



October 25, 2024

Neurophet, Inc.
% Priscilla Chung
Regulatory Affairs Consultant
LK Consulting Group USA, Inc.
18881 Von Karman Ave STE 160
Irvine, California 92612

Re: K242215

Trade/Device Name: Neurophet AQUA (V3.1)
Regulation Number: 21 CFR 892.2050
Regulation Name: Medical image management and processing system
Regulatory Class: Class II
Product Code: QIH, LLZ
Dated: July 25, 2024
Received: July 29, 2024

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 (the 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 available 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.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (<https://www.fda.gov/media/99812/download>) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (<https://www.fda.gov/media/99785/download>).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

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 Part 803) for devices or postmarketing safety reporting (21 CFR Part 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 Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

All medical devices, including Class I and unclassified devices and combination product device constituent parts are required to be in compliance with the final Unique Device Identification System rule ("UDI Rule"). The UDI Rule requires, among other things, that a device bear a unique device identifier (UDI) on its label and package (21 CFR 801.20(a)) unless an exception or alternative applies (21 CFR 801.20(b)) and that the dates on the device label be formatted in accordance with 21 CFR 801.18. The UDI Rule (21 CFR 830.300(a) and 830.320(b)) also requires that certain information be submitted to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). For additional information on these requirements, please see the UDI System webpage at <https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-system-udi-system>.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 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,

A handwritten signature in black ink, appearing to read 'D. Krainak', is written over a large, light blue, semi-transparent watermark of the letters 'FDA'.

Daniel M. Krainak, Ph.D.
Assistant Director
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

Indications for Use

Submission Number (if known)

K242215

Device Name

Neurophet AQUA (V3.1)

Indications for Use (Describe)

Neurophet AQUA 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.

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.

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510(k) Summary

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

1. Date: 10/24/2024

2. Applicant / Submitter

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3. U.S. Designated Agent

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4. Trade/Proprietary Name:

Neurophet AQUA (V3.1)

5. Common Name:

Medical Image Processing Software

6. Classification:

- Automated Radiological Image Processing Software (21CFR 892.2050, Product code QIH, Class 2, Radiology)
- Medical Image Management and Processing System (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 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. In addition, the adjunctive use of the T2 FLAIR MR series allows for improved identification of some brain abnormalities such as lesions, which are often associated with T2 FLAIR hyperintensities.

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 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 and lesions from a set of MR images. Volumetric data may be compared to reference percentile data.

9. Predicate Device:

- Primary Predicate:
Neurophet AQUA v2.1 (K220437) by NEUROPHET, Inc.
- Reference Device:
NeuroQuant® v2.2 (K170981) by CorTechs Labs, Inc.

10. Substantial Equivalence:

Comparison Table

	Subject Device	Primary predicate Device	Reference Device
Device name	Neurophet AQUA V3.1	Neurophet AQUA v2.1	NeuroQuant® v2.2
510(k)	K242215	K220437	K170981
Manufacturer	NEUROPHET, Inc.	NEUROPHET, Inc.	CorTechs Labs, Inc
Product Code	QIH, LLZ	LLZ	LLZ
Indications for Use	Neurophet AQUA 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.	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.
Target Anatomical Sites	Brain	Brain	Brain
Design and Incorporated Technology	• Automated measurement of brain tissue volumes, structures, and lesions ▪ Automatic segmentation and quantification of brain structures using deep learning	• 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
Physical characteristics	• Software package • Operates on off-the-shelf hardware (multiple vendors)	• Software package • Operates on off-the-shelf hardware (multiple vendors)	• Software package • Operates on off-the-shelf hardware (multiple vendors)
Operating System	Windows	Windows	Supports Linux, Mac OS X and Windows.
Processing Architecture	Automated internal pipeline that performs: - segmentation - volume calculation - lesion quantification - report generation	Automated internal pipeline that performs: - segmentation - volume calculation - report generation	Automated internal pipeline that performs: - artifact correction - segmentation - lesion quantification - volume calculation - report generation

Data Source	• MRI scanner: 3D T1 and FLAIR MRI scans acquired with specified protocols • Supports DICOM format as input	• 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
Output	▪ 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 ▪ 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
Safety	• Automated quality control functions - Image artifact check - Scan protocol verification • Results must be reviewed by a trained physician	• 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

Substantial Equivalence Discussion

Neurophet AQUA V3.1 is an update of the previous 510(k) cleared device, Neurophet AQUA v2.1 (K220437).

- Except for the addition of “and lesions” words, both devices have same indications for use.
- Physical characteristics, and operating system are same.
- T1 MR image analysis algorithm and performance is same as previous.

New features of the device are as follows:

- Quantitative analysis function of T2 FLAIR images is added.

A major update in this version is support for quantitative analysis of T2 FLAIR images. This feature was added after verifying the performance of the analysis algorithm. We verified the

accuracy and reproducibility of T2 FLAIR analysis considering various patients ages, ethnicities, and gender. The test results meet acceptance criteria based on the performance of the reference device, NeuroQuant v2.2 (K170981).

In conclusion, Neurophet AQUA V3.1 is substantially equivalent to the predicated device, Neurophet AQUA v2.1 (K220437).

11. Performance Data:

SW verification/validation 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.

About the deep learning algorithm, the analysis performance is tested and validated as below:

To demonstrate the T2-FLAIR analysis performance of Neurophet AQUA, the data primarily sourced from U.S. hospitals were utilized. The data presents a diverse mix of clinical, demographic, and technical variables, providing a foundation for both reliable and reproducible testing, as well as comprehensive accuracy assessment. The ground truth was established by consensus among three U.S.-based neuroradiologists. The multi-site data collection enhances statistical independence, while the inclusion of varied demographic groups, clinical conditions, and MR imaging parameters addresses potential confounders.

The accuracy test dataset comprised 136 images, and the reproducibility test dataset comprised 52 images. The sample size supports robust performance validation. The subjects upon whom the device was trained and tested include healthy subjects, mild cognitive impairment patients, Alzheimer's disease patients, and multiple sclerosis patients from young adults to elderlies. The multicenter study was adapted to collect scans from various vendors including Philips, Siemens, and GE and MR scans using general clinical protocols were collected.

Neurophet AQUA performance was then 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.

Neurophet AQUA's lesion segmentation accuracy compared to expert manual segmentations of T2 FLAIR scan was evaluated using Dice's coefficient metric, which exceeds 0.80. The brain lesion segmentation reproducibility was evaluated using repeated T2 FLAIR scan pairs of subjects with brain lesions. The mean absolute lesion volume difference was less than 0.25cc.

The segmentation accuracy and reproducibility for T1 images were evaluated under K220437.

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.