September 13, 2018

Heidelberg Engineering GmbH
% Lena Sattler
Consultant
Orasi Consulting, LLC.
1655 Forest Drive
Medina, OH 44256

Re: K181594
Trade/Device Name: Spectralis HRA+OCT and variants with OCT Angiography Module
Regulation Number: 21 CFR 886.1570
Regulation Name: Ophthalmoscope
Regulatory Class: Class II
Product Code: OBO, MYC
Dated: June 15, 2018
Received: June 18, 2018

Dear Lena Sattler:

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,

Bradley S. Cunningham -A

for Malvina B. Eydelman, M.D.
Director
Division of Ophthalmic and Ear,
Nose and Throat Devices
Office of Device Evaluation
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)*
K181594

Device Name
SPECTRALIS HRA+OCT and variants with OCT Angiography Module

Indications for Use *(Describe)*
The SPECTRALIS is a non-contact ophthalmic diagnostic imaging device. It is intended for:
- viewing the posterior segment of the eye, including two- and three-dimensional imaging
- cross-sectional imaging (SPECTRALIS HRA+OCT and SPECTRALIS OCT)
- fundus imaging
- fluorescence imaging (fluorescein angiography, indocyanine green angiography; SPECTRALIS HRA+OCT, SPECTRALIS HRA)
- autofluorescence imaging (SPECTRALIS HRA+OCT, SPECTRALIS HRA and SPECTRALIS OCT with BluePeak)
- performing measurements of ocular anatomy and ocular lesions.

The device is indicated as an aid in the detection and management of various ocular diseases, including:
- age-related macular degeneration
- macular edema
- diabetic retinopathy
- retinal and choroidal vascular diseases
- glaucoma

The device is indicated for viewing geographic atrophy.

The SPECTRALIS OCT Angiography Module is indicated as an aid in the visualization of vascular structures of the retina and choroid.

The SPECTRALIS HRA+OCT and SPECTRALIS OCT include the following reference databases:
- a retinal nerve fiber layer thickness reference database, which is used to quantitatively compare the retinal nerve fiber layer in the human retina to values of Caucasian normal subjects – the classification result being valid only for Caucasian subjects
- a reference database for retinal nerve fiber layer thickness and optic nerve head neuroretinal rim parameter measurements, which is used to quantitatively compare the retinal nerve fiber layer and neuroretinal rim in the human retina to values of normal subjects of different races and ethnicities representing the population mix of the USA (Glaucoma Module Premium Edition)

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

Date Prepared August 31, 2018

SPONSOR/510(K) OWNER/ MANUFACTURER

Heidelberg Engineering GmbH
Max-Jarecki-Strasse 8
69115 Heidelberg, Germany
Telephone: +49 6221 / 64 63 0
Facsimile: +49 6221 / 64 63 62
Email: Christoph.Schoess@HeidelbergEngineering.com
Establishment Registration No.: 8043762

OFFICIAL CONTACT PERSON

Lena Sattler
Orasi Consulting, LLC.
1655 Forest Dr.
Medina, OH 44256
Telephone: (440) 554-3706
Facsimile: (866) 904-4315
E-mail: lena@orasiconsulting.com

COMMON/USUAL NAME

Optical Coherence Tomography

PROPRIETARY OR TRADE NAMES

SPECTRALIS HRA+OCT and variants with OCT Angiography Module

CLASSIFICATION INFORMATION

Classification Name:	Tomography, Optical Coherence Ophthalmoscope, Laser, Scanning
Medical Specialty:	Ophthalmic
Device Class:	II
Classification Panel:	Ophthalmic Device Panel
Product Codes:	OBO, MYC

PRODUCT CODE: CLASSIFICATION / CFR TITLE

OBO, MYC: Class II § 21 CFR 886.1570

PRIMARY PREDICATE DEVICE

OptoVue, Inc. RTVue XR OCT Avanti with AngioVue™ Software (K153080), Software Version 2016.1.0

LEGALLY MARKETED UNMODIFIED PREDICATE DEVICE

Trade/Device Name:	SPECTRALIS HRA+OCT and variants
Applicant:	Heidelberg Engineering GmbH
510(k) Premarket Notification number:	K172649
Classification:	Class II
CFR Title:	21 CFR 886.1570
FDA Product Code(s):	OBO, MYC
Classification Name:	Tomography, Optical Coherence Ophthalmoscope, Laser, Scanning
Common Name:	Optical Coherence Tomography
Medical Specialty:	Ophthalmic
Classification Panel:	Ophthalmic Device Panel

GENERAL DEVICE DESCRIPTION

The Heidelberg Engineering SPECTRALIS HRA+OCT is a non-contact ophthalmic device used to image the anterior and posterior segments of the human eye. The SPECTRALIS HRA+OCT is a combination of a confocal laser-scanning ophthalmoscope (cSLO, the HRA portion) and a spectral-domain optical coherence tomographer (SD-OCT). The confocal laser-scanning part of the device allows for acquisition of reflectance images (with blue, green or infrared light), conventional angiography images (using fluorescein or indocyanine green dye) and autofluorescence images. The different imaging modes can be used either alone or simultaneously. The SD-OCT part of the device acquires cross-sectional and volume images, together with an HRA cSLO image.

A blue laser is used for fluorescein angiography, autofluorescence imaging, and blue reflectance imaging, and two infrared lasers are used for indocyanine green angiography and infrared reflectance imaging. A green laser is used for MultiColor imaging (“composite color images”). MultiColor imaging is the simultaneous acquisition of infrared, green and blue reflectance images that can be viewed separately or as a composite color image. For SD-OCT imaging, an infrared super-luminescent diode and a spectral interferometer are used to create the cross-sectional images.

The purpose of this premarket notification [510(k)] is to add OCT Angiography (OCTA) as an optional, add-on functionality to the SPECTRALIS HRA+OCT. Based on OCT imaging, OCTA is a non-invasive method to visualize the retinal and choroidal vasculature without the need for injection of intravenous dyes. The device generates OCTA images from analysis of temporal changes in the intensity of reflected light caused by moving particles, such as erythrocytes flowing through vessels. These changes in the OCT signal are detected by repeatedly capturing OCT images on the retina to allow for the creation of an image contrast between the perfused vessels and the static surrounding tissues.
OCTA volume scans allow for the visualization of en-face images generated from predefined or user-customizable slabs. OCT Angiography is intended for qualitative use only. No quantitative measurements are provided by the OCTA functionality.

Besides the addition of OCT Angiography, the SPECTRALIS device is unchanged. The unmodified device is the predicate device for all functions besides OCT Angiography.

INDICATIONS FOR USE – MODIFIED SPECTRALIS HRA+OCT

The SPECTRALIS is a non-contact ophthalmic diagnostic imaging device. It is intended for:

- viewing the posterior segment of the eye, including two- and three-dimensional imaging
- cross-sectional imaging (SPECTRALIS HRA+OCT and SPECTRALIS OCT)
- fundus imaging
- fluorescence imaging (fluorescein angiography, indocyanine green angiography; SPECTRALIS HRA+OCT, SPECTRALIS HRA)
- autofluorescence imaging (SPECTRALIS HRA+OCT, SPECTRALIS HRA and SPECTRALIS OCT with BluePeak)
- performing measurements of ocular anatomy and ocular lesions.

The device is indicated as an aid in the detection and management of various ocular diseases, including:

- age-related macular degeneration
- macular edema
- diabetic retinopathy
- retinal and choroidal vascular diseases
- glaucoma

The device is indicated for viewing geographic atrophy.

The SPECTRALIS OCT Angiography Module is indicated as an aid in the visualization of vascular structures of the retina and choroid.

The SPECTRALIS HRA+OCT and SPECTRALIS OCT include the following reference databases:

- a retinal nerve fiber layer thickness reference database, which is used to quantitatively compare the retinal nerve fiber layer in the human retina to values of Caucasian normal subjects – the classification result being valid only for Caucasian subjects
- a reference database for retinal nerve fiber layer thickness and optic nerve head neuroretinal rim parameter measurements, which is used to quantitatively compare the retinal nerve fiber layer and neuroretinal rim in the human retina to values of normal subjects of different races and ethnicities representing the population mix of the USA (Glaucoma Module Premium Edition)

SUBSTANTIAL EQUIVALENCE

The modified SPECTRALIS HRA+OCT and variants with OCT Angiography Module is a device modification to the cleared SPECTRALIS HRA+OCT and variants (K172649) predicate device. Technological characteristics of the device are unchanged except for the modification as stated in the General Device Description. The modified SPECTRALIS has an updated Indications for Use statement, but maintains the same fundamental scientific technology as the unmodified device. The modified SPECTRALIS HRA+OCT and variants measures the same ophthalmic features and parameters as the cleared SPECTRALIS HRA+OCT and variants in K172649. The changes applied to the SPECTRALIS since the clearance in K172649 do not change the intended patient populations, the type of acquired images, or how the SPECTRALIS may be used as an aid to clinical evaluation.

