July 1, 2024

Combinostics OY
% Erin Gontang
Senior Consultant
Rqm+
2790 Mosside Boulevard, #800
Monroeville, PA 15146

Re: K233908
Trade/Device Name: cNeuro™ cDAT
Regulation Number: 21 CFR 892.2050
Regulation Name: Medical Image Management And Processing System
Regulatory Class: Class II
Product Code: LLZ
Dated: May 30, 2024
Received: May 30, 2024

Dear Erin Gontang:

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.

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,

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

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

# Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 07/31/2026
*See PRA Statement below.*

510(k) Number *(if known)*
K233908

Device Name
cNeuro™ cDAT

Indications for Use *(Describe)*
cNeuro™ cDAT is intended for use by Nuclear Medicine or Radiology practitioners and referring physicians for display, processing, and reporting of Nuclear Medicine Imaging data.

cNeuro™ cDAT enables visual evaluation and quantification of ioflupane I 123 (DaTscan™) images. The software enables automated quantification of tracer uptake and comparison with the corresponding tracer uptake in healthy subjects as provided by normal population databases of ioflupane I 123 (DaTscan™) images. cNeuro™ cDAT assists in detection of loss of functional dopaminergic neuron terminals in the striatum, which is correlated with Parkinson disease or Dementia with Lewy Bodies (DLB).

cNeuro™ cDAT has not been demonstrated to improve ioflupane I 123 reader performance for distinguishing positive from negative patients. This device should not be used to deviate from ioflupane I 123 dosing and administration instructions. Refer also to ioflupane I 123 prescribing information for instructions.

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
# K233908

**DATE PREPARED**
July 3, 2024

**MANUFACTURER AND 510(k) OWNER**
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**DEVICE INFORMATION**

| | |
|---|---|
| Proprietary Name/Trade Name: | cNeuro™ cDAT |
| Common Name: | System, Image Processing, Radiological |
| Regulation Number: | 21 CFR §892.2050 |
| Class: | Class II |
| Product Code: | LLZ |
| Premarket Review Panel: | Radiology |

**PREDICATE DEVICE IDENTIFICATION**
The cNeuro™ cDAT is substantially equivalent to the following predicate:

| 510(k) Number | Predicate Device Name / Manufacturer | Primary Predicate |
|---|---|---|
| K201103 | Xeleris V Processing and Review Systems (DaTQUANT Application) / GE Medical Systems, LLC. | ✓ |

The predicate device have not been subject to a design related recall.

**DEVICE DESCRIPTION**

cNeuro™ cDAT is Software as a Medical Device (SaMD) intended to aid physicians in the evaluation of the loss of functional dopaminergic neuron terminals in the striatum through the quantification of ioflupane I 123 (DaTscan™) images. cNeuro™ cDAT is a fully automated image analysis software tool that provides tools for viewing DaTscan™ images and quantification of tracer uptake in the striatum with comparison to reference data from healthy controls. The results are summarized in a PDF-report.

cNeuro™ cDAT quantifies DaTscan™ brain images and computes Striatal Binding Ratios (SBRs) for different volumes of interest (VOIs). SBRs are computed by subtracting the uptake in a background VOI from the tracer uptake in the target VOI and then dividing this value with uptake in a background VOI. Results are compared with normative values in a reference database and z-scores are presented.

cNeuro™ cDAT quantifies the data by registering the images to a template where VOIs are defined. Quantification results are summarized in PDF-reports that are sent to the organization's PACS. cNeuro™ cDAT also offers interactive review of the DaTscan™ images and the quantification results in a browser-based viewer.

**INDICATIONS FOR USE**

cNeuro™ cDAT is intended for use by Nuclear Medicine or Radiology practitioners and referring physicians for display, processing, and reporting of Nuclear Medicine Imaging data.

cNeuro™ cDAT enables visual evaluation and quantification of ioflupane I 123 (DaTscan™) images. The software enables automated quantification of tracer uptake and comparison with the corresponding tracer uptake in healthy subjects as provided by normal population databases of ioflupane I 123 (DaTscan™) images. cNeuro™ cDAT assists in detection of loss of functional dopaminergic neuron terminals in the striatum, which is correlated with Parkinson disease or Dementia with Lewy Bodies (DLB).

cNeuro™ cDAT has not been demonstrated to improve ioflupane I 123 reader performance for distinguishing positive from negative patients. This device should not be used to deviate from ioflupane I 123 dosing and administration instructions. Refer also to ioflupane I 123 prescribing information for instructions.

**COMPARISON OF TECHNOLOGICAL CHARACTERISTICS**

Combinostics believes that the cNeuro™ cDAT is substantially equivalent to the predicate device based on the information summarized here:

The subject device and predicate device are software for the automated quantification, visualization, and reporting of ioflupane I 123 (DaTscan™) images. Both devices compute Striatal Binding Ratios (SBRs) where the uptake in a background region is subtracted from the uptake in a target region or voxel and then the difference is divided with the value in a background region. In addition to SBRs, both devices compute asymmetry between striatal

regions as well as putamen/caudate ratios. Both devices compute z-scores by comparing extracted features with corresponding values in reference data from healthy controls.

