Cercare Medical A/S
% Jennifer Willner
President
JW Regulatory Consulting LLC
406 Wacouta Street, Suite 417
SAINT PAUL MN 55101

July 14, 2023

Re: K230016
Trade/Device Name: Cercare Medical Neurosuite (CMN) Capillary Function with Virtual Expert
Regulation Number: 21 CFR 892.2050
Regulation Name: Medical image management and processing system
Regulatory Class: Class II
Product Code: LLZ
Dated: June 6, 2023
Received: June 14, 2023

Dear Jennifer Willner:

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,

Jessica S. Lamb, Ph.D.
Assistant Director
Imaging Software Team
DHT8B: Division of Radiological Imaging Devices and Electronic Products
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: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K230016

Device Name
Cercare Medical Neurosuite (CMN) Capillary Function with Virtual Expert

Indications for Use *(Describe)*
Cercare Medical Neurosuite and associated modules, including the Capillary Function module, is an image processing software package to be used by trained professionals, including physicians and medical technicians.

The software package runs on standard off-the-shelf computer or a virtual platform, such as VMware, and can be used to perform image viewing, processing, and analysis of images. Data and images are acquired through DICOM (Digital Imaging and Communications in Medicine) compliant imaging devices
Cercare Medical Neurosuite provides viewing capabilities, whereas the Capillary Function module provides analysis capabilities for functional and dynamic imaging datasets acquired with MRI including a Diffusion Weighted MRI (DWI) Module and a Dynamic Analysis Module (dynamic contrast-enhanced imaging data for MRI).

The Capillary Function module is used for visualization and analysis of dynamic imaging data, showing properties of changes in contrast over time. This functionality includes calculation of parameters related to tissue flow (perfusion) and tissue blood volume. In addition, the Capillary Function module's DWI technology is used to visualize local water diffusion properties from the analysis of diffusion-weighted MRI data.

The Virtual Expert module allows the calculation of regions of interest and the visual inspection of time attenuation curves. One clinical application is to visualize the apparent blood perfusion and diffusion and to calculate ADC threshold volume, Tmax threshold volume, and Mismatch Ratio in the brain tissue affected by acute stroke.

Areas of decreased perfusion appear as areas of changed signal intensity:
• Lower signal intensity for CBF and CBV
• Higher signal intensity for TTP, MTT, and Tmax

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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510(K) SUMMARY

510(k) Number: K230016

Date Prepared: July 12, 2023

Table 1: Submitter Information

Manufacturer:	Cercare Medical A/S Inge Lehmanns Gade 10 DK-8000 Aarhus Denmark US FDA ERN: 3019844085	Manufacturer's Contact Person: Mikkel Bo Hansen Chief Scientific Officer Phone: +45 22890125 Email: mbh@cercare-medical.com

Table 2: Device Information

Trade Name	Cercare Medical Neurosuite (CMN) Capillary Function with Virtual Expert for MRI
Common Name	CMN Capillary Function with Virtual Expert
Classification Name	System, Image Processing, Radiological
Regulation	21 CFR 892.2050
Product Code	LLZ
Regulatory Classification:	Class II
Device Panel:	Radiology

CMN Capillary Function with Virtual Expert MRI is substantially equivalent to the CMN Capillary Function Predicate Device (**Table 3**) and its modifications are similar to those provided in the iSchemaView RAPID Reference Device (**Table 4**). Neither of these have been subject to a design-related recall.

Table 3: Predicate Device

Predicate Device	Manufacturer	FDA 510(k)
CMN Capillary Function	Cercare Medical A/S	K202793

Table 4: Reference Device

Predicate Device	Manufacturer	FDA 510(k)
RAPID	iSchemaView	K182130

Device Description

Cercare Medical Neurosuite is a software-only device designed to streamline medical image processing by providing for the visualization and study of medical images. CMN can be installed on a customer PC or it can be accessed remotely using remote desktop technologies. CMN provides viewing, quantification, analysis and reporting capabilities. CMN is not intended as a dedicated PACS system for long term persistent storage of patient data.

CMN is software that is intended for use by trained professionals, including physicians and medical technicians. The software provides cerebral image processing capabilities. CMN is

intended to be used as decision support software only and the clinician continues to provide all treatment decisions.