The added OCTA functionality is similar to that of the primary predicate device, RTVue XROCT Avanti with AngioVue software as cleared under K153080.

Non-clinical and clinical performance testing was conducted on the SPECTRALIS HRA+OCT to verify that the device is safe and effective for its intended use and indications for use. The modification to the device does not raise issues of safety and effectiveness. A comparison of technological characteristics and clinical performance testing demonstrate that the SPECTRALIS device is substantially equivalent to the primary predicate device, RTVue XR OCT Avanti with AngioVue software.

The Substantial Equivalence Summary tables below illustrate the comparisons of the modified SPECTRALIS to the predicate devices.

INDICATIONS FOR USE STATEMENT CHART

PRIMARY PREDICATE K153080 RTVue XR	K172649 PREDICATE DEVICE	SUBJECT DEVICE
The RTVue XR OCT Avanti with Normative Database is an optical coherence tomography system indicated for the in vivo imaging and measurement of the retina, retinal nerve fiber layer, and optic disc as a tool and aid in the diagnosis and management of retinal diseases by a clinician. The RTVue XR OCT Avanti with Normative Database is also a quantitative tool for the comparison of retina, retinal nerve fiber layer, and optic disk measurements in the human eye to a database of known normal subjects. It is intended for use as a diagnostic device to aid in the detection and management of ocular diseases. The RTVue XR OCT Avanti with AngioVue Software is indicated as an aid in the visualization of vascular structures of the retina and choroid.	The SPECTRALIS is a non-contact ophthalmic diagnostic imaging device. It is intended for viewing the posterior segment of the eye, including two- and three-dimensional imaging, cross-sectional imaging (SPECTRALIS HRA+OCT and SPECTRALIS OCT), fundus photography, fluorescence imaging (fluorescein angiography, indocyanine green angiography; SPECTRALIS HRA+OCT, SPECTRALIS HRA), autofluorescence imaging (SPECTRALIS HRA+OCT, SPECTRALIS HRA and SPECTRALIS OCT with BluePeak) and to perform measurements of ocular anatomy and ocular lesions. The device is indicated as an aid in the detection and management of various ocular diseases, including age-related macular degeneration, macular edema, diabetic retinopathy, retinal and choroidal vascular diseases, glaucoma, and for viewing geographic atrophy as well as changes in the eye that result from neurodegenerative diseases. The SPECTRALIS HRA+OCT and SPECTRALIS OCT include reference databases for retinal nerve fiber layer thickness and optic nerve head neuroretinal rim parameter measurements, which are used to quantitatively compare the retinal nerve fiber layer and neuroretinal rim in the human retina to values found in normal subjects.	The SPECTRALIS is a non-contact ophthalmic diagnostic imaging device. It is intended for: • viewing the posterior segment of the eye, including two- and three-dimensional imaging • cross-sectional imaging (SPECTRALIS HRA+OCT and SPECTRALIS OCT) • fundus imaging • fluorescence imaging (fluorescein angiography, indocyanine green angiography; SPECTRALIS HRA+OCT, SPECTRALIS HRA) • autofluorescence imaging (SPECTRALIS HRA+OCT, SPECTRALIS HRA and SPECTRALIS OCT with BluePeak) • performing measurements of ocular anatomy and ocular lesions. The device is indicated as an aid in the detection and management of various ocular diseases, including: • age-related macular degeneration • macular edema • diabetic retinopathy • retinal and choroidal vascular diseases • glaucoma The device is indicated for viewing geographic atrophy. The SPECTRALIS OCT Angiography Module is indicated as an aid in the visualization of vascular structures of the retina and choroid. The SPECTRALIS HRA+OCT and SPECTRALIS OCT include the following reference databases: • a retinal nerve fiber layer thickness reference database, which is used to quantitatively compare the retinal nerve fiber layer in the human retina to values of Caucasian normal subjects – the classification result being valid only for Caucasian subjects • a reference database for retinal nerve fiber layer thickness and optic nerve head neuroretinal rim parameter measurements, which is used to quantitatively compare the retinal nerve fiber layer and neuroretinal rim in the human retina to values of normal subjects of different races and ethnicities representing the population mix of the USA (Glaucoma Module Premium Edition)

TECHNOLOGICAL CHARACTERISTICS COMPARISON TABLE

	PRIMARY PREDICATE K153080 RTVUE XR	PREDICATE DEVICE K172649 SPECTRALIS HRA+OCT	SUBJECT DEVICE	Discussion
Device classification name	Optical Coherence Tomographer (OCT)	Optical Coherence Tomographer (OCT)	Optical Coherence Tomographer (OCT)	Same
Technology	Spectral Domain OCT	Spectral Domain OCT	Spectral Domain OCT	Same
Images of posterior segment of eye	Yes	Yes, using standard, WFO/WFO2, or UWF objective lens	Yes, using standard, WFO/WFO2, or UWF objective lens	Same
Images of anterior segment of eye	Yes	With Anterior Segment Module (K113129)	With Anterior Segment Module (K113129)	Same
OCT imaging of the anterior and posterior segment	Anterior segment: with CAM (Cornea and Anterior Module) Posterior Segment: Yes	Anterior segment: With Anterior Segment Module (K113129) Posterior Segment: Yes	Anterior segment: With Anterior Segment Module (K113129) Posterior Segment: Yes	Same
OCT Angiography	AngioVue™ Software	n/a	OCT Angiography Module; 30° OCT/OCTA field of view with standard objective	Similar to the primary predicate
Reference Databases	Comparison of retina, retinal nerve fiber layer, and optic disk measurements in the human eye to a database of known normal subjects.	RNFL thickness in reference database for 12° circle scans (Caucasian only) (K101223) RNFL thickness in reference database for fixed diameter circle scans, and ONH parameters (BMO-MRW, BMO-MRA) reference database (K152205)	RNFL thickness in reference database for 12° circle scans (Caucasian only) (K101223) RNFL thickness in reference database for fixed diameter circle scans, and ONH parameters (BMO-MRW, BMO-MRA) reference database (K152205)	Similar; SPECTRALIS does not include a Retina RDB.

	PRIMARY PREDICATE K153080 RTVUE XR	PREDICATE DEVICE K172649 SPECTRALIS HRA+OCT	SUBJECT DEVICE	Discussion
Imaging modes, lights sources and wavelength of light emitted	Live camera: • Near infrared reflectance images: LED, 735 nm, OCT: 840 nm ± 10 nm	cSLO: • Near infrared reflectance images: diode laser, 815 nm, • Blue light reflectance images: diode laser, 486 nm, or optically pumped semiconductor laser, 488 nm • Green light reflectance images: diode laser, 518 nm • Fluorescein angiography: diode laser, 486 nm, or optically pumped semiconductor laser, 488 nm • Indocyanine green angiography: diode laser, 786 nm OCT: superluminescence diode, 840 nm to 920 nm (weighted average 880 nm)	cSLO: • Near infrared reflectance images: diode laser, 815 nm, • Blue light reflectance images: diode laser, 486 nm, or optically pumped semiconductor laser, 488 nm • Green light reflectance images: diode laser, 518 nm • Fluorescein angiography: diode laser, 486 nm, or optically pumped semiconductor laser, 488 nm • Indocyanine green angiography: diode laser, 786 nm OCT: superluminescence diode, 840 nm to 920 nm (weighted average 880 nm)	Comparable for OCT imaging; Different for fundus imaging: RTVue uses a live camera for fundus imaging; SPECTRALIS uses a cSLO system with several imaging modes
Amount of light irradiated to retina (exposure)	Exposure Power at pupil: less than or equal to 750 µW (Laser Class I)	Low amount, does not exceed Class I laser accessible emission limits	Low amount, does not exceed Class I laser accessible emission limits	Same
Lateral optical resolution (OCT)	15 µm	14 µm	14 µm	Comparable
Optical depth resolution (OCT)	5 µm	7 µm	7 µm	Comparable

	PRIMARY PREDICATE K153080 RTVUE XR	PREDICATE DEVICE K172649 SPECTRALIS HRA+OCT	SUBJECT DEVICE	Discussion
Fundus imaging field of view	32° (horizontal) x 22° (vertical)	SO (standard objective): 15° x 15° to 30° x 30°	SO (standard objective): 15° x 15° to 30° x 30°	Comparable
OCT axial imaging depth	2 to 3 mm	1.9 mm	1.9 mm	RTVue has a slightly higher scanning depth
Lateral field of view (OCT)	2 to 12 mm (approximately 7° to 40°)	10°-30°	10°-30°	RTVue has a higher range for lateral field of view
Digital axial resolution (pixel size OCT)	3 µm	3.9 µm	3.9 µm	Comparable
Indications for Use (OCT Angiography part only)	The RTVue XR OCT Avanti with AngioVue Software is indicated as an aid in the visualization of vascular structures of the retina and choroid.	n/a	The SPECTRALIS OCT Angiography Module is indicated as an aid in the visualization of vascular structures of the retina and choroid.	Same Indications for Use for OCT Angiography.
OCTA acquisition	Motion-contrast technique	n/a	Motion-contrast technique	Same
OCTA algorithm	Split-spectrum amplitude-decorrelation angiography (SSADA); 2 repeats of each B-scan	n/a	Proprietary, probabilistic algorithm; 4-7 repeats of each B-scan	Same purpose (generation of OCTA flow images), but different mathematical approach.
Maximum A-scan rate for OCT and OCTA	70 kHz	85 kHz (OCT only)	85 kHz	Comparable; subject device has slightly faster acquisition rate
OCTA Analysis	Visualization of three-dimensional microvasculature	n/a	Visualization of three-dimensional microvasculature	Same as primary predicate.

