DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
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Silver Spring, MD 20993-0002

March 17, 2016

Nidek Co., Ltd.
% Mr. Ryan Bouchard
Ora, Inc.
300 Brickstone Square
Andover, Massachusetts 01810

Re: K151706
Trade/Device Name: Specular Microscope Cem- 530
Regulation Number: 21 CFR 886.1850
Regulation Name: Ac-Powered Slitlamp Biomicroscope
Regulatory Class: Class II
Product Code: NQE
Dated: February 4, 2016
Received: February 5, 2016

Dear Mr. Bouchard:

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. 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); 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 Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. 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 the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Kesia Alexander

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: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*

K151706

Device Name
Specular Microscope CEM-530

Indications for Use *(Describe)*
The Specular Microscope CEM-530 is a non-contact ophthalmic microscope, optical pachymeter, and camera intended for examination of the corneal endothelium and for measurement of the thickness of the cornea.

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

This summary of the 510(k) premarket notification for the NIDEK Specular Microscope CEM-530 is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR § 807.92.

Date Prepared: March 4, 2016

SPONSER/ 510(k) OWNER/ MANUFACTURER

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NAME OF DEVICE

Trade Name: Specular Microscope CEM-530
Common Name: Specular Microscope

DEVICE CLASSIFICATION/FDA REVIEWING BRANCH

The Ophthalmic Branch has classified AC Powered Slit Lamp Biomicroscopes as Class II devices pursuant to 21 C.F.R. §886.1850.

PRODUCT CODE: CLASSIFICATION / CFR TITLE

NQE, 21 CFR 886.1850

PREDICATE DEVICES

Nidek Specular Microscope CEM-530 (K130565)
Konan Medical, Inc. Cellchek Plus (K120264)

INDICATIONS FOR USE

The Nidek Specular Microscope CEM-530 is a non-contact ophthalmic microscope, optical pachymeter, and camera intended for examination of the corneal endothelium and for measurement of the thickness of the cornea.

PRODUCT DESCRIPTION

The Nidek Specular Microscope CEM-530 provides non-contact, high magnification image capture of the endothelium enabling observation of the size and shape of cells. Information such as the number of endothelial cells, cell density, and cell area is analyzed through the captured images. The captured images and analysis results of the endothelium are used in intraocular or corneal surgery, postoperative follow-up, and corneal observation such as for endothelial disorders or the corneal state of patients who wear extended-wear contact lenses. Observation is possible in the central area (visual angle: 5°) and peripheral area (visual angle: 27°) using a periphery capture function as well as in the center of the cornea. The captured images and analysis results can be printed on the built-in printer or optional video printer, or output to an external device over LAN connection. In addition to the specular microscopy, the corneal thickness can be optically measured in a non-contact method. The CEM-530 has auto-tracking and auto-shooting functions. Results can be printed using the built-in thermal printer or captured images can be transferred to a filing system via LAN connection. The Specular Microscope CEM-530 cleared in this 510(k) is identical to the Specular Microscope CEM-530 cleared in K130565 with the addition of a new analysis mode: Center Point Method. All other aspects of the cleared device remain unchanged.

SUBSTANTIAL EQUIVALENCE

The Specular Microscope CEM-530 and the predicate devices are all non-contact ophthalmic microscopes, optical pachymeters, and cameras intended for examination of the corneal endothelium and for measurement of the thickness of the cornea. Both the Specular Microscope CEM-530 and the predicate device offer automatic capture features and manual capture modes. The Specular Microscope CEM-530 which is the subject of this 510(k) has identical technological characteristics to the Specular Microscope CEM-530 which was cleared in K130565. The only difference is the addition of Center Point Method. With Center Point method, the operator touches the center of a cell on the endothelial image with the touch screen pen. A dot is displayed on the endothelial image. Shapes are surrounded by the vertical lines to the lines made by connecting each dot and is recognized as a cell. Connected dots are top of cells and vertical lines are cell walls. Therefore, this discussion will focus primarily on the substantial equivalence to the Konan Cellchek Plus cleared in K120264.

Both the CEM-530 and the Konan Cellchek Plus have a built-in CCD camera. Both the CEM-530 and the Konan Cellchek Plus include an optical pachymeter with an accuracy of $\pm$ 10 microns. There were no modifications made to the optical pachymeter in the Specular Microscope CEM-530 compared with the device cleared in K130565.

