Quantib B.V.
℅ Floor van Leeuwen
Quality & Regulatory Director
Westblaak 106
Rotterdam, Zuid-Holland 3012KM
NETHERLANDS

January 14, 2022

Re: K213737
Trade/Device Name: Quantib ND
Regulation Number: 21 CFR 892.2050
Regulation Name: Medical image management and processing system
Regulatory Class: Class II
Product Code: LLZ
Dated: November 11, 2021
Received: December 17, 2021

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/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)*
K213737

Device Name
Quantib ND

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.

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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Quantib ND 2.0 Special 510(k) Summary

1 SUBMITTER

Quantib B.V.
Westblaak 106
3012 KM Rotterdam
Phone: (+31) 108 41 17 49
Contact Person: Floor van Leeuwen
Date Prepared: November 11, 2021

2 DEVICE

Name of Device: Quantib ND 2.0
Common or Usual Name: Quantib ND 2.0
Classification Name: System, image processing, radiology (892.2050)
Regulatory Class: II
Product Code: Medical image management and processing system (former Picture archiving and communication system)

3 PREDICATE DEVICE

Device: Quantib ND 1.5
Manufacturer: Quantib B.V.
510(k) Reg. No: K182564
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 an extension for Quantib AI Node software platform. It is intended for automatic labeling, visualization, and volumetric quantification of identifiable brain structures from magnetic resonance images (a 3D T1-weighted MR image for brain structure segmentation, 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 4 workflows: for both segmentation and quantification of brain structures as well as of white matter hyperintensities is there a single time-point analysis workflow, and a longitudinal workflow, which provides longitudinal analysis of images of two or more time-points. 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 2.0

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.

Indications for use predicate device (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 comparison

The intended use of the device is **equivalent** to the intended use of the previously cleared predicate device [K182564]

6 DEVICE MODIFICATIONS

Quantib ND 2.0 is the first update of Quantib ND 1.5 that includes a substantial change. The substantial changes are the following:

1. *Quantib ND 2.0 is an extension for a different platform*

Whereas Quantib ND 1.5 was an add-on for the Windows-based 3rd party platform Myrian® (Intrasense, FR), Quantib ND 2.0 is developed as extension for Quantib's own platform Quantib AI Node (Quantib BV, NL). This platform is Linux-based. Quantib ND 2.0 is designed as a

server-client system, where the server is accessible via a web browser from any configured client system. Both platforms are FDA-cleared.

2. *Simplification of user interaction and results viewing in workflows*

With the exception of the single time-point WMH analysis- which requires review, editing and validation by the user- results of the workflows are now directly added to the report.

- For the brain structures single time point and longitudinal step, the user could previously only view the segmentations in the user interface, with no possibility to edit. Now, results are directly added to the report in the form of volumetric measures and overview images of the segmentations. Complete segmentations are exported as separate files for detailed analysis.
- For the longitudinal WMH analysis workflow the functionality to relabel was never used and has been removed. Longitudinal labeling results are now directly sent to the report.

Numerical values are now only present in the report and no longer in a summary table in the user interface. Each workflow now generates its own report, which removes dependencies between workflows and thereby produces certain reports without waiting for user input.

Report and segmentations are directly and automatically exported to a configured DICOM node (for example PACS system). They can be viewed from the PACS system using any DICOM viewer the user prefers.

7 COMPARISON OF TECHNOLOGICAL CHARACTERISTICS

The following technological characteristics are the same for Quantib ND 2.0 and its predicate device Quantib ND 1.5:

- Indications for use
- Target users, anatomical site, and use environment
- Algorithm design
- Reported measures
- Design control activities and recognized standards
- Required input

The following technological characteristics are different:

- *Software Design:* Architecture of algorithm parts is equivalent for new and predicate device and is using the same C++ library. Architecture of integration is determined by architecture of platform, in the case of Quantib ND 2.0 the Quantib AI Node. Design differences include different programming language for integration architecture and use of additional libraries and packages.
- *Human factors:* user interaction has been revised due to the change of platform, which includes the viewer/editor functionality and sets requirements on how workflows are implemented. Where possible, user interaction steps have been simplified or been left out.
- *Algorithm performance:* Performance numbers show slight changes, attributable to the underlying software packages. No significant performance differences are expected and observed since no changes have been made to algorithms and their implementation.

- *Compatibility with the environment and other devices:* Quantib ND 2.0 is an extension for Quantib AI Node running on a Linux OS, while Quantib ND 1.5 is an add-on for Myrian, using Windows as operating system.

8 PERFORMANCE DATA

8.1 QUALITY AND SAFETY

Quantib ND 2.0 is 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 2.0 development:

- Risk and hazard analysis
- Design and code reviews
- Unit level testing
- Integration and regression testing
- System and UI testing
- Performance testing
- Usability engineering
- Cybersecurity and vulnerability analysis

8.2 ALGORITHM PERFORMANCE

8.2.1 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	1.63 ± 1.06
CSF	A	0.78 ± 0.05	1.67 ± 1.06
ICV	A	0.98 ± 0.00	-
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 ± 0.04	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	1.21 ± 1.22
Frontal lobe right		0.94 ± 0.02	0.76 ± 0.58
Frontal lobe left		0.94 ± 0.02	0.60 ± 0.67
Occipital lobe total	C	0.89 ± 0.03	0.75 ± 0.83
Occipital lobe right		0.88 ± 0.04	0.54 ± 0.48
Occipital lobe left		0.88 ± 0.03	0.44 ± 0.36
Parietal lobe total	C	0.89 ± 0.03	1.21 ± 1.31
Parietal lobe right		0.88 ± 0.04	0.73 ± 0.76
Parietal lobe left		0.88 ± 0.03	0.64 ± 0.67
Temporal lobe total	C	0.91 ± 0.02	0.87 ± 0.74
Temporal lobe right		0.91 ± 0.02	0.46 ± 0.33
Temporal lobe left		0.90 ± 0.03	0.47 ± 0.46
Cerebellum total	C	0.99 ± 0.00	0.19 ± 0.13
Cerebellum right		0.97 ± 0.01	0.12 ± 0.07
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.

8.2.2 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).

9 CONCLUSIONS

By virtue of its intended use and physical and technological characteristics, Quantib ND 2.0 is substantially equivalent to a device that has been approved for marketing in the United States. The performance data shows that Quantib ND 2.0 is as safe and effective as the predicate device.