocampus. The detailed of demographic information about the atlas data was described in Table 1. During processing, AccuBrain selects a number of brain images from the atlas pool based on similarity with the subject images. The similarity measures used in this step is Normalized Cross correlation (NCC). AccuBrain will select 10 images from the atlas pool with highest NCC scores. 3) Image segmentation. The non-rigid image registration is performed to match the selected image with the subject image. The resulting transformation field will be applied to transform the predefined atlas label to the subject image. As 10 template images are selected, 10 segmentation results are obtained and will be merged using STAPLE label fusion method [4] to fuse the final segmentation labels of the subject image.

Table 1. Demographic information of the atlas data

Demographic Categories	Frequency (subject number)	Percentage(%)
Gender		
Female	151	50.3
Male	149	49.7
Disease Status		
AD	123	41
NC	115	38.3
MCI	62	20.7
Age		
51-60	25	8.3
61-70	96	32
71-80	118	39.3
81-90	61	20.3
Magnetic Field Strength		
1.5T	68	22.7
3T	232	77.3
Manufacturer		
GE	131	43.7
Philips	44	14.7
Siemens	125	41.7
In-plane resolution		
1x1	214	71.3
0.9375x0.9375	84	28
0.8594x0.8594	2	0.7
FOV (mm^2)		
220	2	0.7
230	135	45
240	84	28
256	79	26.3
Slice Thickness(mm)		
1	216	72
1.2	84	28

6. Indications for Use

AccuBrain is a fully automated post-processing software that provides automatic labeling, visualization and volumetric quantification of hippocampus from a set of T1W MRIs and returns an analysis report.

7. Comparison of Predicate Devices

Summary Comparison Table for the subject device and predicate devices (K170981 and K140828):

Comparison Elements	Subject Device	Predicate Device（A）	Predicate or Reference Device (B)	Discussion of difference
Device Name	AccuBrain	NeuroQuant	NeuroReader	/
510(k) No	/	K170981	K140828	/

Regulation No	21 CFR 892.2050	21 CFR 892.2050	21 CFR 892.2050	Same
Regulation Description	“Picture archiving and communications system”	“Picture archiving and communications system”	“Picture archiving and communications system”	Same
Classification name	System, Image Processing, Radiological	System, Image Processing, Radiological	System, Image Processing, Radiological	Same
Classification	Class II	Class II	Class II	Same
Product code	LLZ	LLZ	LLZ	Same
Indications for use	AccuBrain is a fully automated post-processing software that provides automatic labeling, visualization and volumetric quantification of hippocampus from a set of T1W MRIs and returns an analysis report.	Automatic labeling, visualization and volumetric quantification of segmentable brain structures and lesions from a set of MR images. Volumetric data may be compared to reference percentile data	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.	SE-within the predicate Both are indicated to automatic labeling, visualization and volumetric quantification of hippocampus from a set of T1W MRIs Is and returns an analysis report.
Design and incorporated technology	• Automated measurement of hippocampus volumes • Automatic atlas-based segmentation and quantification of hippocampus using an atlas pool consisting of difference	• Automated measurement of brain tissue volumes and structures and lesions • Automatic segmentation and quantification of brain structures using a dynamic probabilistic	Information not publicly available	SE Both are indicated to automate measurement of hippocampus volumes through automatic atlas-based segmentation and quantification of hippocampus base on an atlas pool consisting of difference template