The software is intended to visualize and study neuroimaging by image viewing and registration of medical images. CMN works with MRI (Magnetic Resonance Image) technology.

CMN accepts and produces data sets in the DICOM format. DICOM is a standard format for storing and transmitting medical image data in vendor neutral format and is managed by the DICOM Standards Committee.

CMN is a platform that allows for the addition of certain modules for further analysis. One of these modules included in this submission is Capillary Function.

CMN Capillary Function

Capillary Function, when activated in the installed Cercare Medical Neurosuite, provides further functionalities for reading, writing, visualizing and studying medical images.

Capillary Function provides perfusion post-processing technologies, where dynamically acquired perfusion MRI series can be processed to yield information relevant for assessment of the hemodynamic status of a patient.

Capillary Function generates hemodynamic markers, which can be used for management of diseases with possibly compromised hemodynamic function, such as ischemic stroke and tumors.

The generated output maps can be viewed by standard DICOM image viewers. In addition, Capillary Function includes the possibility for post-processing diffusion-weighted imaging (DWI) MRI data. Post-processing of DWI data results in maps reflective of local water diffusion properties. The post-processed DWI-derived maps can be viewed in standard DICOM image viewers. Capillary Function thus works with MRI technology.

CMN Virtual Expert

Virtual Expert, when activated in the installed CMN Capillary Function, provides further functionalities for reading, writing, visualizing, and studying medical images.

Virtual Expert provides automatic delineation of regions of interest (ROI) relevant for stroke patient assessment based on perfusion and diffusion image output generated by the Capillary Function module. Specifically, diffusion MRI images are used to generate threshold masks of perceived core lesions, whereas perfusion MRI images are used to generate threshold masks of perceived perfusion restriction. Virtual Expert thus works with MRI technology.

The generated masks can be combined into a mismatch region of interest.

Volumetric calculations and ratios can be calculated from the computed regions of interest.

Indications for Use

Cercare Medical Neurosuite and associated modules, including the Capillary Function module, is an image processing software package to be used by trained professionals, including physicians and medical technicians.

The software package runs on standard off-the-shelf computer or a virtual platform, such as VMware, and can be used to perform image viewing, processing, and analysis of images. Data and images are acquired through DICOM (Digital Imaging and Communications in Medicine) compliant imaging devices

Cercare Medical Neurosuite provides viewing capabilities, whereas the Capillary Function module provides analysis capabilities for functional and dynamic imaging datasets acquired with MRI including a Diffusion Weighted MRI (DWI) Module and a Dynamic Analysis Module (dynamic contrast-enhanced imaging data for MRI).

The Capillary Function module is used for visualization and analysis of dynamic imaging data, showing properties of changes in contrast over time. This functionality includes calculation of parameters related to tissue flow (perfusion) and tissue blood volume. In addition, the Capillary Function module's DWI technology is used to visualize local water diffusion properties from the analysis of diffusion-weighted MRI data.

The Virtual Expert module allows the calculation of mirrored regions of interest and the visual inspection of time attenuation curves. One clinical application is to visualize the apparent blood perfusion and to calculate Hypoperfused Area and Mismatch Ratio in the brain tissue affected by acute stroke.

Areas of decreased perfusion appear as areas of changed signal intensity:

- Lower signal intensity for CBF and CBV
- Higher signal intensity for TTP, TTD, MTT, and Tmax

Technological Characteristics

CMN with Capillary Function provides the following functions:

- processes DICOM images from multiple sources to provide visualization of changes of tissue perfusion, diffusion and change
- receives DICOM images from external DICOM image providers (modalities (MRI Scanners), PACS and Workstations) and sends DICOM images to external image consumers
- storage of status and results, and references therein, in a searchable database

CMN Capillary Function with Virtual Expert is a DICOM-compliant PACS software that provides comprehensive functionality to transfer, process and display modality specific imaging data. CMN runs on standard off-the-shelf computer and networking hardware and is entirely independent from CT, MRI or PACS platforms. It supports secure VPN networking or

encapsulated Secure Shell (SSH), and seamlessly integrates into an existing radiological data network.

