May 10, 2023

NEUROPHET, Inc.
% Priscilla Chung
Regulatory Affairs Consultant
LK Consulting Group USA, Inc.
18881 Von Karman Ave. STE 160
IRVINE CA 92612

Re: K220437
Trade/Device Name: Neurophet AQUA
Regulation Number: 21 CFR 892.2050
Regulation Name: Medical image management and processing system
Regulatory Class: Class II
Product Code: LLZ
Dated: March 30, 2023
Received: March 31, 2023

Dear Priscilla Chung:

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,

Daniel M. Krainak, Ph.D.
Assistant Director
Magnetic Resonance and Nuclear Medicine Team
DHT8C: Division of Radiological Imaging
and Radiation Therapy Devices
OHT8: Office of 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)*
K220437

Device Name
Neurophet AQUA

Indications for Use *(Describe)*
Neurophet AQUA is intended for Automatic labeling, visualization and volumetric quantification of segmentable brain structures from a set of MR images. Volumetric data may be compared to reference percentile data.

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

(K220437)

This summary of 510(k) information is being submitted in accordance with requirements of 21 CFR Part 807.92.

1. **Date:** 5/2/2023

2. **Applicant / Submitter**

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3. **U.S. Designated Agent**

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4. **Trade/Proprietary Name:**

Neurophet AQUA

5. **Common Name:**

Medical Image Processing Software

6. **Classification:**

System, image processing, radiological (21CFR 892.2050, Product code LLZ, Class 2, Radiology)

7. **Device Description:**

Neurophet AQUA is a fully automated MR imaging post-processing medical device software that provides automatic labeling, visualization, and volumetric quantification of brain structures from a set of MR images and returns segmented images and morphometric reports.

The resulting output is provided in morphometric reports that can be displayed on Picture Archive and Communications Systems (PACS). The high throughput capability makes the software suitable for use in both clinical trial research and routine patient care as a support tool for clinicians in assessment of structural MRIs.
Neurophet AQUA provides morphometric measurements based on T1 MRI series. The output of the software includes volumes that have been annotated with color overlays, with each color representing a particular segmented region, and morphometric reports that provide comparison of measured volumes to age and gender-matched reference percentile data. Neurophet AQUA processing architecture includes a proprietary automated internal pipeline that performs segmentation, volume calculation and report generation.

The results are displayed in a dedicated graphical user interface, allowing the user to:

- Browse the segmentations and the measures,
- Compare the results of segmented brain structures to a reference healthy population,
- Read and print a PDF report

Additionally, automated safety measures include automated quality control functions, such as tissue contrast check, scan protocol verification, which validate that the imaging protocols adhere to system requirements.

8. Indication for use:

Neurophet AQUA is intended for Automatic labeling, visualization and volumetric quantification of segmentable brain structures from a set of MR images. Volumetric data may be compared to reference percentile data.

9. Predicate Device:

- Primary Predicate:
  NeuroQuant® v2.2 (K170981) by CorTechs Labs, Inc

- Reference Device:
  BrainInsight (K202414) by Hyperfine Research, Inc.

10. Substantial Equivalence:

	Subject Device	Primary predicate Device	Reference Device
Device name	Neurophet AQUA v2.1	NeuroQuant® v2.2	BrainInsight
510(k)	K220437	K170981	K202414
Manufacturer	NEUROPHET, Inc.	CorTechs Labs, Inc	Hyperfine Research, Inc
Product Code	LLZ	LLZ	LLZ
Indications for Use	Neurophet AQUA is intended for Automatic labeling, visualization and volumetric quantification of segmentable brain structures from a set of MR images. Volumetric data may be compared to reference percentile data.	NeuroQuant is intended for 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, spatial measurement, and volumetric quantification of brain structures from a set of low-field MR images and returns annotated and segmented images, color overlays, and reports.
Target Anatomical Sites	Brain	Brain	Brain
Design and Incorporated Technology	• Automated measurement of brain tissue volumes and structures ▪ Automatic segmentation and quantification of brain structures using deep learning	• Automated measurement of brain tissue volumes and structures and lesions • Automatic segmentation and quantification of brain structures using a dynamic probabilistic neuroanatomical atlas, with age and gender specificity, based on the MR image intensity	▪ Automated measurement of brain tissue volumes and structures ▪ Automatic segmentation and quantification of brain structures using machine learning
Physical characteristics	• Software package • Operates on off-the-shelf hardware (multiple vendors)	• Software package • Operates on off-the-shelf hardware (multiple vendors)	No software required • Operates in a serverless cloud environment • User interface through PACS (multiple vendors)
Operating System	Windows	Supports Linux, Mac OS X and Windows.	Supports Linux
Processing Architecture	Automated internal pipeline that performs: - segmentation - volume calculation - report generation	Automated internal pipeline that performs: - artifact correction - segmentation - lesion quantification - volume calculation	Automated internal pipeline that performs: - segmentation - volume calculation - distance measurement - numerical information

