



Medis Medical Imaging Systems bv
% B. Goedhart, Ph.D.
VP Corporate R&D
Schuttersveld 9
Leiden, 2316 XG
THE NETHERLANDS

May 30, 2019

Re: K182611

Trade/Device Name: QANGIO XA 3D
Regulation Number: 21 CFR 892.1600
Regulation Name: Angiographic x-ray system
Regulatory Class: Class II
Product Code: QHA, LLZ
Dated: May 1, 2019
Received: May 3, 2019

Dear Dr. Goedhart:

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

Indications for Use

510(k) Number (if known)
K182611

Device Name
QANGIO XA 3D

Indications for Use (Describe)

QANGIO XA 3D is indicated for use in clinical settings where validated and reproducible quantified results are needed to support the assessment of coronary vessels in X-ray angiographic images, for use on individual patients with coronary artery disease.

When the quantified results provided by QAngio XA 3D are used in a clinical setting on X-ray images of an individual patient. The results are only intended for use by the responsible clinicians.

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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5. 510(k) Summary of Safety and Effectiveness

Submission in accordance with the requirements of 21 CFR Part 807.87(h).

Submitter : Medis medical imaging systems bv
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: The Netherlands
Contact Person : B. Goedhart, PhD, Vice President R&D
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Prepared : May 29, 2019
Trade / Device Name : QANGIO XA 3D
Common Name : Radiological Image Processing Software
Regulatory Class : II
Regulation Description : Angiographic X-ray system
Regulation Number : 21 CFR 892.1600
Classification Product Code : QHA
Subsequent Product Code : LLZ

Predicate Device

- The Pie Medical: **CAAS™ Workstation (K180019)**, Regulation Number : 21 CFR 892.1600.

Device Description

QANGIO XA 3D is the Medis software solution for the quantitative analysis of cardiac X-ray Angiography (XA) studies. QANGIO XA 3D features:

- Acquisition guide and series selection guide: A visualization method is provided to find suitable rotation and angulation angles for a second XA image if the first XA image is selected (acquisition guide). Another visualization method is provided to support the selection of matching XA images in a completed patient study (selection guide). Input: XA image. Output: XA image with required angulation compared to input image. Method: Comparing angulation information from DICOM.
- Annotations and basic measurements: User tools are provided for basic textual annotations onto an XA image, to perform a simple distance or area measurement in a 2D XA image, and to create snapshot images of the screen. Input: XA image. Output: simple measurement results. Method: manual delineation.
- 2D and 3D QCA vessel detection: 2D vessel boundaries are (automatically) detected of a user-selected coronary vessel segment in an XA image. The 2D vessel boundaries from two XA images of the same vessel under different angulation are used to reconstruct a 3D model of the user-selected vessel segment. Input: 2 XA images. Output: 3D model of targeted coronary vessel.
- 2D and 3D QCA vessel quantification: From the 3D model of the vessel segment, each ellipse is described by its two diameters, which are stored as a minimum and maximum diameter. The total set of diameters is called the “arterial diameter function”. From the arterial diameter function, a so-called “reference diameter” function is calculated using a recursive method that fits a linear approximation through the diameters, excluding the areas that are considered narrowed portions of the vessel segment. Analogue to 2D X-ray angiographic analysis provided in our predicate device X-RAY VVA, all quantitative parameters provided by QAngio XA 3D with respect to a lesion are calculated from these arterial and reference diameter functions. By default the software will indicate the lesion with the most severe narrowing (minimal lumen diameter / area), which is defined to be the narrowing with the largest percent of area-stenosis. Further, the start and end point of the lesion will be provided, resulting in the calculation of the length of the lesion. Other quantitative results derived from the diameter functions are: maximum diameter / area, average diameter over the lesion or the whole vessel segment.

- QFR calculations:
 - o Quantitative Flow Ratio (QFR) analysis: The QFR value (ratio of the pressure drop) is calculated based on computer calculations of the functional significance of a coronary vessel narrowing. The computation is based on computational fluid dynamics (CFD) principles applied to a 3D reconstruction of the coronary vessel segment (as described above) and one of the flow models. Input: 3D model of targeted coronary vessel and a flow model. Output: QFR curve describing the QFR value at each location along the centerline of the vessel segment. From this QFR curve function the parameters “Vessel QFR”, “Index QFR”, and “Lesion QFR” can be derived. Two different flow models are available:
 - o The so-called fixed flow model, which uses a fixed empiric hyperemic flow velocity, derived from literature. Using this model will yield fQFR values.
 - o The contrast flow model, which models the hyperemic flow velocity derived from coronary angiograms without pharmacologically induced hyperemia (i.e the contrast flow was converted into the virtual hyperemic flow based on data derived from previous studies). Using this model will yield so-called cQFR values.
 - o The agreement between the fQFR and cQFR model has been shown in a comparative study.
 - o The QFR value is validated against the FFR value in several validation studies. The WIFI II study, FAVOR II Europe-Japan, FAVOR II China, QFR and Non Culprit lesions in STEMI Patients (and many others). For FFR, only the value at a specific point along a coronary segment is known, i.e. at the place of the pressure sensor, while the calculated QFR curve describes its value along the entire segment. For the comparison of FFR and QFR at a specific location, the QFR value is sampled from the QFR curve at the location of the FFR wire. Since this sample is at a different position in each analysis, it is admissible to see this as a validation of the entire QFR curve. From the QFR curve, three different QFR values are derived (i.e. samples of the QFR curve) and reported as output:
 - o The vessel QFR is the value at the end of the QFR curve;
 - o The index QFR is a caliper at a user-defined position in the QFR curve;
 - o The lesion QFR is 1 minus the QFR drop between the lesion markers;
- Single vessel report: A report is generated by the software that shows patient information, image acquisition information (both obtained from the DICOM input), analysis results (vessel sizing and QFR value) and snapshot images showing the vessel boundaries.

