510(K) SUMMARY

K083291

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MAY - 5 2009

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(per 21 CFR §807.92)

Cirrus HD-OCT with Retinal Nerve Fiber Layer and Macular Normative Databases

GENERAL INFORMATION

Manufacturer:	Carl Zeiss Meditec, Inc. 5160 Hacienda Drive Dublin, California 94568 (925) 557-4616 (phone) (925) 557-4259 (fax) Est. Reg. No. 2918630
Contact Person:	Judith A. Brimacombe, MA Director, Regulatory/Clinical Affairs Carl Zeiss Meditec Inc. 5160 Hacienda Drive Dublin, California 94568 (925) 557-4616 (phone) (925) 557-4259 (fax)
Classification name:	Tomography, Optical Coherence; Ophthalmoscope
Classification:	Class II (acc. 21 CFR 886.1570)
Product Code:	OBO
Trade/Proprietary name:	Cirrus HD-OCT with Retinal Nerve Fiber Layer (RNFL) and Macular Normative Databases

PREDICATE DEVICES

Company: Device:	Carl Zeiss Meditec, Inc. Cirrus™ HD-OCT (K063378)
Company: Device:	Carl Zeiss Meditec, Inc. StratusOCT™ with Retinal Nerve Fiber Layer (RNFL) & Macula Normative Database (K033123)
Company: Device:	Carl Zeiss Meditec, Inc. Visante OCT (K051789)

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INTENDED USE

The Cirrus™ HD-OCT with Retinal Nerve Fiber Layer and Macular Normative Databases is indicated for in-vivo viewing, axial cross-sectional, and three-dimensional imaging and measurement of anterior and posterior ocular structures.

INDICATIONS FOR USE

The Cirrus™ HD-OCT is a non-contact, high resolution tomographic and biomicroscopic imaging device. It is indicated for in-vivo viewing, axial cross-sectional, and three-dimensional imaging and measurement of anterior and posterior ocular structures, including cornea, retina, retinal nerve fiber layer, macula, and optic disc. The Cirrus HD-OCT with Retinal Nerve Fiber Layer (RNFL) and Macular Normative Database is a quantitative tool for the comparison of retinal nerve fiber layer and the macula in the human retina 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 including, but not limited to, macular holes, cystoid macular edema, diabetic retinopathy, age-related macular degeneration, and glaucoma.

DEVICE DESCRIPTION

The Cirrus™ HD-OCT is a computerized instrument that acquires and analyzes cross-sectional tomograms of anterior and posterior ocular structures (including cornea, retina, retinal nerve fiber layer, macula, and optic disc). It employs non-invasive, non-contact, low-coherence interferometry to obtain these high-resolution images. Using this non-invasive optical technique, Cirrus HD-OCT produces high-resolution cross-sectional tomograms of the eye without contacting the eye.

SUBSTANTIAL EQUIVALENCE

It is the opinion of Carl Zeiss Meditec, Incorporated that the Cirrus HD-OCT with Retinal Nerve Fiber Layer and Macular Normative Databases is substantially equivalent to the Cirrus HD-OCT, Stratus OCT with RNFL and Macula Normative Databases and to the Visante OCT. The indications for use for the Cirrus HD-OCT with Retinal Nerve Fiber Layer and Macular Normative Databases is similar to the indications for the predicate devices cited in this application. A technological comparison and clinical testing demonstrate that the Cirrus HD-OCT with Retinal Nerve Fiber Layer (RNFL) and Macular Normative Database is functionally equivalent to the predicate devices.

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Evaluation performed on the Cirrus HD-OCT with Retinal Nerve Fiber Layer and Macular Normative Databases supports the expanded indications for use statement and demonstrates that the device is substantially equivalent to the predicate devices and does not raise new questions regarding safety and effectiveness.

CLINICAL EVALUATION

Clinical data was collected and evaluated to support the indications for use statement for the Cirrus HD-OCT with Retinal Nerve Fiber Layer and Macular Normative Databases and to demonstrate substantial equivalence to the Cirrus HD-OCT, the Stratus OCT with RNFL and Macula Normative Databases as well as to the Visante OCT. Three of these studies are summarized below.