		- report generation	display
Data Source	• MRI scanner: 3D T1 scans acquired with specified protocols • Supports DICOM format as input	• MRI scanner: 3D T1 and FLAIR MRI scans acquired with specified protocols • Supports DICOM format as input	▪ MRI scanner: Hyperfine FSE MRI scans acquired with specified protocols ▪ Supports DICOM format as input
Output	▪ Provides volumetric measurements of brain structures ▪ 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	▪ Provides volumetric measurements 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	Provides volumetric measurements of brain structures ▪ Includes segmented color overlays and morphometric reports ▪ Supports DICOM format as output of results that can be displayed on DICOM workstations and Picture Archive and Communications Systems
Safety	• Automated quality control functions - Tissue contrast check - Scan protocol verification • Results must be reviewed by a trained physician	• Automated quality control functions - Tissue contrast check - Scan protocol verification - Atlas alignment check • Results must be reviewed by a trained physician	Automated quality control functions ▪ Tissue contrast check ▪ Scan protocol verification ▪ Atlas alignment check ▪ Results must be reviewed by a trained physician

Neurophet AQUA and the predicate device are software for automatically identifying and quantifying the volumes of brain structures, automatic labeling and visualization. The devices have the same intended use and operating principle. They take MR brain images as input and generate an electronic report with similar quantitative information. For both devices, output volumes are compared to a normative dataset of control subjects computed based on MRI data from normal control subjects.

Both devices are DICOM compatible and operate on off-the-shelf hardware. Both devices are used by physicians skilled in brain MR imaging.

Neurophet AQUA is functionally similar and improved from a previous 510(k) market-cleared CorTechs Labs NeuroQuant software device (NeuroQuant K170981).

Both devices have same intended use and basic design and similar operating principle.

Following are the differences between Neurophet AQUA and the predicate device:

	Neurophet AQUA	NeuroQuant
Processing architecture	Segmentation based on deep learning tools, volume calculation and report generation.	Artifact correction, atlas-based segmentation, lesion quantification, volume calculation and report generation.
Operating System	Windows	Supports Linux, Mac OS X and Windows.
Deployment	Installed	Cloud based or installed

Although both are technically similar, in the processing architecture, the subject device performs segmentation based on deep learning and the predicate device performs segmentation based on atlas-based.

Although the predicate device performs artifact correction, the subject device uses the data augmentation technique during deep learning for segmentation, so it robustly performs segmentation on MRI data with artifact correction.

We identified a reference device (BrainInsight, K202414) which also uses a fully automated MR imaging post-processing medical software that image alignment, whole brain segmentation, ventricle segmentation, and midline shift measurements based on machine learning tools. Similarly, the subject device and the reference device segments brain structures from T1 MR images based on a similar principle. Furthermore, for volumes derived from T1 images, the subject device and the reference device provide statistical comparison of normalized values with a normative dataset from a healthy reference population.

However, both systems use clinical MR brain scans as input and automatically identify and measure volumes of brain structures. Both systems provide morphometric measurements based on 3D T1 MRI series. The resulting output is provided in a standard DICOM format as additional MR series that can be displayed on third-party DICOM workstations and PACS. Both systems produce similar reports. The output includes volumes that have been annotated with color overlays, with each color representing a particular segmented region, and morphometric reports that provide comparison of measured volumes to reference percentile data.

They utilize the same automated safety measures and have similar processing architecture. Both devices are DICOM compatible and operate on off-the-shelf hardware. Both systems are used by medical professionals, such as radiologists, neurologists and neuroradiologists, as well as by clinical researchers, as a support tool in assessment of
structural MRIs.

11. Performance Data:

SW verification/validation and the measurement accuracy test were conducted to establish the performance, functionality and reliability characteristics of the subject devices. The device passed all of the tests based on pre-determined Pass/Fail criteria.

Neurophet AQUA performance was evaluated by comparing segmentation accuracy with expert manual segmentations and by measuring segmentation reproducibility between same subject scans. The system yields reproducible results that are well correlated with expert manual segmentation.

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As part of AQUA's training data, 300 T1-weighted MRI scans collected from ten different MRI scanner types were used to train for the brain structural segmentation model.

MRI scanners with 30 scans each contain public datasets, including ADNI, IXI, PPMI, HCP, and AIBL. Ground-truth data were initially generated using FreeSurfer (General Hospital Corporation, Boston, MA, USA, version 6.0) and verified and corrected by four radiologists.

A total of 64 T1 scans (56%, n=36 US-based data; 62.5%, n=40 females; age ranges 20-90) were used for accuracy and 50 repeated T1 scans (62%, n=31 US-based data; 46%, n=23 females; age ranges 10-90) were used for reproducibility. Both sets include cognitive normal, mild cognitive impairments, and Alzheimer's disease patients from MR scanners of three main vendors (Siemens, Phillips, and GE). The data set met the imaging protocol requirements described in the User Manual. Stratified results across race/ethnicity, age, gender, pathology, scanner, vendor, and magnetic field strength were provided. All the testing data was exclusive from the training dataset.

Neurophet AQUA segmentation accuracy compared to expert manual segmentations of T1 MRI scans was evaluated using Dice’s coefficient metric. For major subcortical brain structures Dice’s coefficients are in the range of 80-90% and for major cortical regions are in the range of 75-85%.

Brain structural reproducibility of repeated T1 MRI scans for same subjects was evaluated by using the percentage absolute volume differences. The mean percentage absolute volume differences for all major subcortical structures were in the range of 1-5%.

12. Conclusion:

The subject device is substantially equivalent in the areas of technical characteristics, general function, application, and indications for use. The new device does not introduce a

fundamentally new scientific technology, and the device has been validated through system level test. Therefore, we conclude that the subject device described in this submission is substantially equivalent to the predicate device.