The primary users of CMN software are medical imaging professionals who analyze tissue using CT or MRI images. The images generated by CMN provide additional diagnostic information, which is derived from the temporal/diffusion/density features of the native MRI image.

Differences in Technical Characteristics/Performance with Respect to the Predicate Device

CMN Capillary Function with Virtual Expert is identical to the Predicate CMN Capillary Function (K202793) with the exception of the following features:

- Output from the so-called SVD algorithm for computing perfusion derived markers has been exposed to the end-user and entails the common perfusion markers CBF, CBV, MTT, and Tmax, which to clearly distinguish these from the similarly named markers of the predicate device are called, respectively, CBF-basic, CBV-basic, MTT-basic, and Tmax-basic.

- Image thresholding features have been implemented via the Virtual Expert module, which provide thresholding of images and subsequent volumetric calculations relevant to ischemic stroke patient assessment.

The Subject and Predicate devices are based on the same technological elements of viewing, processing and analyzing DICOM image data to assist the clinician during diagnostic procedures. These differences do not impact the intended use or raise new questions with the safety and performance of the device.

Performance Standards

CMN Capillary Function with Virtual Expert has been developed in conformance with the following standards and FDA guidance, as applicable:

- ISO 13485:2016, Quality management systems – Requirements for regulatory purposes
- ISO 14971:2019, Medical devices – Application of risk management to medical devices
- IEC 62304:2006/Amd 1:2015, Medical device software – Software lifecycle processes
- IEC 82304-1:2016, Health Software Part 1: General Requirements for Product Safety
- IEC 62366-1:2015, Medical devices – Part 1: Application of usability engineering to medical devices
- ISO 15223-1:2021, Medical devices – Symbols to be used with medical device labels, labeling and information to be supplied
- ISO 20417:2021, Medical devices – Information to be supplied by the manufacturer
- NEMA PS 3.1-3.20:2022 Digital Imaging and Communications in Medicine (DICOM)

- Content of Premarket Submissions for Management of Cybersecurity in Medical Devices, October 2018
- Computer-Assisted Detection Devices Applied to Radiology Images and Radiology Device Data – Premarket Notification [510(k)] Submissions, July 2012

Performance Data

CMN Capillary Function with Virtual Expert complies with DICOM (Digital Imaging and Communications in Medicine), developed by the American College of Radiology and the National Electrical Manufacturers Association – NEMA PS 3.1-3.20.

Cercare conducted extensive performance validation testing and software verification and validation testing of the CMN Capillary Function with Virtual Expert. This performance validation testing demonstrated that the CMN system provides accurate representation of key processing parameters under a range of clinically relevant parameters associated with the intended use of the software. Software performance, validation and verification testing demonstrated that the CMN system met all design requirements and specifications.

Comparative performance testing was performed for the Subject Device with respect to the Predicate Device and Reference Device through bench testing including simulated digital phantoms and retrospective clinical data.

For the Capillary Function module, the retrospective clinical data was primarily used for visual inspection due to the relative nature of most perfusion image biomarkers, while rigorous testing was conducted through digital phantoms where the true parameter combinations were known. The simulated phantom data included variations of hemodynamic parameter combinations, while simultaneously simulating various experimental conditions such as patient motion, signal-to-noise ratios, and diffusion gradient schemes. Following the process undertaken with FDA on the Predicate Device (K202793), only human-like phantom testing and analyses were conducted since this approach allows for more realistic experimental settings (motion correction, noise, etc) and performance quantified through comparison of absolute bias, correlation coefficients, and multi-scale structural similarity index obtained for both devices. The established acceptance criteria were reached in all tests conducted.

For the Virtual Expert module, comparison testing of retrospective patient MR perfusion and diffusion imaging consisted of primary analyses of volumetric and spatial agreement per-patient and per-lesion. Secondary clinical application assessments (high-level context of the devices not associated with clinical claims) were then conducted in terms of image-driven decision to treat analysis through the so-called DEFUSE3 criteria. The Virtual Expert comparison testing was modeled by the comparison testing conducted for the Predicate Device (K202213) and in the associated published technical comparison study (Bathla et al, J. Neurointerventional Surg., 12:1028-1032 (2020)).