RNFL Repeatability and Reproducibility

An in-house study was performed on 32 normal subjects to determine the inter-visit and inter-instrument repeatability of Cirrus RNFL thickness measurements. The repeatability and reproducibility (including effects of multiple visits and multiple instruments), along with mean thickness, are shown in the table below. Similar results were also found in an independent study, with a repeatability standard deviation of 1.3 μm in normal subjects and 1.2 μm in patient eyes[1].

Table 1. Mean thickness, Repeatability and Reproducibility of Cirrus RNFL measurements for five sectors, including the overall average thickness, four quadrants (temporal, superior, nasal, and inferior), measured on 32 normal subjects.

	Mean Thickness (μm)	Repeatability SD (μm)	Reproducibility SD (μm)	Repeatability Limit[a] (μm)	Reproducibility Limit[b] (μm)
Average	93.0	1.33 μm	1.35 μm	3.72 μm	3.78 μm
Temporal	64.6	2.03 μm	2.05 μm	5.68 μm	5.74 μm
Superior	118.8	3.42 μm	3.45 μm	9.58 μm	9.66 μm
Nasal	68.6	2.19 μm	2.24 μm	6.13 μm	6.27 μm
Inferior	123.6	3.01 μm	3.14 μm	8.43 μm	8.79 μm

a. Repeatability Limit is the upper 95% limit for the difference between repeated results. Per ISO 5725-1 and ISO 5725-6, Repeatability Limit = 2.8 x Repeatability SD.

b. Reproducibility Limit is the upper 95% limit calculated for the difference between results repeated with different operators on different instruments. Each subject was imaged by a single operator twice during a single visit on five instruments (Phase 1) or three times each during three visits on a single instrument (Phase 2). Per ISO 5725-1 and ISO 5725-6, Reproducibility limit = 2.8 x Reproducibility SD.

[1] Vizzeri, G, Weinreb, RN, Gonzalez-Garcia, AO, Bowd, C, Medeiros, F, Sample, PA, Zangwill, LM: Agreement between spectral-domain and time-domain OCT for measuring RNFL thickness, Br J Ophthalmol, March 2009.

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RNFL Agreement with Stratus OCT

A recent study[2] of normal subjects and patients (N = 130) found that although there were differences between Stratus and Cirrus, the Pearson correlation coefficient for the average RNFL thickness was 0.953, indicating good correlation. However, they also found differences between Cirrus and Stratus RNFL measurements. Cirrus measured thicker than Stratus for thinner RNFL values, and measured thinner than Stratus for thicker (more normal) RNFL values. Measurements from the two systems should not be used interchangeably.

Retinal Segmentation Accuracy

A study was conducted at four sites to evaluate the accuracy and precision of the Cirrus HD-OCT retinal thickness segmentation algorithms and to evaluate the agreement between the resulting measurements and similar measurements made on Stratus OCT.

Both eyes of 370 subjects were scanned, with one eye being chosen as the study eye based on eligibility guidelines. Subjects were classified into the six groups based on the primary diagnosis causing the most pathologic abnormalities in the study eye as follows:

Group 1 - age-related macular degeneration (AMD),
Group 2 - diabetic retinopathy (DR),
Group 3 - vitreoretinal interface abnormalities (including macular holes),
Group 4 - other retinal pathology,
Group 5 - macular edema for which treatment was planned,
Group 6 - no retinal pathology.

Any subjects with a primary diagnosis that placed them within Groups 1 through 4, for whom treatment of macular edema was scheduled, were categorized into Group 5.

Two 200 x 200 scans and two 512 x 128 scans of the study and fellow eyes were acquired using the Cirrus SD-OCT instrument during a single visit. Retinal thickness in every subfield was calculated (based on the ETDRS 6 mm grid centered on the fovea).