	PRIMARY PREDICATE K153080 RTVUE XR	PREDICATE DEVICE K172649 SPECTRALIS HRA+OCT	SUBJECT DEVICE	Discussion
Predefined slabs	Superficial (Plexus) Deep (Plexus) Outer Retina Choroid Cap (Capillaries)	n/a	Full image Vitreoretinal Interface Full Retina Superficial Vascular Complex (SVC) Nerve Fiber Layer Vascular Plexus (NFLVP) Superficial Vascular Plexus (SVP) Deep Vascular Complex (DVC) Intermediate Capillary Plexus (ICP) Deep Capillary Plexus (DCP) Avascular Complex (AC) Choriocapillaris (CC) Choroid	Comparable to primary predicate; SPECTRALIS offers more detailed predefined slabs, but both devices cover the full retinal and choroidal vasculature networks

KEY SOFTWARE DIFFERENCES BETWEEN THE MODIFIED AND UNMODIFIED SPECTRALIS HRA+OCT

Software / firmware	**PREDICATE DEVICE K172649 Final version#**	**SUBJECT DEVICE K181594 Final version#**	**Description of changes**
SPECTRALIS Product Family software	6.6	6.9	Addition of OCT Angiography
Software Level of Concern (LOC)	Moderate	Moderate	Unchanged
Software & firmware changes			
General Product Requirements (GPR)	1.10	1.12	**1.** OCT Angiography **2.** New Glaucoma Overview Report
SPECTRALIS System	1.10	1.12	**1.** OCTA image acquisition **2.** OCTA image review **3.** Hardware requirements updated for OCTA acquisition
Heidelberg Eye Explorer (HX)	1.9	1.10	**1.** Display of GTIN number in the software **2.** Performance improvements
Acquisition Module (AQM)	6.5	6.9	**1.** OCT Angiography Acquisition Mode / UI changes **2.** OCT Angiography Processing **3.** Licensing Mechanism (Activation Codes) **4.** Memory Handling **5.** FLEX mount support (not available in the USA)
Viewing Module (VWM)	6.6	6.9	**1.** New analysis tab: Display OCT Angio **2.** New analysis tab: OCT Angiography **3.** New licensing mechanism **4.** Scan planning tool support for OCTA **5.** Configuration of printouts **6.** New printouts: Glaucoma Overview Report, OCTA Overview Report
OCT Firmware	1.5	1.6	**1.** Support for OCTA volume scans

DESIGN CONTROL

Heidelberg Engineering designed and developed the modified SPECTRALIS per the company's Design Control procedure, which complies with the FDA Quality System Regulations CFR Part 820 and ISO 13485:2016. The Design Control procedure also incorporates Risk Management procedures, which comply with ISO 14971:2007.

Risk assessment was conducted on the modified SPECTRALIS, and the impact of the design modifications were assessed on the predicate 510(k) cleared device.

The modified SPECTRALIS is manufactured and tested in the exact manner as the predicate 510(k) cleared device.

Heidelberg Engineering performed bench testing, and software verification and validation, to confirm that the modified SPECTRALIS HRA+OCT functions as intended, and that the addition of OCT Angiography does not interfere with existing SPECTRALIS functionality.

NON-CLINICAL PERFORMANCE TESTING

The modified SPECTRALIS was evaluated according to the requirements of FDA recognized consensus standards ISO 14971, Medical Devices - Application of Risk Management to Medical Devices and AAMI / ANSI / IEC 62304:2006 Medical Device Software - Software Life Cycle Processes and was found to meet the requirements of the applicable parts.

Laser safety testing, biocompatibility, electromagnetic compatibility, and electrical safety testing was conducted on the previously cleared SPECTRALIS HRA+OCT device. Since there were no hardware changes for the addition of OCT Angiography, these performance and safety tests were not required to be repeated for this change.

Software documentation was provided, and software verification and validation was conducted as recommended by FDA's Guidance for Industry and FDA Staff, "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices."

CLINICAL PERFORMANCE TESTING

A prospective, case series study was conducted at a single clinical site in the United States to compare the clinical performance of the OCTA functionality between the SPECTRALIS and the RTVue XR devices. 79 participants age 22 or older meeting eligibility criteria in at least one eye were enrolled into a single study cohort with two sub-groups, the "Normal group" (without ocular pathology) and the "Pathology group" (those with retinal vascular pathologies affecting different anatomic depths throughout the retina and choroid). One eye of each participant was selected to be the study eye, (randomly determined when both eyes were eligible). After completion of a baseline clinical evaluation, eligible participants underwent the following imaging:

1. OCTA imaging with the Spectralis (HR10 and HS20 scan patterns) and the RTVue XR (AngioRetina 3.0 mm and 6.0 mm scan patterns);
2. structural (non-OCTA) OCT imaging;
3. color fundus photography (CFP);
4. fluorescein angiography (FA) and, when clinically indicated, indocyanine green angiography (ICGA).

"Normal group" participants were randomized to having OCTA imaging performed before dilation or after dilation. All "Pathology group" participants underwent dilated OCTA imaging unless the location of relevant pathology was already known. For those included into the "Pathology group," the investigator determined a "primary pathology of interest" (PPOI) and corresponding "region of interest" (ROI) to which reading center (RC) grading is directed. Device operators were instructed to image only the designated ROI, and were masked to the determined PPOI. Up to three re-attempts were allowed when the proper ROI was not acquired. The clinical site reviewed the imaging and selected the first acceptable OCTA image set from each OCTA device; any manual segmentation correction was performed by the clinical site at the investigator's discretion. Acquired images were submitted to an independent RC (two sets of three qualified, masked graders, one set for OCTA image grading, one set for FA/ICGA grading) for evaluation of image quality and clinically relevant content.

The following endpoints were evaluated:

1) "Response rate":
   - The percentage of eye with SPECTRALIS image quality score (of OCTA images) greater than or equal to that of the RTVue XR; scoring is based on a scale (0 = poor, 1 = average, 2 = good).
   - The percentage of eye with SPECTRALIS anatomical structure score greater than or equal to that of the RTVue XR for clinically relevant vascular structures (foveal avascular zone, large vessels, small vessels, end capillaries); scoring is based on a scale (0 = unable to distinguish, 1 = difficult, 2 = easy).

2) Agreement between OCTA images and FA/ICGA images (the defined reference standard) in the ease in identification of the following:
   - The pre-specified PPOI;
   - Pertinent vascular pathology (microaneurysms, retinal vascular tortuosity, choroidal neovascularization, retinal ischemia, retinal neovascularization, other types).

   This endpoint was evaluated based on the analysis of the boxed area of the FA/ICGA images that best represented the area scanned by each device's respective OCTA scan pattern.

3) The frequency and nature of adverse events.

A total of 95 participants were enrolled, 37 "Normal," 58 "Pathology." 32 "Normal" and 47 "Pathology" participants completed the study; the rest were discontinued as screen failures. The primary analyses were based on data from these 79 participants. The median age in the "Normal" and "Pathology" sub-groups are 36.5 and 68, respectively (range, 24-77 "Normal," 27-90 "Pathology"). The proportion of women was 75% and 49% in the "Normal" and "Pathology" sub-groups, respectively. The majority (86%) of the entire cohort was racially white. In the "Normal" sub-group, the mean Q values (a signal strength indicator) were 41.5±2.7 (range 37-46) for the HR10 scan pattern and 38.6±2.6 (range 33-43) for the HS20 scan pattern; in the "Pathology" sub-group, the mean Q values were 35.8±3.4 (range 28-42) and 34.3±2.9 (range 26-39) for the HR10 and HS20 scan patterns, respectively. The RTVue SSI values in the "Normal" sub-group were 75.0±7.1 (range 57-89) and 70.5±7.3 (range 52-84) for the AngioRetina 3.0 mm and 6.0 mm scan patterns, respectively. In the "Pathology" sub-group, the RTVue SSI values were 61.4±10.3 (range 41-84) and 56.9±9.6 (range 37-75) for the AngioRetina 3.0 mm and 6.0 mm scan patterns, respectively. The distribution of vascular pathologies in the "Pathology" sub-group is shown in Table 1.