QANGIO XA 3D will be used by interventional cardiologists and researchers to obtain quantifications of lesions in coronary vessels, to determine the functional significance of the individual or consecutive multiple lesions, prior, during or after percutaneous coronary intervention treatment. QANGIO XA 3D has been developed as a standalone application to run on a Windows based operating system. The import of images and the export of analysis results are via CD / DVD, a PACS or network environment.

Intended Use

QANGIO XA 3D is software intended to be used for performing calculations in X-ray angiographic images of the coronary arteries. QANGIO XA 3D enables interventional cardiologists and researchers to obtain quantifications of one or more lesions in the analyzed coronary vessel segment. In particular, QANGIO XA 3D provides:

- Quantitative results of coronary vessel segments based on a 3D reconstructed model;
- Dimensions of the cardiovascular vessels and lesions;
- Quantification of the pressure drop in coronary vessels.

Indications for Use

QANGIO XA 3D is indicated for use in clinical settings where validated and reproducible quantified results are needed to support the assessment of coronary vessels in X-ray angiographic images, for use on individual patients with coronary artery disease.

When the quantified results provided by QANGIO XA 3D are used in a clinical setting on X-ray images of an individual patient, the results are only intended for use by the responsible clinicians.

Substantial Equivalence Information

The predicate device for QANGIO XA 3D is the CAASTTM Workstation.

Especially this 2D vessel analysis (for the 2D XA project imaging) forms the basis for the 3D vessel analysis in QANGIO XA 3D. This analysis produces a 3D model of a coronary vessel from two 2D vessels detected in regular X-ray projection images. Similar functionality is provided by the CAAS™ Workstation (where it is called “QCA3D”). Further, QANGIO XA 3D provides visualization functionalities for 3D review of the model, which are also supported by CAAS™ Workstation.

QANGIO XA 3D provides (see Intended Use description above) a quantification parameter called QFR (Quantitative Flow Ratio), for which a similar parameter is also provided by the CAAS™ Workstation (where it is called “vFFR”).

From the Intended Use comparison it is concluded that the CAAS Workstation offers comparable (and more) functionality to the QANGIO XA 3D device. The main functionality, being 3D vessel reconstruction and the calculation of the pressure drop, are explicitly mentioned in the intended use and indications for use.

All functionality (including 3D vessel reconstruction and the calculation of the QFR pressure drop) is specified in the QANGIO XA 3D system requirements. All requirements are tested and all results of the tests performed are summarized in the software test statement and especially the requirements coverage matrix of QANGIO XA 3D proving traceability between requirements and tests successfully executed.

Extensive clinical evaluation has been performed based on both scientific literature review and clinical studies executed with the device. The quantified results provided by QANGIO XA 3D for the main functionality (including 3D vessel reconstruction and the calculation of the QFR pressure drop) have all been validated, both technically and clinically:

- 3D vessel reconstruction: The reconstruction of a 3D model from the 2D vessel boundaries detected on two XA images of the same vessel under different angulation have been validated clinically in studies using QCA parameters and IVUS pullbacks in patients.
- Quantitative Flow Ratio (QFR) analysis: The calculation of the QFR value is both technically and clinically validated. Estimates for precision of QFR are based on a strong body of evidence derived from multiple prospective studies. Two of the multicenter studies (FAVOR II Europe-Japan and FAVOR II China) show excellent results of true in-procedure QFR analyzed by end-users. In these prospective, observational, investigator-initiated multi-center studies QFR was evaluated for feasibility and diagnostic performance and agreement with pressure-wire derived fractional flow reserve (FFR) as reference standard. QFR and FFR were analyzed separately by different observers. The primary endpoints of sensitivity and specificity of QFR were compared to two-dimensional QCA (2D-QCA) with FFR as reference standard.

Conclusions

QANGIO XA 3D has the same intended use as the predicate device.

QANGIO XA 3D complies with international process standards (ISO 13485, ISO 14971, IEC 62304, IEC 62366 and ISO 15223).

Testing, validation and clinical evaluation have produced results consistent with design input requirements. QANGIO XA 3D is a software-only device for which there no applicable mandatory performance standards.

During the development, potential hazards were controlled by a risk management plan, including risk analysis, risk mitigation, verification and evaluation.

Medis concludes that QANGIO XA 3D is a safe and effective medical device, and is at least as safe and effective as its predicate devices. The use of QANGIO XA 3D does not change the intended use of X-ray Angiography acquisition, nor does the use of this software result in any new potential hazards.