Together with software verification and validation, the performance validation demonstrated that CMN Capillary Function with Virtual Expert satisfies all design requirements and device specifications and is substantially equivalent to the Predicate Device and Reference Device.

Substantial Equivalence

In comparison with the Predicate CMN Capillary Function device (K202793) and Reference RAPID device (K182130), CMN Capillary Function with Virtual Expert has the same intended use and similar indications, technological characteristics, and principles of operation as described in the comparison table below.

Description	Subject Device	Predicate Device CMN Capillary Function (K202793)	Reference Device IschemaView Rapid (K182130)
Product Name	CMN Capillary Function with Virtual Expert	CMN Capillary Function	ISchemaView Rapid
Product Code / Regulation	LLZ / 21CFR/892.2050	LLZ / 21CFR/892.2050	LLZ / 21CFR/892.2050
Indications for Use	CMN and associated modules, including the Capillary Function module, is an image processing software package to be used by trained professionals, including physicians and medical technicians. The software package runs on standard off-the-shelf computer or a virtual platform, such as VMware, and can be used to perform image viewing, processing and analysis of images. Data and images are acquired through DICOM compliant imaging devices. CMN provides viewing capabilities, whereas the Capillary Function module provides analysis capabilities for functional and dynamic imaging datasets acquired with MRI including a Diffusion Weighted MRI (DWI) Module and a Dynamic Analysis Module (dynamic contrast-enhanced imaging data for MRI). The Capillary Function module is used for visualization and analysis of dynamic imaging data, showing properties of	CMN and associated modules, including the Capillary Function module, is an image processing software package to be used by trained professionals, including physicians and medical technicians. The software package runs on standard off-the-shelf computer or a virtual platform, such as VMware, and can be used to perform image viewing, processing and analysis of images. Data and images are acquired through DICOM compliant imaging devices. CMN provides viewing capabilities, whereas the Capillary Function module provides analysis capabilities for functional and dynamic imaging datasets acquired with MRI including a Diffusion Weighted MRI (DWI) Module and a Dynamic Analysis	iSchemaView RAPID is an image processing software package to be used by trained professionals, including but not limited to physicians and medical technicians. The software runs on a standard off-the-shelf computer or a virtual platform, such as VMware, and can be used to perform image viewing, processing and analysis of images. Data and images are acquired through DICOM compliant imaging devices. The iSchemaView RAPID provides both viewing and analysis capabilities for functional and dynamic imaging datasets acquired with CT Perfusion (CT-P), CT Angiography (CTA), and MRI including a Diffusion Weighted MRI (DWI) Module and a Dynamic Analysis Module (dynamic contrast-enhanced imaging data for MRI and CT).

Description	Subject Device	Predicate Device CMN Capillary Function (K202793)	Reference Device IschemaView Rapid (K182130)
	changes in contrast over time. This functionality includes calculation of parameters related to tissue flow (perfusion) and tissue blood volume. In addition, the Capillary Function module's DWI technology is used to visualize local water diffusion properties from the analysis of diffusion-weighted MRI data. The Virtual Expert module allows the calculation of mirrored regions of interest and the visual inspection of time attenuation curves. One clinical application is to visualize the apparent blood perfusion and to calculate Hypoperfused Area and Mismatch Ratio in the brain tissue affected by acute stroke. Areas of decreased perfusion appear as areas of changed signal intensity: • Lower signal intensity for CBF and CBV • Higher signal intensity for TTP, TTD, MTT, and TMax	Module (dynamic contrast-enhanced imaging data for MRI). The Capillary Function module is used for visualization and analysis of dynamic imaging data, showing properties of changes in contrast over time. This functionality includes calculation of parameters related to tissue flow (perfusion) and tissue blood volume. In addition, the Capillary Function module's DWI technology is used to visualize local water diffusion properties from the analysis of diffusion-weighted MRI data.	The DWI Module is used to visualize local water diffusion properties from the analysis of diffusion - weighted MRI data. The Dynamic Analysis Module is used for visualization and analysis of dynamic imaging data, showing properties of changes in contrast over time. This functionality includes calculation of parameters related to tissue flow (perfusion) and tissue blood volume. RAPID CT-Perfusion and RAPID MR-Perfusion can be used by physicians to aid in the selection of acute stroke patients (with known occlusion of the intracranial internal carotid artery or proximal middle cerebral artery) for endovascular thrombectomy. Instructions for use of contrast agents for this indication can be found in Appendix A of the User's Manual. Additional information for safe and effective drug use is available in product specific iodinated CT and gadolinium-based MR contrast drug labeling.