TABLE 1: VASCULAR PATHOLOGY OF STUDY EYES

	Normal (N=32)	Pathology (N=47)	Total (N=79)
Primary vascular pathology of interest			
None	32 (100)	0 (0)	32 (41)
Retinal ischemia	0 (0)	8 (17)	8 (10)
Microaneurysms	0 (0)	18 (38)	18 (23)
Choroidal neovascularization	0 (0)	14 (30)	14 (18)
Retinal neovascularization	0 (0)	1 (2)	1 (1)
Retinal vascular tortuosity	0 (0)	3 (6)	3 (4)
Other	0 (0)	3 (6)	3 (4)
Vascular pathology[1]			
None	32 (100)	0 (0)	32 (41)
Retinal ischemia	0 (0)	16 (34)	16 (20)
Microaneurysms	0 (0)	22 (47)	22 (28)
Choroidal neovascularization	0 (0)	14 (30)	14 (18)
Retinal neovascularization	0 (0)	3 (6)	3 (4)
Retinal vascular tortuosity	0 (0)	10 (21)	10 (13)
Other	0 (0)	3 (6)	3 (4)

[1] Eyes may have more than 1 pathology.

SPECTRALIS OCTA images rejection frequencies for the HR10 scan pattern were 5% and 15% in the “Normal” and “Pathology” sub-groups, respectively, and 14% and 9% for the HS20 scan pattern. RTVue OCTA image rejection frequencies for the AngioRetina 3.0 mm scan pattern were 3% and 12% in the “Normal” and “Pathology” sub-groups, respectively, and 3% and 18% for the AngioRetina 6.0 mm scan pattern. Manual segmentation correction frequencies for the HR10 scan pattern were 16% and 52% in the “Normal” and “Pathology” sub-groups, respectively, and 38% and 63% for the HS20 scan pattern. Manual segmentation correction frequencies for the AngioRetina 3.0 mm scan pattern were 47% and 52% in the “Normal” and “Pathology” sub-groups, respectively, and 22% and 38% for the AngioRetina 6.0 mm scan pattern.

For image quality assessment for each OCTA device and scan pattern, all but one image were graded as average or good (score ≥ 1) by the graders. The consensus OCTA image quality score response rates are summarized in Table 2.

TABLE 2: COMPARISON OF CONSENSUS OCTA IMAGE QUALITY BETWEEN SPECTRALIS AND RTVUE FOR NORMAL SUBJECTS AND VASCULAR PATHOLOGY SUBJECTS

	SPECTRALIS Score[1]				Response Rate (%)[3]
RTVue Score[1], n (%)	0	1	2	Total	(95% CI)
Normal Subjects					
Scan pattern 1[2] (N=32)					75.0 (56.6, 88.5)
0	0 (0)	0 (0)	0 (0)	0 (0)	
1	0 (0)	3 (9)	2 (6)	5 (16)	
2	0 (0)	8 (25)	19 (59)	27 (84)	
Total	0 (0)	11 (34)	21 (66)	32	
Scan pattern 2[2] (N=32)					71.9 (53.3, 86.3)
0	0 (0)	0 (0)	0 (0)	0 (0)	
1	0 (0)	3 (9)	6 (19)	9 (28)	
2	0 (0)	9 (28)	14 (44)	23 (72)	
Total	0 (0)	12 (38)	20 (63)	32	
Vascular Pathology Subjects					
Scan pattern 1[2] (N=47)					93.6 (82.5, 98.7)
0	0 (0)	0 (0)	0 (0)	0 (0)	
1	0 (0)	32 (68)	3 (6)	35 (74)	
2	0 (0)	3 (6)	9 (19)	12 (26)	
Total	0 (0)	35 (74)	12 (26)	47	
Scan pattern 2[2] (N=47)					89.4 (76.9, 96.5)
0	0 (0)	0 (0)	0 (0)	0 (0)	
1	1 (2)	29 (62)	8 (17)	38 (81)	
2	0 (0)	4 (9)	5 (11)	9 (19)	
Total	1 (2)	33 (70)	13 (28)	47	

N = Number of subjects with image quality scores from both devices
[1] Score: 0=Poor; 1=Average; 2=Good
[2] Scan pattern 1: SPECTRALIS 10° x 10° and RTVue 3mm x 3mm; Scan pattern 2: SPECTRALIS 20° x 20° and RTVue 6mm x 6mm
[3] Percentage of eyes with SPECTRALIS score greater than or equal to RTVue score. 95% confidence interval is calculated by exact method.

Total inter-grader agreement on image quality scoring (where the same image quality score was determined by all three graders for an OCTA image) is summarized in Table 3.

TABLE 3: INTER-GRADER AGREEMENT IN OCTA IMAGE QUALITY

	Normal (N=32)	Pathology (N=47)	Total (N=79)
SPECTRALIS 10° x 10°			
Number of subjects	32	47	79
Same score from 3 graders	27 (84)	37 (79)	64 (81)
95% CI[1]	67.2, 94.7	64.3, 89.3	70.6, 89.0
Same score from 2 graders	5 (16)	10 (21)	15 (19)
Different scores from 3 graders	0 (0)	0 (0)	0 (0)
RTVue 3mm x 3mm			
Number of subjects	32	47	79
Same score from 3 graders	25 (78)	28 (60)	53 (67)
95% CI[1]	60.0, 90.7	44.3, 73.6	55.6, 77.3
Same score from 2 graders	7 (22)	19 (40)	26 (33)
Different scores from 3 graders	0 (0)	0 (0)	0 (0)
SPECTRALIS 20° x 20°			
Number of subjects	32	47	79
Same score from 3 graders	23 (72)	39 (83)	62 (78)
95% CI[1]	53.3, 86.3	69.2, 92.4	67.8, 86.9
Same score from 2 graders	9 (28)	8 (17)	17 (22)
Different scores from 3 graders	0 (0)	0 (0)	0 (0)
RTVue 6mm x 6mm			
Number of subjects	32	47	79
Same score from 3 graders	23 (72)	30 (64)	53 (67)
95% CI[1]	53.3, 86.3	48.5, 77.3	55.6, 77.3
Same score from 2 graders	9 (28)	17 (36)	26 (33)
Different scores from 3 graders	0 (0)	0 (0)	0 (0)

[1] Exact 95% confidence interval

The consensus overall anatomical structure score response rate (percentage of eyes with SPECTRALIS anatomical structure score greater than or equal to RTVue anatomical structure score) ranged from 85.3% to 97.5% for the four key anatomical structures [Table 4: foveal avascular zone (FAZ), Table 5: large vessels (LV), Table 6: small vessels (SV), and Table 7: end capillaries (EC)].

TABLE 4: COMPARISON OF CONSENSUS VISUALIZATION OF FOVEAL AVASCULAR ZONE BORDER BETWEEN SPECTRALIS AND RTVUE

	SPECTRALIS Score[1]				Response Rate (%)[3]
RTVue Score[1], n (%)	0	1	2	Total	(95% CI)
All Subjects					
Scan pattern 1[2] (N=68)					95.6 (87.6, 99.1)
0	0 (0)	0 (0)	0 (0)	0 (0)	
1	0 (0)	12 (18)	2 (3)	14 (21)	
2	0 (0)	3 (4)	51 (75)	54 (79)	
Total	0 (0)	15 (22)	53 (78)	68	
Scan pattern 2[2] (N=75)					85.3 (75.3, 92.4)
0	1 (1)	0 (0)	0 (0)	1 (1)	
1	3 (4)	14 (19)	11 (15)	28 (37)	
2	1 (1)	7 (9)	38 (51)	46 (61)	
Total	5 (7)	21 (28)	49 (65)	75	
Normal Subjects					
Scan pattern 1[2] (N=32)					100.0 (89.1, 100.0)
0	0 (0)	0 (0)	0 (0)	0 (0)	
1	0 (0)	0 (0)	0 (0)	0 (0)	
2	0 (0)	0 (0)	32 (100)	32 (100)	
Total	0 (0)	0 (0)	32 (100)	32	
Scan pattern 2[2] (N=32)					96.9 (83.8, 99.9)
0	0 (0)	0 (0)	0 (0)	0 (0)	
1	0 (0)	1 (3)	3 (9)	4 (13)	
2	0 (0)	1 (3)	27 (84)	28 (88)	
Total	0 (0)	2 (6)	30 (94)	32	
Vascular Pathology Subjects					
Scan pattern 1[2] (N=36)					91.7 (77.5, 98.2)
0	0 (0)	0 (0)	0 (0)	0 (0)	
1	0 (0)	12 (33)	2 (6)	14 (39)	
2	0 (0)	3 (8)	19 (53)	22 (61)	
Total	0 (0)	15 (42)	21 (58)	36	
Scan pattern 2[2] (N=43)					76.7 (61.4, 88.2)
0	1 (2)	0 (0)	0 (0)	1 (2)	
1	3 (7)	13 (30)	8 (19)	24 (56)	
2	1 (2)	6 (14)	11 (26)	18 (42)	
Total	5 (12)	19 (44)	19 (44)	43	

Number of subjects with OCTA image quality scores from either device. The anatomical structure score for a poor quality OCTA image is assigned to 0.