The Cirrus inner limited membrane (ILM) and retinal pigment epithelium (RPE) segmentations were deemed accurate if software-segmentations and hand-segmentations agreed for 100% of the A-scans that were evaluated, where agreement was defined as being within 16 μm for the central 1mm of the scan and within 32 μm

[2] O.J. Knight, R.T. Chang, W.J. Feuer, D.L. Budenz, "Comparison of Retinal Nerve Fiber Layer Measurements Using Stratus OCT and Cirrus Spectral Domain OCT," Poster 4628, ARVO 2008

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elsewhere in the scan. The accuracy of segmentation was found to depend on layer (RPE or ILM) and disease category, and is summarized below in Tables 2 and 3.

Table 2. Accuracy of segmentations for RPE layer by pathology category

Category	200x200		512x218	
	n/N (%)	95% CI	n/N (%)	95% CI
AMD	60/70 (85.7%)	(77.5%, 91.3%)	62/72 (86.1%)	(78.1%, 98.5%)
Diabetic Retinopathy	40/42 (95.2%)	(86.6%, 98.4%)	41/42 (97.6%)	(90.0%, 99.5%)
VRI Disorder	27/28 (96.4%)	(85.5%, 99.2%)	25/28 (89.3%)	(76.0%, 95.5%)
Other Retinal Disease	44/51 (86.3%)	(76.5%, 92.4%)	46/52 (88.5%)	(79.2%, 93.9%)
Macular Edema	27/28 (96.4%)	(85.5%, 99.2%)	27/29 (93.1%)	(82.2%, 97.7%)
No Retinal Disease	37/37 (100.0%)	(93.2%, 100%)	40/40 (100.0%)	(93.7%, 100%)

Table 3. Accuracy of segmentations for ILM layer by pathology category

Category	200x200		512x218	
	n/N (%)	95% CI	n/N (%)	95% CI
AMD	68/70 (97.1%)	(91.7%, 99.1%)	73/74 (98.6%)	(94.2%, 99.7%)
Diabetic Retinopathy	40/42 (95.2%)	(86.6%, 98.4%)	40/42 (95.2%)	(86.6%, 98.4%)
VRI Disorder	26/28 (92.9%)	(80.6%, 97.6%)	26/27 (96.3%)	(85.0%, 99.2%)
Other Retinal Disease	50/51 (98.0%)	(91.7%, 99.6%)	51/52 (98.1%)	(91.8%, 99.6%)
Macular Edema	28/28 (100.0%)	(91.2%, 100%)	28/29 (96.6%)	(85.9%, 99.2%)
No Retinal Disease	37/37 (100.0%)	(93.2%, 100%)	40/40 (100.0%)	(93.7%, 100%)

Retinal Segmentation Precision

The repeatability of Cirrus HD-OCT retinal thickness measurements varied with pathology. Table 4 shows the repeatability standard deviation for each disease category for the central subfield average thickness. Repeatability can be improved by

ensuring that two scans are registered to each other, as when the Macular Change Analysis is used. Repeatability can also be improved using the Macular Thickness Analysis when the fovea is correctly identified and used as the reference point for subfield average thickness calculations. These repeatability improvements are also shown in Table 4.

Table 4. Repeatability Standard Deviation[a] in micrometers for central subfield macular thickness (CSMT) measurements on the 200x200 scan using Macular Thickness Analysis (MTA), MTA with the ability to adjust the fovea position, and Macular Change Analysis (MCA), which uses registration and fovea placement. The total number of subjects for each disease category, and their means and standard deviations (SD) are also shown for reference.

Category	N	Mean ± SD CSMT (μm) for Cirrus 4.0 MTA	Central Subfield Macular Thickness Repeatability Standard Deviation (μm)		
			Cirrus 3.0 MTA	Cirrus 4.0 MTA with Fovea Placement	Cirrus 4.0 MCA with Registration and Fovea Placement
AMD	77	255 ± 65	17.5	6.3	8.7
DR	51	335 ± 109	16.8	9.8	8.1
VRI Disorder	44	360 ± 128	14.4	5.4	4.3
Other	62	303 ± 114	10.1	7.5	4.5
ME	41	339 ± 141	13.5	7.9	7.0
No Disease	44	256 ± 21	4.8	2.2	2.5

a. Repeatability Limit is the upper 95% limit for the difference between repeated results. For this study, two scans were acquired per subject during a single visit on a single system by a single operator at one of four sites. Per ISO 5725-1 and ISO 5725-6, Repeatability limit = 2.8 x Repeatability SD.