	template images with highly variable appearance together with their prior encoded radiologist-specified anatomy information	neuroanatomical atlas, with age and gender specificity, based on the MR image intensity		images with highly variable appearance together with their prior encoded radiologist-specified anatomy information. The difference does not affect the determination of substantial equivalence.
Physical characteristics	• Web-based application • Operates on off-the -shelf hardware (multiple vendors)	• Software package • Operates on off-the-shelf hardware (multiple vendors)	Information not publicly available	SE The Cybersecurity of Subject Device was verified (Cybersecurity Information Document, section 005). And the Subject Device was verified according to the ANSI AAMI IEC 62304:2006/A1:2016 (section 004) and the Accuracy and Reproducibility of the Subject Device was verified (section 006). The difference does not affect the determination of substantial equivalence.
Operating system	Supports Windows	Supports Linux, Mac OS X and Windows.	Information not publicly available	SE--within the predicate. The Operating system of Subject Device is fewer than Predicate Device (A), the risk of the Subject Device is fewer than Predicate Device (A). And the Subject Device was verified

				according to the ANSI AAMI IEC 62304:2006/A1:2016 (Software Documentation, section 004) and the Accuracy and Reproducibility of the Subject Device was verified (section 006). The difference does not affect the determination of substantial equivalence.
Processing architecture	Automated internal pipeline that performs: -artifact correction -segmentation -hippocampus quantification -volume calculation -report generation	Automated internal pipeline that performs: -artifact correction -segmentation -lesion quantification -volume calculation -report generation	Information not publicly available	SE-within the predicate Both are performed: -artifact correction -segmentation -hippocampus quantification -volume calculation -report generation The difference does not affect the determination of substantial equivalence.
Data source	• MRI scanner: 3D T1 MRI scans acquired with specified protocols • AccuBrain supports DICOM format as input	• MRI scanner: 3D T1 MRI scans acquired with specified protocols • NeuroQuant supports DICOM format as input	Information not publicly available	Same
Output	-Provides volumetric	▪ Provides volumetric measurements	Information not publicly available	SE-within the predicate

	measurements of hippocampus -Includes segmented color overlays and an analysis report (just volumetric of the hippocampus)	of brain structures and lesions ▪ Includes segmented color overlays and morphometric reports ▪ Automatically compares results to reference percentile data and to prior scans when available ▪ Supports DICOM format as output of results that can be displayed on DICOM workstations and Picture Archive and Communications Systems		Both provide volumetric measurements of hippocampus -Includes segmented color overlays and an analysis report including the volumetric of the hippocampus. The difference does not affect the determination of substantial equivalence.
Accuracy	The mean DICE of AccuBrain results and manual segmentation results is 0.89, 0.89 and 0.89 for right, left and total hippocampus, respectively.	For major subcortical brain structures Dice's coefficients are in the range of 80%-90%.	NeuroReader can segment the hippocampus with a Dice similarity index of 0.87 for both the right and left hippocampus.	SE The accuracy and reproducibility of hippocampus segmentation of AccuBrain with T1W MRI images are comparable with Predicate Device（A）and Predicate Device（B）. The accuracy and reproducibility of Subject Device was verified (Accuracy and Reproducibility Test Report, section 006).

				The difference does not affect the determination of substantial equivalence.
Safety	• Automated quality control functions - DICOM check - Age check - Image resolution check - Image quality check Diagnostic decisions should be made by trained clinicians.	• Automated quality control functions - Tissue contrast check - Scan protocol verification - Atlas alignment check • Results must be reviewed by a trained physician	Information not publicly available	SE Both are conducted the - DICOM check, Age check, Image resolution check, Image quality check. The Cybersecurity of Subject Device was verified (Cybersecurity Information Document, section 005). And the Subject Device was verified according to the IEC 62304(Software Documentation, section 004) and the Accuracy and Reproducibility of the Subject Device was verified (Accuracy and Reproducibility test report, section 006). The difference does not affect the determination of substantial equivalence.

Subject device and predicate devices are softwares for automatically identifying and quantifying volumes of brain structures. Subject and predicate devices take 3D MR images of the brain as input and generate electronic report with similar quantitative information.
AccurBrain and NeuroQuant achieve the intended use based on similar principle and processing architecture, since the quantification systems implement brain segmentation and quantification using atlas-based segmentation scheme. Both hippocampi are segmented and the volumes are calculated.