1 Score: 0=Unable to be distinguished; 1=Difficult; 2=Easy

2 Scan pattern 1: SPECTRALIS 10° x 10° and RTVue 3mm x 3mm; Scan pattern 2: SPECTRALIS 20° x 20° and RTVue 6mm x 6mm

3 Percentage of eyes with SPECTRALIS score greater than or equal to RTVue score. 95% confidence interval is calculated by exact method.

TABLE 5: COMPARISON OF CONSENSUS VISUALIZATION OF LARGE VESSELS BETWEEN SPECTRALIS AND RTVUE

	SPECTRALIS Score[1]				Response Rate (%)[3]
RTVue Score[1], n (%)	0	1	2	Total	(95% CI)
All Subjects					
Scan pattern 1[2] (N=79)					97.5 (91.2, 99.7)
0	0 (0)	0 (0)	0 (0)	0 (0)	
1	0 (0)	1 (1)	0 (0)	1 (1)	
2	0 (0)	2 (3)	76 (96)	78 (99)	
Total	0 (0)	3 (4)	76 (96)	79	
Scan pattern 2[2] (N=79)					97.5 (91.2, 99.7)
0	0 (0)	0 (0)	0 (0)	0 (0)	
1	1 (1)	0 (0)	0 (0)	1 (1)	
2	0 (0)	1 (1)	77 (97)	78 (99)	
Total	1 (1)	1 (1)	77 (97)	79	
Normal Subjects					
Scan pattern 1[2] (N=32)					100.0 (89.1, 100.0)
0	0 (0)	0 (0)	0 (0)	0 (0)	
1	0 (0)	0 (0)	0 (0)	0 (0)	
2	0 (0)	0 (0)	32 (100)	32 (100)	
Total	0 (0)	0 (0)	32 (100)	32	
Scan pattern 2[2] (N=32)					100.0 (89.1, 100.0)
0	0 (0)	0 (0)	0 (0)	0 (0)	
1	0 (0)	0 (0)	0 (0)	0 (0)	
2	0 (0)	0 (0)	32 (100)	32 (100)	
Total	0 (0)	0 (0)	32 (100)	32	
Vascular Pathology Subjects					
Scan pattern 1[2] (N=47)					95.7 (85.5, 99.5)
0	0 (0)	0 (0)	0 (0)	0 (0)	
1	0 (0)	1 (2)	0 (0)	1 (2)	
2	0 (0)	2 (4)	44 (94)	46 (98)	
Total	0 (0)	3 (6)	44 (94)	47	
Scan pattern 2[2] (N=47)					95.7 (85.5, 99.5)
0	0 (0)	0 (0)	0 (0)	0 (0)	
1	1 (2)	0 (0)	0 (0)	1 (2)	
2	0 (0)	1 (2)	45 (96)	46 (98)	
Total	1 (2)	1 (2)	45 (96)	47	

Number of subjects with OCTA image quality scores from either device. The anatomical structure score for a poor quality OCTA image is assigned to 0.

1 Score: 0=Unable to be distinguished; 1=Difficult; 2=Easy

2 Scan pattern 1: SPECTRALIS 10° x 10° and RTVue 3mm x 3mm; Scan pattern 2: SPECTRALIS 20° x 20° and RTVue 6mm x 6mm

3 Percentage of eyes with SPECTRALIS score greater than or equal to RTVue score. 95% confidence interval is calculated by exact method.

TABLE 6: COMPARISON OF CONSENSUS VISUALIZATION OF SMALL VESSELS BETWEEN SPECTRALIS AND RTVUE

	SPECTRALIS Score[1]				Response Rate (%)[3]
RTVue Score[1], n (%)	0	1	2	Total	(95% CI)
All Subjects					
Scan pattern 1[2] (N=79)					94.9 (87.5, 98.6)
0	0 (0)	0 (0)	0 (0)	0 (0)	
1	0 (0)	6 (8)	3 (4)	9 (11)	
2	0 (0)	4 (5)	66 (84)	70 (89)	
Total	0 (0)	10 (13)	69 (87)	79	
Scan pattern 2[2] (N=79)					88.6 (79.5, 94.7)
0	0 (0)	0 (0)	0 (0)	0 (0)	
1	1 (1)	2 (3)	4 (5)	7 (9)	
2	0 (0)	8 (10)	64 (81)	72 (91)	
Total	1 (1)	10 (13)	68 (86)	79	
Normal Subjects					
Scan pattern 1[2] (N=32)					100.0 (89.1, 100.0)
0	0 (0)	0 (0)	0 (0)	0 (0)	
1	0 (0)	0 (0)	0 (0)	0 (0)	
2	0 (0)	0 (0)	32 (100)	32 (100)	
Total	0 (0)	0 (0)	32 (100)	32	
Scan pattern 2[2] (N=32)					100.0 (89.1, 100.0)
0	0 (0)	0 (0)	0 (0)	0 (0)	
1	0 (0)	0 (0)	0 (0)	0 (0)	
2	0 (0)	0 (0)	32 (100)	32 (100)	
Total	0 (0)	0 (0)	32 (100)	32	
Vascular Pathology Subjects					
Scan pattern 1[2] (N=47)					91.5 (79.6, 97.6)
0	0 (0)	0 (0)	0 (0)	0 (0)	
1	0 (0)	6 (13)	3 (6)	9 (19)	
2	0 (0)	4 (9)	34 (72)	38 (81)	
Total	0 (0)	10 (21)	37 (79)	47	
Scan pattern 2[2] (N=47)					80.9 (66.7, 90.9)
0	0 (0)	0 (0)	0 (0)	0 (0)	
1	1 (2)	2 (4)	4 (9)	7 (15)	
2	0 (0)	8 (17)	32 (68)	40 (85)	
Total	1 (2)	10 (21)	36 (77)	47	

Number of subjects with OCTA image quality scores from either device. The anatomical structure score for a poor quality OCTA image is assigned to 0.

1 Score: 0=Unable to be distinguished; 1=Difficult; 2=Easy

2 Scan pattern 1: SPECTRALIS 10° x 10° and RTVue 3mm x 3mm; Scan pattern 2: SPECTRALIS 20° x 20° and RTVue 6mm x 6mm

3 Percentage of eyes with SPECTRALIS score greater than or equal to RTVue score. 95% confidence interval is calculated by exact method.

TABLE 7: COMPARISON OF CONSENSUS VISUALIZATION OF END CAPILLARIES BETWEEN SPECTRALIS AND RTVUE

	SPECTRALIS Score[1]				Response Rate (%)[3]
RTVue Score[1], n (%)	0	1	2	Total	(95% CI)
All Subjects					
Scan pattern 1[2] (N=79)					89.9 (81.0, 95.5)
0	0 (0)	0 (0)	0 (0)	0 (0)	
1	1 (1)	19 (24)	5 (6)	25 (32)	
2	0 (0)	7 (9)	47 (59)	54 (68)	
Total	1 (1)	26 (33)	52 (66)	79	
Scan pattern 2[2] (N=79)					92.4 (84.2, 97.2)
0	1 (1)	0 (0)	0 (0)	1 (1)	
1	0 (0)	26 (33)	22 (28)	48 (61)	
2	0 (0)	6 (8)	24 (30)	30 (38)	
Total	1 (1)	32 (41)	46 (58)	79	
Normal Subjects					
Scan pattern 1[2] (N=32)					100.0 (89.1, 100.0)
0	0 (0)	0 (0)	0 (0)	0 (0)	
1	0 (0)	0 (0)	0 (0)	0 (0)	
2	0 (0)	0 (0)	32 (100)	32 (100)	
Total	0 (0)	0 (0)	32 (100)	32	
Scan pattern 2[2] (N=32)					90.6 (75.0, 98.0)
0	0 (0)	0 (0)	0 (0)	0 (0)	
1	0 (0)	0 (0)	11 (34)	11 (34)	
2	0 (0)	3 (9)	18 (56)	21 (66)	
Total	0 (0)	3 (9)	29 (91)	32	
Vascular Pathology Subjects					
Scan pattern 1[2] (N=47)					83.0 (69.2, 92.4)
0	0 (0)	0 (0)	0 (0)	0 (0)	
1	1 (2)	19 (40)	5 (11)	25 (53)	
2	0 (0)	7 (15)	15 (32)	22 (47)	
Total	1 (2)	26 (55)	20 (43)	47	
Scan pattern 2[2] (N=47)					93.6 (82.5, 98.7)
0	1 (2)	0 (0)	0 (0)	1 (2)	
1	0 (0)	26 (55)	11 (23)	37 (79)	
2	0 (0)	3 (6)	6 (13)	9 (19)	
Total	1 (2)	29 (62)	17 (36)	47	

Number of subjects with OCTA image quality scores from either device. The anatomical structure score for a poor quality OCTA image is assigned to 0.