Regarding image analysis, both the CEM-530 and the predicate device offer automatic image analysis. The CEM-530, which is the subject of this 510(k), also offers manual analysis of images, as does the Konan predicate device. Clinical performance data is provided which evaluates the precision and agreement of the manual measurements performed by the CEM-530 compared to manual measurements performed with the Konan predicate device. The clinical performance data demonstrates the substantial equivalence of the CEM-530 manual mode to the Konan predicate device's manual mode.

Both the CEM-530 and the predicate device comply with applicable electrical safety and light safety standards.

Therefore, in regards to technological characteristics, the Specular Microscope CEM-530 is similar to the Konan but there are some minor differences between the devices which have been evaluated with non-clinical and clinical performance data. The differences are shown in Table 1.

TABLE 1
SPECULAR MICROSCOPE CEM-530
SUBSTANTIAL EQUIVALENCE CHART

Manufacturer	Nidek	Nidek	Konan
Device Name	CEM-530	CEM-530	Cellchek Plus
510(k) Number	NA	K130565	K120264
Product Classification	Class II, NQE	Class II, NQE	Class II, NQE
Indications for Use	Non-contact ophthalmic microscope, optical pachymeter, and camera intended for examination of the corneal endothelium and for measurement of the thickness of the cornea.	Non-contact ophthalmic microscope, optical pachymeter, and camera intended for examination of the corneal endothelium and for measurement of the thickness of the cornea.	Non-contact ophthalmic microscope, optical pachymeter, and camera intended for examination of corneal endothelium and for the measurement of the thickness of the cornea.
Device Type	Non-contact specular microscope and pachymeter	Non-contact specular microscope and pachymeter	Non-contact specular microscope and pachymeter
Capturing Method	Auto capture, auto alignment, auto focus (3D, 2D)/Manual	Auto capture, auto alignment, auto focus (3D, 2D)/Manual	Auto capture, auto alignment, auto focus(3D)/Manual
Capture Field	0.25x 0.55 mm	0.25x 0.55 mm	0.24 x 0.4 mm
Fixation Lamp (Central)	1 point	1 point	1 point
Fixation Lamp (Paracentral)	8 points (5 degrees of visual angle for each point)	8 points (5 degrees of visual angle for each point)	4 points (direction of 12, 2, 10 and 6 o'clock)
Fixation Lamp (Periphery)	6 points (27 degrees of visual angle for direction of 12, 2, 10, 6, 4 and 8 o'clock)	6 points (27 degrees of visual angle for direction of 12, 2, 10, 6, 4 and 8 o'clock)	
Camera	Built-in CCD camera	Built-in CCD camera	Built-in CCD image sensing element camera
Flash	Cyan LED	Cyan LED	Konan Xe tube
Illumination for	InfraRed LED	InfraRed LED	Konan halogen lamp

focusing			
Pachymetry Technology	Optical	Optical	Optical
Measurement Range Pachymetry	300 to 1000 microns	300 to 1000 microns	Unknown
Accuracy of pachymetry	± 10 microns	± 10 microns	± 10 microns
Auto Analysis	Yes	Yes	Yes
Manual Analysis	Yes	No	Yes
Analysis Speed	2 seconds	2 seconds	Unknown
Record (1 patient)	Single mode: 1 endothelial image for both right and left eyes Paracentral and Peripheral modes: 15 endothelial images for both right and left eyes	Single mode: 1 endothelial image for both right and left eyes Paracentral and Peripheral modes: 15 endothelial images for both right and left eyes	1 endothelial image for both right and left eyes
Built-in Printer	Thermal Line Printer with auto cutter	Thermal Line Printer with auto cutter	NA
External Interface	USB-A: barcode, card reader, LAN for data output, Video output: BNC terminal	USB-A: barcode, card reader, LAN for data output, Video output: BNC terminal	Video output: BNC terminal Input port for mouse and remote control
Connection to Filing System	Connectable	Connectable	Connectable
Monitor	8.4” SVGA color LCD with touch panel	8.4” SVGA color LCD with touch panel	19” color LCD monitor
Input Power	100 VA	100 VA	70 VA
Dimensions	291 (W) x 495 (D) x 457 (H) mm	291 (W) x 495 (D) x 457 (H) mm	334 (W) x 486 (D) x 420 (H) mm
Weight	20 Kg	20 Kg	20.5 Kg
Compliance with Safety Standards	IEC 60601-1 IEC 60601-1-2 ISO 15004-1 ISO 15004-2	IEC 60601-1 IEC 60601-1-2 ISO 15004-1 ISO 15004-2	IEC 60601-1 IEC 60601-1-2 ISO 15004-1 ISO 15004-2