The subject device and predicate device achieve their intended use based on the identical principle, which is the quantification system relies on registering the SPECT data to a template space where a volume of interest template is defined.

A comparison of the subject device and predicate device is provided below.

| | ***Subject Device*** | ***Predicate Device*** |
|---|---|---|
| | Combinostics OY<br>cNeuro™ cDAT<br><br>K233908 | GE Healthcare<br>Xeleris V Processing and Review Systems<br>(DaTQUANT Application)<br>K201103 |
| Indications for Use | cNeuro™ cDAT is intended for use by Nuclear Medicine or Radiology practitioners and referring physicians for display, processing, and reporting of Nuclear Medicine Imaging data.<br><br>cNeuro™ cDAT enables visual evaluation and quantification of ioflupane I 123 (DaTscan™) images. The software enables automated quantification of tracer uptake and comparison with the corresponding tracer uptake in healthy subjects as provided by normal population databases of ioflupane I 123 (DaTscan™) images. cNeuro™ cDAT assists in detection of loss of functional dopaminergic neuron terminals in the striatum, which is correlated with Parkinson disease or Dementia with Lewy Bodies (DLB).<br><br>cNeuro™ cDAT has not been demonstrated to improve ioflupane I 123 reader performance for distinguishing positive from negative patients. This device should not be used to deviate from ioflupane I 123 dosing and administration instructions. Refer also to ioflupane I 123 prescribing information for instructions. | The system is intended for use by Nuclear Medicine (NM) or Radiology practitioners and referring physicians for display, processing, archiving, printing, reporting and networking of NMI data, including planar scans (Static, Whole Body, Dynamic, Multi-Gated) and tomographic scans (SPECT, Gated SPECT, dedicated PET or Camera-Based-PET) acquired by gamma cameras or PET scanners. The system can run on dedicated workstation or in a server-client configuration. The NM or PET data can be coupled with registered and/or fused CT or MR scans, and with physiological signals in order to depict, localize, and/or quantify the distribution of radionuclide tracers and anatomical structures in scanned body tissue for clinical diagnostic purposes.<br><br>The DaTQUANT optional application enables visual evaluation and quantification of 123I-ioflupane (DaTscan™) images. DaTQUANT Normal Database option enables quantification relative to normal population databases of 123 I ioflupane (DaTscan™) images. These applications may assist in detection of loss of functional dopaminergic neuron terminals in the striatum, which is correlated with Parkinson disease. |

| | | |
|---|---|---|
| Product Code(s) | LLZ – System, Image Processing, Radiological | LLZ – System, Image Processing, Radiological |
| Regulation Number/ Description | 21 CFR 892.2050 / Medical image management and processing system | 21 CFR 892.2050 / Medical image management and processing system |
| Import of SPECT Images | Can only take reconstructed DaTscan™ SPECT images as input. | Can take both raw and reconstructed DaTscan™ SPECT images as input. If raw images are provided, there is a reconstruction pre-processing step. |
| Supported Tracers | DaTscan™ only | DaTscan™ only |
| Method for Quantification | A VOI template outlining caudate, anterior putamen, posterior putamen and a background region is defined in template space. The patient's SPECT image is registered to the template and the regions are applied to the data and counts within each region. | A VOI template outlining caudate, anterior putamen, posterior putamen and a background region is defined in template space. The patient's SPECT image is registered to the template and the regions are applied to the data and counts within each region. |
| Quality Check of Registration | There is an automated check of the registration parameters and if they are outside the expected range, the image is automatically repositioned, and a new registration is started. This is repeated 5 times. There is also a check if the occipital reference region is outside the brain.<br><br>If registration was not successful, no quantification results are presented.<br><br>If registration is successfully completed, the user is provided with images to review the quality of the image registration and fitting of the VOIs, but there is no explicit "I have approved" button. | The user needs visually check registration and click "Passed" before quantification results are shown. If registration was not successful, the user has the ability to manually reposition the images and rerun the image registration. |
| Ability for User to Move Regions | User does not have the ability to interactively move regions. | User has the ability to interactively move regions. |
| Normal Database | Data from DaTscan™ studies of healthy controls is used to define a reference normal database. | Data from DaTscan™ studies of healthy controls is used to define a reference normal database. |