1 Score: 0=Unable to be distinguished; 1=Difficult; 2=Easy

2 Scan pattern 1: SPECTRALIS 10° x 10° and RTVue 3mm x 3mm; Scan pattern 2: SPECTRALIS 20° x 20° and RTVue 6mm x 6mm

3 Percentage of eyes with SPECTRALIS score greater than or equal to RTVue score. 95% confidence interval is calculated by exact method.

The agreement in identification of vascular pathology and the PPOI between SPECTRALIS OCTA images and RTVue OCTA images is summarized in Table 8 through Table 13.

TABLE 8: AGREEMENT IN CONSENSUS IDENTIFICATION OF MICROANEURYSMS BETWEEN SPECTRALIS AND RTVUE USING BOXED AREA OF FA/ICGA

SPECTRALIS	RTVue 3mm x 3mm			SPECTRALIS	RTVue 6mm x 6mm		
10° x 10°	Match[1]	Not Match[2]	Total	20° x 20°	Match[1]	Not Match[2]	Total
All Subjects							
Match[1]	71 (90)	1 (1)	72 (91)	Match[1]	71 (90)	3 (4)	74 (94)
Not Match[2]	0 (0)	7 (9)	7 (9)	Not Match[2]	1 (1)	4 (5)	5 (6)
Total	71 (90)	8 (10)	79	Total	72 (91)	7 (9)	79
PoA (95% CI)[3]	98.7 (93.1, 100.0)			PoA (95% CI)[3]	94.9 (87.5, 98.6)		
Ratio (95% CI)[4]	1.014 (0.987, 1.042)			Ratio (95% CI)[4]	1.028 (0.974, 1.084)		
Normal Subjects							
Match[1]	29 (91)	0 (0)	29 (91)	Match[1]	29 (91)	1 (3)	30 (94)
Not Match[2]	0 (0)	3 (9)	3 (9)	Not Match[2]	0 (0)	2 (6)	2 (6)
Total	29 (91)	3 (9)	32	Total	29 (91)	3 (9)	32
PoA (95% CI)[3]	100.0 (89.1, 100.0)			PoA (95% CI)[3]	96.9 (83.8, 99.9)		
Ratio (95% CI)[4]	1.000 (1.000, 1.000)			Ratio (95% CI)[4]	1.034 (0.968, 1.106)		
Vascular Pathology Subjects							
Match[1]	42 (89)	1 (2)	43 (91)	Match[1]	42 (89)	2 (4)	44 (94)
Not Match[2]	0 (0)	4 (9)	4 (9)	Not Match[2]	1 (2)	2 (4)	3 (6)
Total	42 (89)	5 (11)	47	Total	43 (91)	4 (9)	47
PoA (95% CI)[3]	97.9 (88.7, 99.9)			PoA (95% CI)[3]	93.6 (82.5, 98.7)		
Ratio (95% CI)[4]	1.024 (0.978, 1.072)			Ratio (95% CI)[4]	1.023 (0.946, 1.106)		

1 Between the FA/ICGA image and the OCTA image from a device, the pathology is present in both images or is absent from both images.

2 Between the FA/ICGA image and the OCTA image from a device, the pathology is present in one image and is absent from the other image, or at least one image is ungradable.

3 PoA = Percent of agreement between SPECTRALIS and RTVue. 95% confidence interval is calculated by exact method.

4 Ratio of the percentages of matching with FA/ICGA (SPECTRALIS to RTVue). 95% confidence interval is estimated by a log-linear regression with device as a single covariate using generalized estimating equation. NE = Not evaluable

TABLE 9: AGREEMENT IN CONSENSUS IDENTIFICATION OF RETINAL VASCULAR TORTUOSITY BETWEEN SPECTRALIS AND RTVUE USING BOXED AREA OF FA/ICGA

SPECTRALIS	RTVue 3mm x 3mm			SPECTRALIS	RTVue 6mm x 6mm		
10° x 10°	Match[1]	Not Match[2]	Total	20° x 20°	Match[1]	Not Match[2]	Total
All Subjects							
Match[1]	66 (84)	4 (5)	70 (89)	Match[1]	72 (91)	1 (1)	73 (92)
Not Match[2]	0 (0)	9 (11)	9 (11)	Not Match[2]	1 (1)	5 (6)	6 (8)
Total	66 (84)	13 (16)	79	Total	73 (92)	6 (8)	79
PoA (95% CI)[3]	94.9 (87.5, 98.6)			PoA (95% CI)[3]	97.5 (91.2, 99.7)		
Ratio (95% CI)[4]	1.061 (1.001, 1.124)			Ratio (95% CI)[4]	1.000 (0.963, 1.039)		
Normal Subjects							
Match[1]	31 (97)	1 (3)	32 (100)	Match[1]	32 (100)	0 (0)	32 (100)
Not Match[2]	0 (0)	0 (0)	0 (0)	Not Match[2]	0 (0)	0 (0)	0 (0)
Total	31 (97)	1 (3)	32	Total	32 (100)	0 (0)	32
PoA (95% CI)[3]	96.9 (83.8, 99.9)			PoA (95% CI)[3]	100.0 (89.1, 100.0)		
Ratio (95% CI)[4]	1.032 (NE)			Ratio (95% CI)[4]	1.000 (NE)		
Vascular Pathology Subjects							
Match[1]	35 (74)	3 (6)	38 (81)	Match[1]	40 (85)	1 (2)	41 (87)
Not Match[2]	0 (0)	9 (19)	9 (19)	Not Match[2]	1 (2)	5 (11)	6 (13)
Total	35 (74)	12 (26)	47	Total	41 (87)	6 (13)	47
PoA (95% CI)[3]	93.6 (82.5, 98.7)			PoA (95% CI)[3]	95.7 (85.5, 99.5)		
Ratio (95% CI)[4]	1.086 (0.989, 1.192)			Ratio (95% CI)[4]	1.000 (0.935, 1.070)		

1 Between the FA/ICGA image and the OCTA image from a device, the pathology is present in both images or is absent from both images.

2 Between the FA/ICGA image and the OCTA image from a device, the pathology is present in one image and is absent from the other image, or at least one image is ungradable.

3 PoA = Percent of agreement between SPECTRALIS and RTVue. 95% confidence interval is calculated by exact method.

4 Ratio of the percentages of matching with FA/ICGA (SPECTRALIS to RTVue). 95% confidence interval is estimated by a log-linear regression with device as a single covariate using generalized estimating equation. NE = Not evaluable

TABLE 10: AGREEMENT IN CONSENSUS IDENTIFICATION OF CHOROIDAL NEOVASCULARIZATION BETWEEN SPECTRALIS AND RTVUE USING BOXED AREA OF FA/ICGA

SPECTRALIS	RTVue 3mm x 3mm			SPECTRALIS	RTVue 6mm x 6mm		
10° x 10°	Match[1]	Not Match[2]	Total	20° x 20°	Match[1]	Not Match[2]	Total
All Subjects							
Match[1]	71 (90)	3 (4)	74 (94)	Match[1]	72 (91)	0 (0)	72 (91)
Not Match[2]	0 (0)	5 (6)	5 (6)	Not Match[2]	1 (1)	6 (8)	7 (9)
Total	71 (90)	8 (10)	79	Total	73 (92)	6 (8)	79
PoA (95% CI)[3]	96.2 (89.3, 99.2)			PoA (95% CI)[3]	98.7 (93.1, 100.0)		
Ratio (95% CI)[4]	1.042 (0.995, 1.092)			Ratio (95% CI)[4]	0.986 (0.960, 1.013)		
Normal Subjects							
Match[1]	32 (100)	0 (0)	32 (100)	Match[1]	32 (100)	0 (0)	32 (100)
Not Match[2]	0 (0)	0 (0)	0 (0)	Not Match[2]	0 (0)	0 (0)	0 (0)
Total	32 (100)	0 (0)	32	Total	32 (100)	0 (0)	32
PoA (95% CI)[3]	100.0 (89.1, 100.0)			PoA (95% CI)[3]	100.0 (89.1, 100.0)		
Ratio (95% CI)[4]	1.000 (NE)			Ratio (95% CI)[4]	1.000 (NE)		
Vascular Pathology Subjects							
Match[1]	39 (83)	3 (6)	42 (89)	Match[1]	40 (85)	0 (0)	40 (85)
Not Match[2]	0 (0)	5 (11)	5 (11)	Not Match[2]	1 (2)	6 (13)	7 (15)
Total	39 (83)	8 (17)	47	Total	41 (87)	6 (13)	47
PoA (95% CI)[3]	93.6 (82.5, 98.7)			PoA (95% CI)[3]	97.9 (88.7, 99.9)		
Ratio (95% CI)[4]	1.077 (0.990, 1.171)			Ratio (95% CI)[4]	0.976 (0.930, 1.024)		

1 Between the FA/ICGA image and the OCTA image from a device, the pathology is present in both images or is absent from both images.