NON-CLINICAL PERFORMANCE SUMMARY

The performance testing conducted using the NIDEK Specular Microscope CEM-530 verified that the device operates as intended. The specifications to which the CEM-530 was verified to are substantially equivalent to the predicate devices and therefore, support a determination of substantial equivalence. The pachymetry functionality was evaluated in model eyes and the measurement accuracy of ± 10 microns was confirmed.

Additionally, the CEM-530 was subjected to electrical safety testing in accordance with IEC 60601-1, electromagnetic compatibility (EMC) testing in accordance with IEC 60601-1-2, and optical radiation safety testing in accordance with ISO 15004-1 and ISO 15004-2.

CLINICAL PERFORMANCE SUMMARY

A prospective clinical study was conducted to assess the agreement, accuracy and precision of the Specular Microscope CEM-530 Center Point Method by comparing results across three machines/operators to those obtained with the predicate device, the Cellchek Plus. Three populations were studied: young (18-28 years of age) and adult (29-80 years of age) healthy subjects and pathologic adult eyes (29-80 years of age).

There were 79 subjects enrolled in the study: 28 in the non-pathologic young eye population, 28 in the non-pathologic adult eye population, and 23 in the pathologic adult eye population. Of those, 74 are included in the effectiveness population (28, 27, and 19, respectively). The agreement population consisted of all 74 subjects (28, 27 and 19, respectively). The precision population included a subset of the effectiveness population, 47 total with 15, 16 and 16 respectively. The pathologic adult subjects consisted of 19 subjects with the following pathologies which qualified them for the subgroup: Guttata (16, 84.2%) and Long Term Fuch's Dystrophy (3, 15.8%). The mean (SD) age of the non-pathologic young population was 22.2 (3.28) years; that of the non-pathologic adult population was 53.0 (13.42) years, and that of the pathologic adult population was 63.9 (12.39) years. All subjects combined had a mean age of 44.1 (20.54) years. The gender distribution of the total population was 27 males (36.5%) and 47 females (63.5%). The gender distribution of the non-pathologic young population was 15 males (53.6%) and 13 females (46.4%); that of the non-pathologic adult population was 8 males (29.6%) and 19 females (70.4%), and that of the pathologic adult population was 4 males (21.1%) and 15 females (78.9%). The majority of subjects were white (66/74 subjects, 89.2%). All of the pathologic adult subjects were white (19/19). The non-pathologic adult were white (21/27), American Indian (1/27), Asian (1/27), African American (1/27) and other (3/27). The non-pathologic young subjects were white (26/28) and other (2/28). With regard to iris color, the highest percentage of subjects had study eyes with brown irides (43.2%), followed by blue irides (28.4%), green irides (6.8%), black irides (1.4%) and gray irides (1.4%).

The result of Agreement study

Table 2 provides a summary of the agreement data for all subjects with the Center Point Method while Tables 3, 4 and 5 provide the same data by subgroup (non-pathologic young eyes, non-pathologic adult eyes, pathologic adult eyes, respectively).