| | | |
|---|---|---|
| Formula for Normal Values | By default, a line is fitted to the mean of values in the normal database. From the user interface, it is possible to enable visualization of z-scores for normative data at ±1.0, ±1.5, ±1.7, and ±2.0. The lines are fitted using the ordinary least squares (OLS) method, i.e., linear regression, and was performed separately for two age segments ([31, 55] and [68, 84]). Additionally, quadratic Bezier curves are fitted to connect the two linear segments.<br><br>The mean and standard deviation for a certain age are defined from these fitted curves. | By default, a line is fitted to the mean of values in the normal database. From the user interface, it is possible to enable visualization of z-scores for normative data at ±1.0, ±1.5, ±1.7, and ±2.0. The lines are fitted using the ordinary least squares (OLS) method, i.e., linear regression, and was performed separately for two age segments ([31, 55] and [68, 84]). Additionally, quadratic Bezier curves are fitted to connect the two linear segments.<br><br>The mean and standard deviation for a certain age are defined from these fitted curves. |
| User Created Normal Database | User does not have the ability to create their own database. | User has the ability to create their own database. |
| Output from Quantification | Striatal Binding Ratios (SBRs) are computed for Caudate, anterior Putamen, posterior Putamen, Putamen as a whole, and Striatum as a whole. In addition, asymmetry is computed for the Striatum as a whole, for the Caudate and for the Putamen.<br><br>Z-scores are computed for each feature by comparing the value with the corresponding mean and standard deviation in the normal database. | Striatal Binding Ratios (SBRs) are computed for Caudate, anterior Putamen, posterior Putamen, Putamen as a whole, and Striatum as a whole. In addition, asymmetry is computed for the Striatum as a whole, for the Caudate and for the Putamen.<br><br>Z-scores are computed for each feature by comparing the value with the corresponding mean and standard deviation in the normal database |
| Database selection and warnings | The recommended reconstruction method is OSEM, 2 iterations, 10 subsets, Butterworth 3D post-filtering with power factor = 10, cut off = 0.6.<br><br>The default normal database is configured in the organizations settings. The reconstruction method used is displayed in the UI and in the report and if the user selects a different database, a warning is shown in the UI and in the report. | The recommended reconstruction method is OSEM, 2 iterations, 10 subsets, Butterworth 3D post-filtering with power factor = 10, cut off = 0.6.<br><br>If data is reconstructed within the device, i.e., reconstruction methods is known, the system will select the correct database. If already reconstructed images are imported, the user will have to enter information so a database can be selected unless the necessary information can be derived from DICOM tags.<br>The reconstruction method used is displayed in the UI and in the report and if the user selects a different database, a warning is shown in the UI and in the report. |

| | | |
|---|---|---|
| Graphical User Interface (GUI) | The GUI allows the user to scroll images, view images with and without regions outlined, change color scale and window levels, view regional results and plots with comparison to the normal database. | The GUI allows the user to scroll images, view images with and without regions outlined, change color scale and window levels, view regional results and plots with comparison to the normal database. |
| Report | A PDF report is generated. The report format is fixed. | A PDF report can be generated. The user has some flexibility in the tailoring of the report. |

**SUMMARY OF PERFORMANCE TESTING**

The cNeuro™ cDAT software complies with NEMA PS 3.1 - 3.20 (2021) Digital Imaging and Communications in Medicine (DICOM) Set (Radiology) standard.

cNeuro™ cDAT employs the same fundamental scientific technology as its predicate device, Xeleris/DaTQUANT. cNeuro™ cDAT uses the equivalent DICOM image data input requirements. It has equivalent display, formatting, archiving and visualization technologies compared to the predicate device. cNeuro™ cDAT utilizes the same methodology to quantify and assess uptake in ioflupane I 123 (DaTscan™) images. The information is presented using volumes of interest. Thorough testing of these capabilities has not raised any safety or effectiveness issues.

The following quality assurance measures were applied to the development of the system:

- Risk Analysis
- Requirements Reviews
- Design Reviews
- Integration testing (System verification)
- Performance testing (Bench testing, verification)
- Safety testing (Verification)

Combinostics believes that a failure or latent flaw of the cNeuro™ cDAT software function, such as inadequate quality of displayed images, would not present a hazardous situation with a probable risk of death or serious injury to either a patient, user of the device, or others in the environment of use, prior to the implementation of risk control measures. Based on the implementation of the Documentation Level risk-based approach, Combinostics has provided Basic Documentation in support of the cNeuro™ cDAT premarket notification.

Combinostics has conducted testing on the cNeuro™ cDAT software. For performance testing, imaging of 370 patients was available to Combinostics following third-party clinical investigations (NCT01952678, NCT01141023). A subset of 48 images could not be processed with the predicate device and were excluded from further testing. Combinostics used the imaging from each included patient as input to both the subject and predicate devices so that paired z-value outputs from each device could be compared. The upper bound of the 95% confidence interval for the percentage of patients with paired z-value outputs differing by >0.5 was tested. This patient percentage ranged from 5.4% to 7.6% for the left and right putamen, caudate, anterior putamen, and posterior putamen, suggesting 92.4% to 94.6% of patients representative of the studied population have equivalent-to-predicate (±0.5) z-value outputs.

The software passed all performance requirements and met specifications.

**CONCLUSION**

The subject device does not raise different issues of safety or effectiveness compared to the predicate device. The similar indications for use, technological characteristics, and performance characteristics for the proposed cNeuro™ cDAT are assessed to be substantially equivalent to the predicate device.