2 Between the FA/ICGA image and the OCTA image from a device, the pathology is present in one image and is absent from the other image, or at least one image is ungradable.

3 PoA = Percent of agreement between SPECTRALIS and RTVue. 95% confidence interval is calculated by exact method.

4 Ratio of the percentages of matching with FA/ICGA (SPECTRALIS to RTVue). 95% confidence interval is estimated by a log-linear regression with device as a single covariate using generalized estimating equation. NE = Not evaluable

TABLE 11: AGREEMENT IN CONSENSUS IDENTIFICATION OF RETINAL ISCHEMIA BETWEEN SPECTRALIS AND RTVUE USING BOXED AREA OF FA/ICGA

SPECTRALIS	RTVue 3mm x 3mm			SPECTRALIS	RTVue 6mm x 6mm		
10° x 10°	Match[1]	Not Match[2]	Total	20° x 20°	Match[1]	Not Match[2]	Total
All Subjects							
Match[1]	62 (78)	4 (5)	66 (84)	Match[1]	65 (82)	3 (4)	68 (86)
Not Match[2]	3 (4)	10 (13)	13 (16)	Not Match[2]	1 (1)	10 (13)	11 (14)
Total	65 (82)	14 (18)	79	Total	66 (84)	13 (16)	79
PoA (95% CI)[3]	91.1 (82.6, 96.4)			PoA (95% CI)[3]	94.9 (87.5, 98.6)		
Ratio (95% CI)[4]	1.015 (0.938, 1.099)			Ratio (95% CI)[4]	1.030 (0.972, 1.092)		
Normal Subjects							
Match[1]	32 (100)	0 (0)	32 (100)	Match[1]	32 (100)	0 (0)	32 (100)
Not Match[2]	0 (0)	0 (0)	0 (0)	Not Match[2]	0 (0)	0 (0)	0 (0)
Total	32 (100)	0 (0)	32	Total	32 (100)	0 (0)	32
PoA (95% CI)[3]	100.0 (89.1, 100.0)			PoA (95% CI)[3]	100.0 (89.1, 100.0)		
Ratio (95% CI)[4]	1.000 (NE)			Ratio (95% CI)[4]	1.000 (NE)		
Vascular Pathology Subjects							
Match[1]	30 (64)	4 (9)	34 (72)	Match[1]	33 (70)	3 (6)	36 (77)
Not Match[2]	3 (6)	10 (21)	13 (28)	Not Match[2]	1 (2)	10 (21)	11 (23)
Total	33 (70)	14 (30)	47	Total	34 (72)	13 (28)	47
PoA (95% CI)[3]	85.1 (71.7, 93.8)			PoA (95% CI)[3]	91.5 (79.6, 97.6)		
Ratio (95% CI)[4]	1.030 (0.883, 1.203)			Ratio (95% CI)[4]	1.059 (0.947, 1.184)		

1 Between the FA/ICGA image and the OCTA image from a device, the pathology is present in both images or is absent from both images.

2 Between the FA/ICGA image and the OCTA image from a device, the pathology is present in one image and is absent from the other image, or at least one image is ungradable.

3 PoA = Percent of agreement between SPECTRALIS and RTVue. 95% confidence interval is calculated by exact method.

4 Ratio of the percentages of matching with FA/ICGA (SPECTRALIS to RTVue). 95% confidence interval is estimated by a log-linear regression with device as a single covariate using generalized estimating equation. NE = Not evaluable

TABLE 12: AGREEMENT IN CONSENSUS IDENTIFICATION OF RETINAL NEOVASCULARIZATION BETWEEN SPECTRALIS AND RTVUE USING BOXED AREA OF FA/ICGA

SPECTRALIS	RTVue 3mm x 3mm			SPECTRALIS	RTVue 6mm x 6mm		
10° x 10°	Match[1]	Not Match[2]	Total	20° x 20°	Match[1]	Not Match[2]	Total
All Subjects							
Match[1]	77 (97)	0 (0)	77 (97)	Match[1]	75 (95)	0 (0)	75 (95)
Not Match[2]	0 (0)	2 (3)	2 (3)	Not Match[2]	1 (1)	3 (4)	4 (5)
Total	77 (97)	2 (3)	79	Total	76 (96)	3 (4)	79
PoA (95% CI)[3]	100.0 (95.4, 100.0)			PoA (95% CI)[3]	98.7 (93.1, 100.0)		
Ratio (95% CI)[4]	1.000 (1.000, 1.000)			Ratio (95% CI)[4]	0.987 (0.962, 1.013)		
Normal Subjects							
Match[1]	32 (100)	0 (0)	32 (100)	Match[1]	32 (100)	0 (0)	32 (100)
Not Match[2]	0 (0)	0 (0)	0 (0)	Not Match[2]	0 (0)	0 (0)	0 (0)
Total	32 (100)	0 (0)	32	Total	32 (100)	0 (0)	32
PoA (95% CI)[3]	100.0 (89.1, 100.0)			PoA (95% CI)[3]	100.0 (89.1, 100.0)		
Ratio (95% CI)[4]	1.000 (NE)			Ratio (95% CI)[4]	1.000 (NE)		
Vascular Pathology Subjects							
Match[1]	45 (96)	0 (0)	45 (96)	Match[1]	43 (91)	0 (0)	43 (91)
Not Match[2]	0 (0)	2 (4)	2 (4)	Not Match[2]	1 (2)	3 (6)	4 (9)
Total	45 (96)	2 (4)	47	Total	44 (94)	3 (6)	47
PoA (95% CI)[3]	100.0 (92.5, 100.0)			PoA (95% CI)[3]	97.9 (88.7, 99.9)		
Ratio (95% CI)[4]	1.000 (1.000, 1.000)			Ratio (95% CI)[4]	0.977 (0.934, 1.022)		

1 Between the FA/ICGA image and the OCTA image from a device, the pathology is present in both images or is absent from both images.

2 Between the FA/ICGA image and the OCTA image from a device, the pathology is present in one image and is absent from the other image, or at least one image is ungradable.

3 PoA = Percent of agreement between SPECTRALIS and RTVue. 95% confidence interval is calculated by exact method.

4 Ratio of the percentages of matching with FA/ICGA (SPECTRALIS to RTVue). 95% confidence interval is estimated by a log-linear regression with device as a single covariate using generalized estimating equation. NE = Not evaluable

TABLE 13: AGREEMENT IN CONSENSUS IDENTIFICATION OF PRIMARY PATHOLOGY OF INTEREST (PPOI) BETWEEN SPECTRALIS AND RTVUE USING BOXED AREA OF FA/ICGA

SPECTRALIS	RTVue 3mm x 3mm			SPECTRALIS	RTVue 6mm x 6mm		
10° x 10°	Match[1]	Not Match[2]	Total	20° x 20°	Match[1]	Not Match[2]	Total
All Subjects							
Match[1]	65 (82)	3 (4)	68 (86)	Match[1]	64 (81)	4 (5)	68 (86)
Not Match[2]	0 (0)	11 (14)	11 (14)	Not Match[2]	1 (1)	10 (13)	11 (14)
Total	65 (82)	14 (18)	79	Total	65 (82)	14 (18)	79
PoA (95% CI)[3]	96.2 (89.3, 99.2)			PoA (95% CI)[3]	93.7 (85.8, 97.9)		
Ratio (95% CI)[4]	1.046 (0.994, 1.101)			Ratio (95% CI)[4]	1.046 (0.979, 1.117)		
Normal Subjects							
Match[1]	29 (91)	0 (0)	29 (91)	Match[1]	29 (91)	1 (3)	30 (94)
Not Match[2]	0 (0)	3 (9)	3 (9)	Not Match[2]	0 (0)	2 (6)	2 (6)
Total	29 (91)	3 (9)	32	Total	29 (91)	3 (9)	32
PoA (95% CI)[3]	100.0 (89.1, 100.0)			PoA (95% CI)[3]	96.9 (83.8, 99.9)		
Ratio (95% CI)[4]	1.000 (1.000, 1.000)			Ratio (95% CI)[4]	1.034 (0.968, 1.106)		
Vascular Pathology Subjects							
Match[1]	36 (77)	3 (6)	39 (83)	Match[1]	35 (74)	3 (6)	38 (81)
Not Match[2]	0 (0)	8 (17)	8 (17)	Not Match[2]	1 (2)	8 (17)	9 (19)
Total	36 (77)	11 (23)	47	Total	36 (77)	11 (23)	47
PoA (95% CI)[3]	93.6 (82.5, 98.7)			PoA (95% CI)[3]	91.5 (79.6, 97.6)		
Ratio (95% CI)[4]	1.083 (0.989, 1.186)			Ratio (95% CI)[4]	1.056 (0.949, 1.174)		

1 Between the FA/ICGA image and the OCTA image from a device, the pathology is present in both images or is absent from both images.