Description	Subject Device	Predicate Device CMN Capillary Function (K202793)	Reference Device IschemaView Rapid (K182130)
			In addition to the RAPID imaging criteria, patients must meet the clinical requirements for thrombectomy, as assessed by the physician, and have none of the following contraindications or exclusions. Contraindications/Exclusions: • Bolus Quality: absent or inadequate bolus. • Patient Motion: excessive motion leading to artifacts that make the scan technically inadequate. • Presence of Hemorrhage.
PACS Functionality			
Basic PACS Functions	View, process and analyze medical images. Communication of results through service class user protocols.	Yes	Yes
Computer Platform	Standard off-the-shelf PC workstation / server	Yes	Yes
	Virtual platform such as VMware	Yes	Yes
DICOM Compliance	Yes	Yes	Yes
Functional Overview	CMN is software package that provides for the visualization and study of changes of tissue in digital images captured by MRI. CMN provides viewing and quantification.	Same	Same

Description	Subject Device	Predicate Device CMN Capillary Function (K202793)	Reference Device IschemaView Rapid (K182130)
Data Acquisition	Acquires medical image data from DICOM compliant imaging devices and modalities	Same	Same
Data / Image Types	MRI via DICOM format	Same	Same
Acquisition and Modalities Features			
MRI	Diffusion Weighted Image (DWI)	Yes	Yes
	Dynamic Analysis tissue flow (perfusion) and tissue blood volume	Yes	Yes
Computed Parameter Maps			
Diffusion MRI	Isotropic DWI (isoDWI)	Yes	Yes
	ADC	Yes	Yes
	Zero=gradient image (B=0 image)	Yes	Yes
Perfusion MRI	Relative cerebral blood flow (rCBF)	Yes	No
	Relative cerebral blood volume (rCBV)	Yes	No
	Mean transit time (MTT)	Yes	No
	Delay	Yes	No
	Capillary transit time heterogeneity (CTH)	Yes	No
	Coefficient of variation (COV)	Yes	No
	Model-based oxygen extraction fraction (OEF (model-based))	Yes	No
	Model-based relative cerebral metabolic rate of oxygen (rCMRO2 (model-based))	Yes	No
	Relative extravasation correction (rLeakage)	Yes	No

Description	Subject Device	Predicate Device CMN Capillary Function (K202793)	Reference Device IschemaView Rapid (K182130)
	rCBF-basic	No	Yes Denoted rCBF but likely based on the same (or similar) algorithm (SVD)
	rCBV-basic	No	Yes Denoted rCBV but likely based on the same (or similar) algorithm (SVD)
	MTT-basic	No	Yes Denoted MTT but likely based on the same (or similar) algorithm (SVD)
	Tmax-basic	No	Yes Denoted Tmax but likely based on the same (or similar) algorithm (SVD)
Measurement Tools			
MRI Tools	Arterial input function (AIF)	Yes	Yes
	Time-course	Yes	Yes
	Brain mask	Yes	Yes
	Region of interest (ROI) and Volumetry	No	Yes
	Volumetric comparison between 2 ROIs	No	Yes
	Motion correction	Yes	Yes
	Export parameter maps PACS and DICOM file systems	Yes	Yes
	Acquire, transmit, process, and store medical images	Yes	Yes

Conclusions

The CMN Capillary Function with Virtual Expert performs as intended and presents no unacceptable risks to the intended patient population. The non-clinical bench data support the safety of the device and demonstrate that CMN Capillary Function with Virtual Expert performs as intended in the specified use conditions. CMN Capillary Function with Virtual Expert is substantially equivalent in intended use, technological characteristics, safety, and performance characteristics to the legally marketed Predicate device, CMN Capillary Function (K202793).