Quantib BV
Floor Van Leeuwen
Quality & Regulatory Manager
Westblaak 106
ROTTERDAM, NL 3012 KM ZUID-HOLLAND

December 27, 2018

Re: K182564
Trade/Device Name: Quantib ND
Regulation Number: 21 CFR 892.2050
Regulation Name: Picture Archiving And Communications System
Regulatory Class: Class II
Product Code: LLZ
Dated: November 12, 2018
Received: November 14, 2018

Dear Floor Van Leeuwen:

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/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm); 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 http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm.

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) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Michael D. O'Hara 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

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)*
K182564

Device Name
Quantib™ ND 1.5

Indications for Use *(Describe)*
Quantib™ ND is a non-invasive medical imaging processing application that is intended for automatic labeling, visualization, and volumetric quantification of segmentable brain structures from a set of magnetic resonance (MR) images. The Quantib™ ND output consists of segmentations, visualizations and volumetric measurements of brain structures and white matter hyperintensities. Volumetric measurements may be compared to reference centile data. It is intended to provide the trained medical professional with complementary information for the evaluation and assessment of MR brain images and to aid the trained medical professional in quantitative reporting. Quantib™ ND is a software application on top of Myrian®.

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.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 79 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

Quantib™ ND 1.5
510(k) Summary

K182564

1 SUBMITTER

Quantib B.V.
Westblaak 106
3012 KM Rotterdam
Phone: (+31) 108 41 17 49
Contact Person: Floor van Leeuwen
Date Prepared: September 17th, 2018

2 DEVICE

Name of Device: Quantib™ ND 1.5
Common or Usual Name: Quantib™ ND
Classification Name: System, image processing, radiology (892.2050)
Regulatory Class: II
Product Code: Picture archiving and communication system (LLZ)

3 PREDICATE DEVICE

Device: Quantib™ Brain 1.3
Manufacturer: Quantib B.V.
510(k) Reg. No: K173939
This predicate has not been subject to a design-related recall.
Classification Name: System, image processing, radiology (892.2050)
Regulatory Class: II
Product Code: Picture archiving and communication system (LLZ)

4 DEVICE DESCRIPTION

Quantib™ ND is a post-processing analysis module for Myrian®, which provides 3D image visualization tools that create and display user-defined views and streamlines interpretation and reporting. It is intended for automatic labeling, visualization, and volumetric quantification of identifiable brain structures from magnetic resonance images (a 3D T1-weighted MR image, with an additional T2-weighted FLAIR MR image for white matter hyperintensities (WMH) segmentation). The segmentation system relies on a number of atlases each consisting of a 3D T1-weighted MR image and a label map dividing the MR image into different tissue segments.

Quantib™ ND provides quantitative information on both the absolute and relative volume of the segmented regions. The automatic WMH segmentation is to be reviewed and if necessary, edited by the user before validation of the segmentation, after which volumetric information is accessible. Quantib ND consists of Quantib ND Baseline, which provides analysis of images of one time-point, and Quantib ND Follow-Up, which provides longitudinal analysis of images of two time-points. Quantib ND Follow-Up can only process images that have been processed by Quantib_ND Baseline. Quantib ND is intended to provide the trained medical professional with complementary information for the evaluation and assessment of MR brain images and to aid the radiology specialist in quantitative reporting.

5 INDICATIONS FOR USE

Indications for use Quantib™ ND 1.5

Quantib™ ND is a non-invasive medical imaging processing application that is intended for automatic labeling, visualization, and volumetric quantification of segmentable brain structures from a set of magnetic resonance (MR) images. The Quantib™ ND output consists of segmentations, visualizations and volumetric measurements of brain structures and white matter hyperintensities. Volumetric measurements may be compared to reference centile data. It is intended to provide the trained medical professional with complementary information for the evaluation and assessment of MR brain images and to aid the trained medical professional in quantitative reporting. Quantib™ ND is a software application on top of Myrian®.

Indications for use predicate device (Quantib™ ND 1.3)

Quantib™ Brain is a non-invasive medical imaging processing application that is intended for automatic labeling, visualization, and volumetric quantification of segmentable brain structures from a set of magnetic resonance (MR) images. The Quantib™ Brain output consists of segmentations, visualizations and volumetric measurements of grey matter (GM), white matter (WM), and cerebrospinal fluid (CSF). The output also visualizes and quantifies white matter hyperintensity (WMH) candidates. Users need to review and if necessary, edit WMH candidates using the provided tools, before validation of the WMHs. It is intended to provide the trained medical professional with complementary information for the evaluation and assessment of MR brain images and to aid the trained medical professional in quantitative reporting. Quantib™ Brain is a post-processing plugin for the GE Advantage Workstation (AW 4.7) or AW Server (AWS 3.2) platforms.