2 Between the FA/ICGA image and the OCTA image from a device, the pathology is present in one image and is absent from the other image, or at least one image is ungradable.

3 PoA = Percent of agreement between SPECTRALIS and RTVue. 95% confidence interval is calculated by exact method.

4 Ratio of the percentages of matching with FA/ICGA (SPECTRALIS to RTVue). 95% confidence interval is estimated by a log-linear regression with device as a single covariate using generalized estimating equation. NE = Not evaluable

Total inter-grader agreement frequencies are summarized in Table 14 through Table 19 and range from 94-100% in the "Normal" sub-group and 87-98% in the "Pathology" sub-group.

TABLE 14: INTER-GRADER AGREEMENT IN OCTA IDENTIFICATION OF MICROANEURYSMS

	SPECTRALIS			RTVue		
	Normal (N=32)	Pathology (N=47)	Total (N=79)	Normal (N=32)	Pathology (N=47)	Total (N=79)
Scan pattern 1[1]						
Number of subjects	32	47	79	32	47	79
Total Agreement	31 (97)	44 (94)	75 (95)	31 (97)	42 (89)	73 (92)
95% CI[2]	83.8, 99.9	82.5, 98.7	87.5, 98.6	83.8, 99.9	76.9, 96.5	84.2, 97.2
Scan pattern 2[1]						
Number of subjects	32	47	79	32	47	79
Total Agreement	32 (100)	41 (87)	73 (92)	32 (100)	42 (89)	74 (94)
95% CI[2]	89.1, 100.0	74.3, 95.2	84.2, 97.2	89.1, 100.0	76.9, 96.5	85.8, 97.9

1 Scan pattern 1: SPECTRALIS 10° x 10° and RTVue 3mm x 3mm; Scan pattern 2: SPECTRALIS 20° x 20° and RTVue 6mm x 6mm

2 95% confidence interval is calculated by exact method.

TABLE 15: INTER-GRADER AGREEMENT IN OCTA IDENTIFICATION OF RETINAL VASCULAR TORTUOSITY

	SPECTRALIS			RTVue		
	Normal (N=32)	Pathology (N=47)	Total (N=79)	Normal (N=32)	Pathology (N=47)	Total (N=79)
Scan pattern 1[1]						
Number of subjects	32	47	79	32	47	79
Total Agreement	32 (100)	43 (91)	75 (95)	31 (97)	44 (94)	75 (95)
95% CI[2]	89.1, 100.0	79.6, 97.6	87.5, 98.6	83.8, 99.9	82.5, 98.7	87.5, 98.6
Scan pattern 2[1]						
Number of subjects	32	47	79	32	47	79
Total Agreement	32 (100)	44 (94)	76 (96)	32 (100)	46 (98)	78 (99)
95% CI[2]	89.1, 100.0	82.5, 98.7	89.3, 99.2	89.1, 100.0	88.7, 99.9	93.1, 100.0

1 Scan pattern 1: SPECTRALIS 10° x 10° and RTVue 3mm x 3mm; Scan pattern 2: SPECTRALIS 20° x 20° and RTVue 6mm x 6mm

2 95% confidence interval is calculated by exact method.

TABLE 16: INTER-GRADER AGREEMENT IN OCTA IDENTIFICATION OF CHOROIDAL NEOVASCULARIZATION

	SPECTRALIS			RTVue		
	Normal (N=32)	Pathology (N=47)	Total (N=79)	Normal (N=32)	Pathology (N=47)	Total (N=79)
Scan pattern 1[1]						
Number of subjects	32	47	79	32	47	79
Total Agreement	32 (100)	44 (94)	76 (96)	32 (100)	45 (96)	77 (97)
95% CI[2]	89.1, 100.0	82.5, 98.7	89.3, 99.2	89.1, 100.0	85.5, 99.5	91.2, 99.7
Scan pattern 2[1]						
Number of subjects	32	47	79	32	47	79
Total Agreement	32 (100)	46 (98)	78 (99)	32 (100)	46 (98)	78 (99)
95% CI[2]	89.1, 100.0	88.7, 99.9	93.1, 100.0	89.1, 100.0	88.7, 99.9	93.1, 100.0

1 Scan pattern 1: SPECTRALIS 10° x 10° and RTVue 3mm x 3mm; Scan pattern 2: SPECTRALIS 20° x 20° and RTVue 6mm x 6mm

2 95% confidence interval is calculated by exact method.

TABLE 17: INTER-GRADER AGREEMENT IN OCTA IDENTIFICATION OF RETINAL ISCHEMIA

	SPECTRALIS			RTVue		
	Normal (N=32)	Pathology (N=47)	Total (N=79)	Normal (N=32)	Pathology (N=47)	Total (N=79)
Scan pattern 1[1]						
Number of subjects	32	47	79	32	47	79
Total Agreement	32 (100)	45 (96)	77 (97)	30 (94)	44 (94)	74 (94)
95% CI[2]	89.1, 100.0	85.5, 99.5	91.2, 99.7	79.2, 99.2	82.5, 98.7	85.8, 97.9
Scan pattern 2[1]						
Number of subjects	32	47	79	32	47	79
Total Agreement	32 (100)	43 (91)	75 (95)	32 (100)	44 (94)	76 (96)
95% CI[2]	89.1, 100.0	79.6, 97.6	87.5, 98.6	89.1, 100.0	82.5, 98.7	89.3, 99.2

1 Scan pattern 1: SPECTRALIS 10° x 10° and RTVue 3mm x 3mm; Scan pattern 2: SPECTRALIS 20° x 20° and RTVue 6mm x 6mm

2 95% confidence interval is calculated by exact method.

TABLE 18: INTER-GRADER AGREEMENT IN OCTA IDENTIFICATION OF RETINAL NEOVASCULARIZATION

	SPECTRALIS			RTVue		
	Normal (N=32)	Pathology (N=47)	Total (N=79)	Normal (N=32)	Pathology (N=47)	Total (N=79)
Scan pattern 1[1]						
Number of subjects	32	47	79	32	47	79
Total Agreement	32 (100)	46 (98)	78 (99)	32 (100)	46 (98)	78 (99)
95% CI[2]	89.1, 100.0	88.7, 99.9	93.1, 100.0	89.1, 100.0	88.7, 99.9	93.1, 100.0
Scan pattern 2[1]						
Number of subjects	32	47	79	32	47	79
Total Agreement	32 (100)	45 (96)	77 (97)	32 (100)	46 (98)	78 (99)
95% CI[2]	89.1, 100.0	85.5, 99.5	91.2, 99.7	89.1, 100.0	88.7, 99.9	93.1, 100.0

1 Scan pattern 1: SPECTRALIS 10° x 10° and RTVue 3mm x 3mm; Scan pattern 2: SPECTRALIS 20° x 20° and RTVue 6mm x 6mm

2 95% confidence interval is calculated by exact method.

TABLE 19: INTER-GRADER AGREEMENT IN OCTA IDENTIFICATION OF PRIMARY PATHOLOGY OF INTEREST (PPOI)

	SPECTRALIS			RTVue		
	Normal (N=32)	Pathology (N=47)	Total (N=79)	Normal (N=32)	Pathology (N=47)	Total (N=79)
Scan pattern 1[1]						
Number of subjects	32	47	79	32	47	79
Total Agreement	31 (97)	44 (94)	75 (95)	30 (94)	41 (87)	71 (90)
95% CI[2]	83.8, 99.9	82.5, 98.7	87.5, 98.6	79.2, 99.2	74.3, 95.2	81.0, 95.5
Scan pattern 2[1]						
Number of subjects	32	47	79	32	47	79
Total Agreement	32 (100)	43 (91)	75 (95)	32 (100)	42 (89)	74 (94)
95% CI[2]	89.1, 100.0	79.6, 97.6	87.5, 98.6	89.1, 100.0	76.9, 96.5	85.8, 97.9

1 Scan pattern 1: SPECTRALIS 10° x 10° and RTVue 3mm x 3mm; Scan pattern 2: SPECTRALIS 20° x 20° and RTVue 6mm x 6mm

2 95% confidence interval is calculated by exact method.

There were two adverse events that occurred during the course of the study. Both of the adverse events were directly associated with the fluorescein angiography imaging. Neither of these two events was considered related to the study devices.
There were no adverse events related to the OCTA devices.

The results of this case series study demonstrate that the SPECTRALIS HRA+OCT generates OCTA images of similar quality as those of the RTVue XR and that these images can allow for visualization of key anatomical vascular structures and vascular pathologies of the retina and choroid.

CONCLUSION

Comparison of technological characteristics and evaluation of non-clinical and clinical performance testing show that the modifications to the SPECTRALIS HRA+OCT and variants with OCT Angiography Module do not introduce any new potential safety risk and the device is as safe and effective as the predicate devices, therefore supporting a determination of substantial equivalence.