Table 2 Center Point Method: Four Corneal Specular Microscopic Variables Assessed with the Two Devices – All Configurations − All Subjects − Effectiveness Population

	CD	CV	% HEX
Nidek Specular Microscope CEM-530			
N	74	74	74
Mean (SD)	2784.3 (428.52)	22.1 (3.36)	59.8 (7.30)
Median	2795.0	21.5	60.0
Min-Max	1754 - 3637	15 - 35	41 - 81
Konan CellChek Plus			
N	74	74	74
Mean (SD)	2738.6 (412.67)	29.6 (4.16)	62.6 (7.42)
Median	2754.5	29.0	63.0
Min- Max	1757 - 3484	22 - 42	41 - 76
Device Comparisons			
Mean Difference (SD)	45.7 (104.11)	-7.6 (3.00)	-2.9 (5.90)
Mean Difference (SD) as a % of the CellChek reading	1.71% (3.976%)	-25.20% (8.391%)	-4.07% (9.662%)
95% LOA	(-162.5, 253.9)	(-13.6, -1.6)	(-14.6, 8.9)
Correlation (R^2)	0.9701	0.7019	0.6791
Deming Regression Intercept (95% CI)	-62.9 (-224.4, 98.6)	0.1 (-6.4, 6.7)	-1.3 (-20.2, 17.5)
Deming Regression Slope (95% CI)	1.0 (1.0, 1.1)	0.7 (0.5, 1.0)	1.0 (0.7, 1.3)

Table 3 Center Point Method: Corneal Specular Microscopic Variables − All Configurations – Non-Pathologic Young Eyes − Effectiveness Population

	CD	CV	% HEX
Nidek Specular Microscope CEM-530			
N	28	28	28
Mean (SD)	3069.5 (346.41)	20.3 (1.90)	63.0 (6.33)
Median	3104.0	21.0	63.0
Min-Max	2437 - 3637	15 - 24	52 - 81
Konan CellChek Plus XL			
N	28	28	28
Mean (SD)	3030.3 (296.93)	27.4 (2.99)	67.0 (5.03)
Median	3053.5	27.0	67.5
Min- Max	2398 - 3484	22 - 34	57 - 76
Device Comparisons			
Mean Difference (SD)	39.2 (93.37)	-7.2 (2.94)	-4.0 (5.31)
Mean Difference (SD) as a % of the CellChek reading	1.19% (3.069%)	-25.59%, (8.660%)	-5.79% (7.933%)
95% LOA	(-147.5, 226.0)	(-13.1, -1.3)	(-14.6, 6.7)
Correlation (R^2)	0.9695	0.3398	0.5841
Deming Regression Intercept (95% CI)	-482.7 (-892.1, -73.4)	11.4 (-0.8, 23.5)	-35.9 (-82.1, 10.3)
Deming Regression Slope (95% CI)	1.2 (1.0, 1.3)	0.3 (-0.1, 0.8)	1.5 (0.8, 2.2)

For subjects in the Precision and Agreement cohort, the measurements from the first acceptable images from each machine within the same configuration are used for the agreement analyses.
The mean differences are calculated as (Nidek Specular Microscope CEM-530) - (Konan CellChek Plus XL).
The mean differences as a % of the CELLCHEK reading are calculated for each subject first and then summarized.

Table 4 Center Point Method: Corneal Specular Microscopic Variables − All Configurations – Non-Pathologic Adult Eyes − Effectiveness Population

	CD	CV	% HEX
Nidek Specular Microscope CEM-530			
N	27	27	27
Mean (SD)	2678.6 (391.33)	23.3 (3.27)	57.1 (6.66)
Median	2772.0	23.0	56.0
Min-Max	1956 - 3399	19 - 35	47 - 73
Konan CellChek Plus XL			
N	27	27	27
Mean (SD)	2627.3 (348.93)	31.1 (4.29)	59.3 (8.11)
Median	2674.0	31.0	60.0
Min- Max	2033 - 3344	22 - 42	45 – 74
Device Comparisons			
Mean Difference (SD)	51.3 (100.35)	-7.8 (3.04)	-2.2 (6.10)
Mean Difference (SD) as a % of the CellChek reading	1.82% (3.753%)	-24.70% (7.780%)	-2.94% (10.324%)
95% LOA	(-149.4, 252.0)	(-13.9, -1.7)	(-14.4, 10.0)
Correlation (R^2)	0.9697	0.7075	0.6750
Deming Regression Intercept (95% CI)	-278.5 (-566.9, 9.9)	2.0 (-13.1, 17.1)	12.7 (-7.5, 32.9)
Deming Regression Slope (95% CI)	1.1 (1.0, 1.2)	0.7 (0.2, 1.2)	0.7 (0.4, 1.1)

For subjects in the Precision and Agreement cohort, the measurements from the first acceptable images from each machine within the same configuration are used for the agreement analyses.
The mean differences are calculated as (Nidek Specular Microscope CEM-530) - (Konan CellChek Plus XL).
The mean differences as a % of the CELLCHEK reading are calculated for each subject first and then summarized.