Retinal Thickness Measurements: Agreement with Stratus

The segmentation algorithms in Cirrus HD-OCT and Stratus OCT are designed to search for different layers. Specifically, Stratus OCT locates the top of the bright reflective layer that is now known to represent the junction between inner and outer segments of the photoreceptors as the lower boundary of the retinal for its thickness calculations; Cirrus locates the brightest layer in the retinal pigment epithelium (RPE)/outer segment complex, which is thought to correspond to the RPE.

Because of this difference in segmentation strategy, there is a mean difference in the retinal thickness found by each instrument. Because the integrity of the layers sought varies with pathology, the mean difference between instruments varies with pathology, as can be seen in Table 5. Even after the mean difference has been accounted for, there is a residual difference that can be seen in the standard deviation of the difference reported in the last column of Table 5. Because of the residual

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difference, for an individual patient, it is better to compare scans between Stratus and Cirrus qualitatively, looking for changes in retinal morphology, rather than making decisions based on quantitative evaluation.

Table 5. Difference between Cirrus HD-OCT and Stratus OCT for the Central Subfield Mean Thickness for each of six categories of pathology

Category	Mean (SD) Difference Cirrus – Stratus (μm)			
	N	Cirrus	Stratus	Difference
AMD	63	271.3 (60.6)	217.7 (54.2)	53.6 (35.0)
Diabetic Retinopathy	39	356.6 (118.7)	316.6 (135.8)	40.0 (47.1)
VRI Disorder	45	386.3 (128.0)	342.5 (125.0)	43.8 (35.9)
Other	53	310.6 (99.5)	268.9 (101.6)	41.7 (47.1)
Macular Edema	35	351.1 (140.3)	305.7 (127.9)	45.5 (45.3)
Normal	48	256.1 (18.6)	196.7 (18.6)	59.4 (11.7)

RNFL and Macula Normative Databases

The Cirrus RNFL and Macula normative databases were developed utilizing 284 subjects (aged 19-84) and 282 subjects (aged 19-84); respectively, collected from seven sites. The normative databases have a similar gender distribution (134 males, 150 females and 133 males, 149 females; respectively). Ethnicity breakdown of the Cirrus RNFL and Macula normative databases is as follows: 43% Caucasians, 24% Asians, 18% African American, 12% Hispanic, 1% Indian, and 6% mixed ethnicity. Note that Cirrus RNFL and Macula normative databases are adjusted only by age, not by axial length, refraction, optic disc area, signal strength or any other parameter.

Results revealed that the mean difference in the average thickness between any two race groups is within 6 um Caucasians have thinner mean average thickness, superior quadrant average, and inferior quadrant average. Asians seem to have thinner mean nasal quadrant average and thicker temporal quadrant average. The largest difference in the RNFL thickness between two race groups is for the temporal quadrant average between Asian and African American, with a difference of 16 um. The normative limits do not take into account differences that may be present due to ethnicity.

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Central Corneal Thickness Measurements

A study was conducted to determine repeatability and reproducibility of the Cirrus HD-OCT instrument measurements of central corneal thickness (CCT). Phase I of the study enrolled 28 subjects and was designed to determine inter-device variability, wherein each subject was imaged 3 times during a single visit on each of three Cirrus OCT instruments by one operator. Phase II enrolled 22 subjects and was designed to determine inter-operator variability, wherein each subject was imaged three times during a single visit by each of three operators. Phases I and II enrolled different subjects.

The Cirrus HD-OCT repeatability and reproducibility are shown in Table 6. Mean thickness of each phase and overall (Phase I and II combined) are also shown. Since the random error variability from Phase II of the study was larger than that from Phase I, the variance components from Phase II were used to estimate the random measurement variability and the repeatability standard deviation.