Indications for use comparison

The intended use of the device is **partially equivalent** to the intended use of the previously cleared predicate device [K173939]

6 COMPARISON OF TECHNOLOGICAL CHARACTERISTICS

The following technological characteristics are the same for Quantib™ ND 1.5 and its predicate device Quantib™ Brain 1.3:

- Target users, anatomical site, and usage location
- Design
- Standards met

- Required input

The following technological characteristics are different:

- *Indications for use and Intended use:* The device is a software application on top of Myrian®; Segmentation and quantification of separate lobes and hippocampus, comparison of whole brain, lobes, and hippocampus volumes to reference centile curves of a group representing the general population, and improved longitudinal volume change calculation using automated image registration are added.
- *Human factors:* Similar workflow, but implementation is slightly different based on existing workflow of underlying software packages
- *Algorithm design*
  For hippocampus segmentation, a slightly different refinement step is used than for other brain structures. Brain structures follow-up analysis is done using technological characteristics also applied elsewhere in Quantib ND and the predicate device.
- *Performance:* For measures reported by both devices, performance numbers show slight changes, attributable to the underlying software packages. Assessment of the performance of segmentation of separate lobes, hippocampus, and reference centile curves is added.
- *Compatibility with the environment and other devices:* Quantib™ ND is an add-on for Myrian, which can be installed on regular hardware using Windows as operating system.
- *Reported measures:* Whole brain measures (sum of Grey Matter [GM] and White Matter [WM]) are reported instead of GM and WM separately. To the reported measures the volumes of the following structures are added: Hippocampus, Frontal Lobe, Occipital Lobe, Parietal Lobe, Temporal Lobe, and Cerebellum. Reference centile curves are added, comparing these results to a group representing the general population.

7 PERFORMANCE DATA

7.1 QUALITY AND SAFETY

Quantib™ ND 1.5 was designed in compliance with the following process standards:

- ISO 14971 – Medical devices - Application of risk management to medical devices
- IEC 62304 – Medical device software – Software life cycle processes
- IEC 62366 – Medical devices - Application of usability engineering to medical devices

The following quality assurance measures were applied to Quantib™ ND 1.5 development:

- Risk and hazard analysis
- Design reviews
- Unit level testing
- Integration testing
- System testing
- Performance testing
- Usability engineering

7.2 ALGORITHM PERFORMANCE

7.2.1 Brain Structures

To validate the quality of Quantib™ ND volume measurements and segmentations, these were compared to manual segmentations of the same scan and their derived volumes. This analysis was performed for Brain Tissue, CSF, ICV, Hippocampus, Frontal Lobe, Occipital Lobe, Parietal Lobe, Temporal Lobe, and Cerebellum.

For brain tissue, CSF, and ICV, the test set included 33 T1w MR images (Dataset A). The set was carefully selected to include data from multiple vendors and a series of representative scan settings. For each scan we selected six (6) slices for comparison. For the hippocampus the test set included 89 T1w images (Dataset B) and for the lobes the test set included 13 T1w MR images (Dataset C). For test sets B and C all slices were segmented manually for the comparison. The results are summarized below.

	Dataset	Dice index	Absolute difference of the relative volumes [pp]
Brain	A	0.96 ± 0.01	1.7 ± 1.3
CSF	A	0.78 ± 0.05	1.8 ± 1.3
ICV	A	0.98 ± 0.01	-
Hippocampus total	B	0.84 ± 0.03	0.03 ± 0.02
Hippocampus right		0.84 ± 0.03	0.01 ± 0.01
Hippocampus left		0.84 ± 0.03	0.01 ± 0.01

Results of comparison between manual and automatic brain structure segmentation. Reported values are averages ± std. dev., computed over 6 segmented slices of 33 scans (Dataset A). For Dataset B all slices were segmented. The Dice index provides a measure for overlap of manual and automatic segmentations (1 = perfect overlap). The absolute differences of the relative volumes are averages ± std. dev. in percentage points.

	Dataset	Dice index	Absolute difference of the relative volumes [pp]
Frontal lobe total	C	0.95 ± 0.01	1.95 ± 0.90
Frontal lobe right		0.94 ± 0.02	1.02 ± 0.61
Frontal lobe left		0.94 ± 0.01	0.93 ± 0.50
Occipital lobe total	C	0.88 ± 0.03	0.87 ± 0.75
Occipital lobe right		0.88 ± 0.03	0.43 ± 0.36
Occipital lobe left		0.87 ± 0.04	0.53 ± 0.53
Parietal lobe total	C	0.89 ± 0.03	2.81 ± 1.13
Parietal lobe right		0.88 ± 0.04	1.45 ± 0.80
Parietal lobe left		0.88 ± 0.02	1.36 ± 0.56
Temporal lobe total	C	0.91 ± 0.01	1.33 ± 0.76
Temporal lobe right		0.91 ± 0.02	0.72 ± 0.46
Temporal lobe left		0.91 ± 0.01	0.61 ± 0.39
Cerebellum total	C	0.98 ± 0.01	0.47 ± 0.20

Cerebellum right		0.97 ± 0.00	0.31 ± 0.13
Cerebellum left		0.97 ± 0.01	0.17 ± 0.11

Results of comparison between manual and automatic brain structure segmentation of the lobes. Reported values are averages ± std. dev., computed over 13 scans of which all slices were segmented (Dataset C). The Dice index provides a measure for overlap of manual and automatic segmentations (1 = perfect overlap). The absolute differences of the relative volumes are averages ± std. dev. in percentage points.

7.2.2 White Matter Hyperintensities

The test set for the White Matter Hyperintensities analysis included 45 3D T1w images, of which 7 contrast-enhanced, all with corresponding T2w FLAIR images. This set also represented various scan settings. WMHs were manually segmented on the T2w FLAIR images and compared to Quantib™ ND automatic segmentation output. The average Dice overlap between the manual segmentations and Quantib™ ND segmentations was 0.61 ± 0.13 (over all cases). The absolute difference of the relative volumes (for WMHs) was 0.2 ± 0.2 percentage points (over 38 cases without contrast-enhancement).

8 CONCLUSIONS

By virtue of its intended use and physical and technological characteristics, Quantib™ ND 1.5 is substantially equivalent to a device that has been approved for marketing in the United States. The performance data shows that Quantib™ ND 1.5 is as safe and effective as the predicate device.