Table 5 Center Point Method: Corneal Specular Microscopic Variables − All Configurations – Pathologic Adult Eyes − Effectiveness Population

	CD	CV	% HEX
Nidek Specular Microscope CEM-530			
N	19	19	19
Mean (SD)	2514.2 (351.02)	23.0 (4.11)	58.7 (7.96)
Median	2522.0	22.0	60.0
Min-Max	1754 - 3078	17 – 33	41 - 71
Konan CellChek Plus XL			
N	19	19	19
Mean (SD)	2466.9 (392.01)	30.8 (4.26)	60.8 (6.41)
Median	2564.0	30.0	61.0
Min- Max	1757 - 3058	24 - 40	41 - 68
Device Comparisons			
Mean Difference (SD)	47.3 (127.36)	-7.8 (3.11)	-2.1 (6.47)
Mean Difference (SD) as a % of the CellChek reading	2.32% (5.367%)	-25.34% (9.218%)	-3.15% (11.085%)
95% LOA	(-207.5, 302.0)	(-14.1, -1.6)	(-15.0, 10.8)
Correlation (R^2)	0.9472	0.7237	0.6134
Deming Regression Intercept (95% CI)	318.7 (-127.8, 765.3)	-6.4 (-23.1, 10.4)	-27.7 (-176.4, 121.0)
Deming Regression Slope (95% CI)	0.9 (0.7, 1.1)	1.0 (0.4, 1.5)	1.4 (-1.0, 3.8)

For subjects in the Precision and Agreement cohort, the measurements from the first acceptable images from each machine within the same configuration are used for the agreement analyses.
The mean differences are calculated as (Nidek Specular Microscope CEM-530) - (Konan CellChek Plus XL).
The mean differences as a % of the CELLCHEK reading are calculated for each subject first and then summarized.

The result of Precision study

Table 6 provides a summary of the precision data for all subjects with the Center Point Method while Tables 7, 8 and 9 provide the same data by subgroup (non-pathologic young eyes, non-pathologic adult eyes, pathologic adult eyes, respectively). Data from a previous Nidek study, CEM-530-US-001, was used as the comparative data with respect to the Konan Cell Chek Plus results for the precision analysis detailed below. In the evaluation of the suitability of using the historical data it was found that the sample size, age, gender, ethnicity/race, iris color and clinical diagnosis of the pathologic sub group were all similar to allow the usage of the data.

Table 6 Center Point Method: Precision Analyses − All Subjects − Effectiveness Population

Variable	NIDEK CEM-530 N=47	Konan CellChek Plus N=62
Endothelial Cell Density		
Repeatability SD	48.9	62.4
Repeatability SD as a % of the Mean	1.8%	2.4%
Repeatability Limit	136.8	174.8
Repeatability Ratio (NIDEK CEM-530/ Konan CellChek Plus XL	0.7829	---
Reproducibility SD	60.9	95.2
Reproducibility SD as a % of the Mean	2.2%	3.7%
Reproducibility Limit	170.4	266.7
Reproducibility Ratio (NIDEK CEM-530/ Konan CellChek Plus XL	0.6391	---
Coefficient of Variation of Endothelial Cell Area (CV)		
Repeatability SD	1.5	2.7
Repeatability SD as a % of the Mean	6.7%	8.5%
Repeatability Limit	4.1	7.5
Repeatability Ratio (NIDEK CEM-530/ Konan CellChek Plus XL	0.5521	---
Reproducibility SD	1.8	2.7
Reproducibility SD as a % of the Mean	8.4%	8.6%
Reproducibility Limit	5.1	7.6
Reproducibility Ratio (NIDEK CEM-530/ Konan CellChek Plus XL	0.6778	---
% Hexagonality		
Repeatability SD	3.5	5.4
Repeatability SD as a % of the Mean	5.8%	8.8%
Repeatability Limit	9.9	15.0
Repeatability Ratio (NIDEK CEM-530/ Konan CellChek Plus XL	0.6586	---
Reproducibility SD	4.0	5.4
Reproducibility SD as a % of the Mean	6.5%	8.9%
Reproducibility Limit	11.1	15.2
Reproducibility Ratio (NIDEK CEM-530/ Konan CellChek Plus XL	0.7267	---

N represents the total number of subjects in each eye population in the precision and agreement cohort. If any variance component was negative, it was reported as 0. The repeatability limit is 2.8 times the repeatability standard deviation, which is the square root of the residual within subject variance component. The reproducibility limit is 2.8 times the reproducibility standard deviation, which is the square root of the sum of the variance components of operator+device, operator+device x subject interaction, and residual within subject.