Table 6. Repeatability and reproducibility of central corneal thickness measurements

Cirrus HD-OCT Repeatability[a]		Cirrus HD-OCT Reproducibility[b]		Mean Thickness		
SD (µm)	Limits (µm)	SD (µm)	Limits (µm)	Phase I (µm)	Phase II (µm)	Overall (µm)
4.08	11.42	4.23	11.84	544.25	532.25	538.25

a. Repeatability Limit is the upper 95% limit for the difference between repeated results. Per ISO 5725-1 and ISO 5725-6, Repeatability Limit = 2.8 x Repeatability SD.

b. Reproducibility Limit is the upper 95 % limit calculated for the difference between results repeated using different operators. Each subject was imaged three times during a single visit by each of three operators. Per ISO 5725-1 and ISO 5725-6, Reproducibility Limit = 2.8 x Reproducibility SD.

Difference in Central Corneal Thickness Measurement between Cirrus HD-OCT and Ultrasound Pachymetry

A study was conducted to determine the difference in central corneal thickness measurement between Cirrus HD-OCT and ultrasound pachymetry. A total of 50 eyes were enrolled at one site and measured by a single operator for each device. The results of this study, provided in Table 7, show that the mean difference in central corneal thickness measurements between Cirrus HD-OCT and ultrasound pachymetry is -9.06. The negative difference indicates that the Cirrus CCT measurement is thinner than the ultrasound CCT measurement. OCT devices in general measure thinner than ultrasound pachymetry. The Visante OCT user

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manual reports that Visante OCT measurements are thinner, on average, by 15.1 microns as compared to ultrasound pachymetry.

Table 7. Difference in Central Corneal Thickness Measurement between Cirrus HD-OCT and Ultrasound Pachymetry

	Mean Difference	SD	95% CI of the Difference	
			Lower	Upper
Cirrus CCT-Ultrasound pachymetry CCT (µm)	-9.06	5.63	-10.66	-7.46

SUMMARY

As described in this 510(k) Summary, all testing deemed necessary was conducted on the Cirrus HD-OCT with Retinal Nerve Fiber Layer and Macular Normative Databases to ensure that the device is safe and effective for its intended use when used in accordance with its Instructions for Use.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

MAY - 5 2009

Carl Zeiss Meditec, Inc.
c/o Judith A. Brimacombe
Director, Clinical & Regulatory Affairs
Carl Zeiss Meditec, Inc.
5160 Hacienda Blvd.
Dublin, CA 94568

Re: K083291
Trade/Device Name: Cirrus HD-OCT with Retinal Nerve Fiber Layer and Macular Normative Databases, Model 4000
Regulation Number: 21 CFR 886.1570
Regulation Name: Ophthalmoscope
Regulatory Class: II
Product Code: OBO
Dated: April 15, 2009
Received: April 16, 2009

Dear Ms. Brimacombe:

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. 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.

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); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Center for Devices and Radiological Health's (CDRH's) Office of Compliance at (240) 276-0115. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please contact the CDRH/Office of Surveillance and Biometrics/Division of Postmarket Surveillance at 240-276-3464. For more information regarding the reporting of adverse events, please go to http://www.fda.gov/cdrh/mdr/.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (240) 276-3150 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Malvina B. Eydelman, M.D.

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

INDICATIONS FOR USE STATEMENT

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510(k) Number (if known): K083291

Device Name: Cirrus HD-OCT with Retinal Nerve Fiber Layer (RNFL) and Macular Normative Databases

Indications for Use:

The Cirrus™ HD-OCT is a non-contact, high resolution tomographic and biomicroscopic imaging device. It is indicated for in-vivo viewing, axial cross-sectional, and three-dimensional imaging and measurement of anterior and posterior ocular structures, including cornea, retina, retinal nerve fiber layer, macula, and optic disc. The Cirrus HD-OCT with Retinal Nerve Fiber Layer (RNFL) and Macular Normative Databases is a quantitative tool for the comparison of retinal nerve fiber layer and the macula in the human retina 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 including, but not limited to, macular holes, cystoid macular edema, diabetic retinopathy, age-related macular degeneration, and glaucoma.

Prescription Use __x____ (Part 21 CFR 801 Subpart D) AND/OR Over-The-Counter Use _____ (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Daryl L. Kaufman

(Division Sign-Off)
Division of Ophthalmic and Ear, Nose and Throat Devices

510(k) Number K083291