AccurBrain and NeuroQuant are DICOM compatible and operate on off-the-shelf hardware. Meanwhile, both devices are used by medical professional, such as radiologists, neurologists and neuroradiologists, as well as by clinical researchers, as a support tool in assessment of structural MRIs.
The output volumes which both devices provide include volumes of left hippocampus, right hippocampus and whole hippocampi.

8. Performance Testing

To demonstrate the performance of AccuBrain (model: AccuBrain_Intl), the measured volumes and volume differences of hippocampus are validated for accuracy and reproducibility. The subjects upon whom the device was tested include healthy subjects, Alzheimer's disease patients and Mild Cognitive Impairment patients. AccuBrain segmentation accuracy with 3D T1 MRI scans was evaluated using Dice coefficient metric. With 135 data provided by the EADC-ADNI HarP, the mean Dice coefficient by comparing AccuBrain results and manual segmentation results was 0.89 (std: 0.03), 0.89 (std: 0.03) and 0.89 (std: 0.03) for right, left and total hippocampal volumes, respectively. Segmentation reproducibility of repeated 3D T1 MRI scans for the same subjects was evaluated using Coefficient of Variation (CV). The mean intra-scanner CV values were 3.20% and 1.23%, the mean percentage absolute volume differences DIFF values were 4.52% and 1.74% for left and right hippocampus, respectively. Compared with the performances of the predicate devices, the results presented above shows that the subject device is safe and effective and performs as well as the predicate devices. The AccuBrain (Model: AccuBrain_Intl) was designed, verified, and validated according to the company's Design Control process and has been subjected to extensive safety and performance testing as shown in the test results provided in this submission. Verification and Validation testing data demonstrate that the device meets all of its specifications.

The Accuracy and Reproducibility of AccuBrain (Model: AccuBrain_Intl) was verified please see section 006 for the Accuracy and Reproducibility Test Report.
The software of AccuBrain (Model: AccuBrain_Intl) was verified according to the ANSI AAMI IEC 62304:2006/A1:2016 Medical device software - Software life cycle processes [Including Amendment 1 (2016)]. Please see section 004 for the Software Documentation.
The Cybersecurity of AccuBrain (Model: AccuBrain_Intl) was verified. Please see section 005 for the Cybersecurity Information Document.

During the verification and validation activity the following guidance documents were used:
General Principles of Software Validation: Guidance for Industry and FDA Staff
Postmarket Management of Cybersecurity in Medical Devices: Guidance for Industry and Food and Drug Administration Staff
Content of Premarket Submissions for Management of Cybersecurity in Medical Devices: Draft Guidance for Industry and Food and Drug Administration Staff
Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices: Guidance for Industry and FDA Staff

9. Conclusions

The performance testing presented above shows that the device is as safe, as effective and performs as well as the predicate devices(A) and predicate devices(B),

and as well as gold standard-computer-aided expert manual segmentation. By virtue of the physical characteristics and intended user, AccuBrain(AccuBrain_Intl) is substantially equivalent to its predicate devices (A) (K170981) and predicate devices (B)(K140828).

10. Bibliography

[1] Coll, Bartomeu & Morel, Jean-Michel. (2005). A non-local algorithm for image denoising. Proceedings of the IEEE Computer Society Conference on Computer Vision and Pattern Recognition. 2. 60- 65 vol. 2.

[2] Tustison NJ, Avants BB, Cook PA, et al. N4ITK: improved N3 bias correction. IEEE Trans Med Imaging. 2010;29(6):1310-1320.

[3] Laszlo G. Nyul, Jayaram K. Udupa, and Xuan Zhang, "New Variants of a Method of MRI Scale Standardization", IEEE Transactions on Medical Imaging, 19(2):143-150, 2000.

[4] Warfield SK, et al. Simultaneous truth and performance level estimation (STAPLE): an algorithm for the validation of image segmentation. Medical Imaging, IEEE Transactions on. 2004;23:903–921.