Table 7 Center Point Method: Precision Analyses − Non-Pathologic Young Eye − Effectiveness Population

Variable	NIDEK CEM-530	Konan CellChek Plus

	N=15	XL N= 20
Endothelial Cell Density		
Repeatability SD	46.0	59.3
Repeatability SD as a % of the Mean	1.5%	2.1%
Repeatability Limit	128.8	166.0
Repeatability Ratio (NIDEK CEM-530/ Konan CellChek Plus XL)	0.7758	---
Reproducibility SD	51.9	70.2
Reproducibility SD as a % of the Mean	1.7%	2.5%
Reproducibility Limit	145.4	196.6
Reproducibility Ratio (NIDEK CEM-530/ Konan CellChek Plus XL)	0.7395	---
Coefficient of Variation of Endothelial Cell Area (CV)		
Repeatability SD	1.3	2.6
Repeatability SD as a % of the Mean	6.4%	8.9%
Repeatability Limit	3.5	7.4
Repeatability Ratio (NIDEK CEM-530/ Konan CellChek Plus XL)	0.4806	---
Reproducibility SD	1.5	2.7
Reproducibility SD as a % of the Mean	7.5%	9.1%
Reproducibility Limit	4.2	7.6
Reproducibility Ratio (NIDEK CEM-530/ Konan CellChek Plus XL)	0.5515	---
% Hexagonality		
Repeatability SD	3.1	4.2
Repeatability SD as a % of the Mean	4.8%	6.4%
Repeatability Limit	8.6	11.7
Repeatability Ratio (NIDEK CEM-530/ Konan CellChek Plus XL)	0.7391	---
Reproducibility SD	3.8	4.3
Reproducibility SD as a % of the Mean	5.8%	6.7%
Reproducibility Limit	10.6	12.1
Reproducibility Ratio (NIDEK CEM-530/ Konan CellChek Plus XL)	0.8705	---

N represents the total number of subjects in each eye population in the precision and agreement cohort. If any variance component was negative, it was reported as 0. The repeatability limit is 2.8 times the repeatability standard deviation, which is the square root of the residual within subject variance component. The reproducibility limit is 2.8 times the reproducibility standard deviation, which is the square root of the sum of the variance components of operator+device, operator+device x subject interaction, and residual within subject.

Table 8 Center Point Method: Precision Analyses − Non-Pathologic Adult Eye − Effectiveness Population

Variable	NIDEK CEM-530 N=16	Konan CellChek Plus XL N=22
Endothelial Cell Density		
Repeatability SD	47.6	58.9
Repeatability SD as a % of the Mean	1.8%	2.3%
Repeatability Limit	133.1	165.0
Repeatability Ratio (NIDEK CEM-530/ Konan CellChek Plus XL)	0.8072	---
Reproducibility SD	56.9	60.8
Reproducibility SD as a % of the Mean	2.2%	2.3%
Reproducibility Limit	159.4	170.2
Reproducibility Ratio (NIDEK CEM-530/ Konan CellChek Plus XL)	0.9364	---
Coefficient of Variation of Endothelial Cell Area (CV)		
Repeatability SD	1.4	2.3
Repeatability SD as a % of the Mean	6.2%	7.1%
Repeatability Limit	3.9	6.4
Repeatability Ratio (NIDEK CEM-530/ Konan CellChek Plus XL)	0.6125	---
Reproducibility SD	1.7	2.4
Reproducibility SD as a % of the Mean	7.4%	7.3%
Reproducibility Limit	4.7	6.6
Reproducibility Ratio (NIDEK CEM-530/ Konan CellChek Plus XL)	0.7056	---
% Hexagonality		
Repeatability SD	3.1	4.1
Repeatability SD as a % of the Mean	5.3%	6.8%
Repeatability Limit	8.6	11.4
Repeatability Ratio (NIDEK CEM-530/ Konan CellChek Plus XL)	0.7557	---
Reproducibility SD	3.4	4.6
Reproducibility SD as a % of the Mean	5.9%	7.7%
Reproducibility Limit	9.7	13.0
Reproducibility Ratio (NIDEK CEM-530/ Konan CellChek Plus XL)	0.7449	---

N represents the total number of subjects in each eye population in the precision and agreement cohort. If any variance component was negative, it was reported as 0. The repeatability limit is 2.8 times the repeatability standard deviation, which is the square root of the residual within subject variance component. The reproducibility limit is 2.8 times the reproducibility standard deviation, which is the square root of the sum of the variance components of operator+device, operator+device x subject interaction, and residual within subject.

Table 9 Center Point Method: Precision Analyses − Pathologic Adult Eye − Effectiveness Population

Variable	NIDEK CEM-530 N=16	Konan CellChek Plus XL N=20
Endothelial Cell Density		
Repeatability SD	52.7	68.9
Repeatability SD as a % of the Mean	2.1%	3.0%
Repeatability Limit	147.4	192.9
Repeatability Ratio (NIDEK CEM-530/ Konan CellChek Plus XL)	0.7641	---
Reproducibility SD	72.4	138.8
Reproducibility SD as a % of the Mean	2.9%	6.1%
Reproducibility Limit	202.7	388.6
Reproducibility Ratio (NIDEK CEM-530/ Konan CellChek Plus XL)	0.5218	---
Coefficient of Variation of Endothelial Cell Area (CV)		
Repeatability SD	1.7	3.1
Repeatability SD as a % of the Mean	7.3%	9.4%
Repeatability Limit	4.8	8.7
Repeatability Ratio (NIDEK CEM-530/ Konan CellChek Plus XL)	0.5561	---
Reproducibility SD	2.3	3.2
Reproducibility SD as a % of the Mean	9.8%	9.7%
Reproducibility Limit	6.4	8.9
Reproducibility Ratio (NIDEK CEM-530/ Konan CellChek Plus XL)	0.7236	---
% Hexagonality		
Repeatability SD	4.3	7.3
Repeatability SD as a % of the Mean	7.3%	12.6%
Repeatability Limit	11.9	20.4
Repeatability Ratio (NIDEK CEM-530/ Konan CellChek Plus XL)	0.5837	---
Reproducibility SD	4.6	7.3
Reproducibility SD as a % of the Mean	7.9%	12.6%
Reproducibility Limit	12.9	20.4
Reproducibility Ratio (NIDEK CEM-530/ Konan CellChek Plus XL)	0.6326	---

N represents the total number of subjects in each eye population in the precision and agreement cohort. If any variance component was negative, it was reported as 0. The repeatability limit is 2.8 times the repeatability standard deviation, which is the square root of the residual within subject variance component. The reproducibility limit is 2.8 times the reproducibility standard deviation, which is the square root of the sum of the variance components of operator+device, operator+device x subject interaction, and residual within subject.

Overall, within eye/subject variability was acceptable, and similar for both machines. The precision of the two devices was assessed with repeatability and reproducibility measures: the first within a given subject and the second within and among configurations. With regard to overall precision, using the Center Point Method, the largest component of variation was the subject to subject variation. The CEM-530 machine was less variable than the Cellchek Plus machine for endothelial cell density and % Hexagonality. The CEM-530 was also less variable than the Cellchek Plus machine for the coefficient of variation.

In summary, the agreement and precision of the Specular Microscope CEM-530 Center Point Method were found to be substantially equivalent to the Konan CellChek Plus center method.

CONCLUSIONS

The Nidek Specular Microscope CEM-530 has the same intended use and indications for use, technological characteristics, and principles of operation as the previously cleared predicate. The minor differences between the subject device and the predicate device have been assessed in a human clinical trial which found agreement, accuracy and precision between the two devices. Therefore, the Nidek Specular Microscope CEM-530 is as safe and effective as its predicate device, and thus, substantially equivalent.