June 16, 2023

Eyenuk, Inc.
Kaushal Solanki, PhD
CEO
5850 Canoga Ave, Suite 250
Los Angeles, California 91367

Re: K223357
Trade/Device Name: EyeArt v2.2.0
Regulation Number: 21 CFR 886.1100
Regulation Name: Retinal Diagnostic Software Device
Regulatory Class: Class II
Product Code: PIB
Dated: May 5, 2023
Received: May 5, 2023

Dear Dr. Kaushal Solanki:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's

requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Elvin Y. Ng -S

Elvin Ng
Assistant Director
DHT1A: Division of Ophthalmic Devices
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Respiratory, ENT and Dental Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K223357

Device Name
EyeArt

Indications for Use *(Describe)*
EyeArt is indicated for use by healthcare providers to automatically detect more than mild diabetic retinopathy and vision-threatening diabetic retinopathy (severe non-proliferative diabetic retinopathy or proliferative diabetic retinopathy and/or diabetic macular edema) in eyes of adults diagnosed with diabetes who have not been previously diagnosed with diabetic retinopathy. EyeArt is indicated for use with Canon CR-2 AF, Canon CR-2 Plus AF, and Topcon NW400 cameras.

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
Eyenuk's EyeArt

I. Submitter

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Contact Person: Kaushal Solanki

Date Prepared: 15 June 2023

II. Device

Name of Device: EyeArt v2.2.0
Classification Name: Retinal diagnostic software device
Regulatory Class: Class II
Regulation: 21 CFR 886.1100
Product Code: PIB

III. Predicate device

Trade name of the device: EyeArt
Manufacturer's Name: Eyenuk, Inc.
Premarket notification number: K200667

IV. Device Description

EyeArt is a software as a medical device that consists of three components – Client, Server, and Analysis Computation Engine (Figure 1).

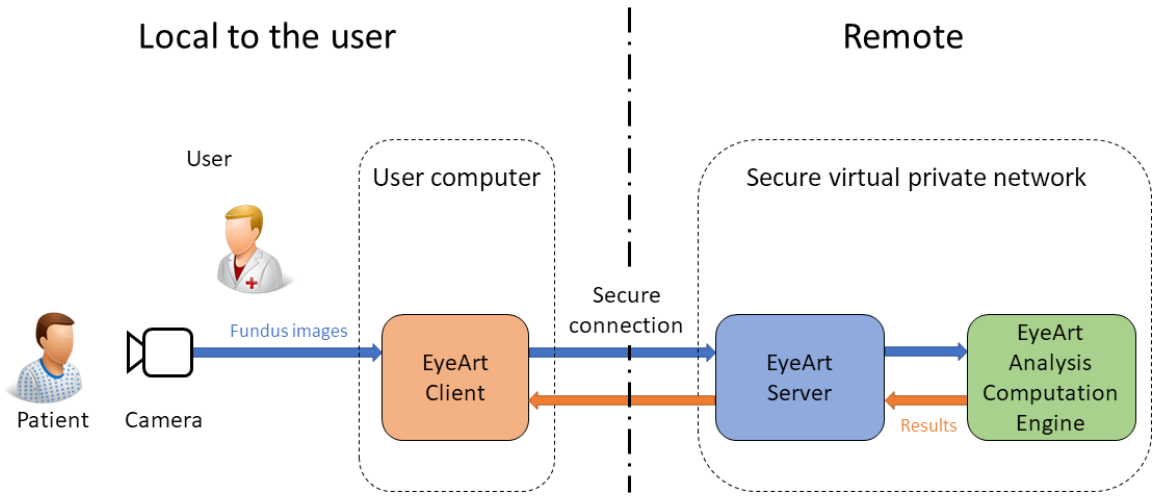

Figure 1: EyeArt components: Client, Server, and Analysis Compute Engine.

A retinal fundus camera, used to capture retinal fundus images of the patient, is connected to a computer where the EyeArt Client software is installed. The EyeArt Client software provides a graphical user interface (GUI) that allows the EyeArt operator to transfer the appropriate fundus images to and receive results from the remote EyeArt Analysis Computation Engine through the EyeArt Server. The EyeArt Analysis Computation Engine is installed on remote computer(s) in a secure data center and uses artificial intelligence algorithms to analyze the fundus images and return results. EyeArt is intended to be used with retinal fundus images of resolution 1.69 megapixels or higher captured using one of the indicated retinal fundus cameras (Canon CR-2 AF, Canon CR-2 Plus AF, and Topcon NW400) with 45 degrees field of view. EyeArt is specified for use with two retinal fundus images per eye: optic nerve head (ONH) centered and macula centered. For each patient eye, the EyeArt results separately indicate whether "more than mild diabetic retinopathy (mtmDR)" and "vision-threatening diabetic retinopathy (vtDR)" are detected. "More than mild diabetic retinopathy" is defined as the presence of moderate non-proliferative diabetic retinopathy or worse on the International Clinical Diabetic Retinopathy (ICDR) severity scale and/or the presence of diabetic macular edema. "Vision-threatening diabetic retinopathy" is defined as the presence of severe non-proliferative diabetic retinopathy or proliferative diabetic retinopathy on the ICDR severity scale and/or the presence of diabetic macular edema. Description of EyeArt components is provided below.

- EyeArt Client: This component is installed on the computer connected to a fundus camera and used by the EyeArt operator. It allows the operator to transfer images to the EyeArt Analysis Computation Engine and receive results. Its functioning requires an internet connection. If images from a patient encounter cannot be analyzed, due to poor image quality or due to lack of all required image fields, live image quality feedback is provided to the operator to help successfully obtain results upon image recapture.

- EyeArt Server: This component provides an interface that securely handles incoming requests and securely stores user information including images and results. It enables the EyeArt Client to use the EyeArt Analysis Computation Engine through an application programming interface (API).

- EyeArt Analysis Computation Engine: This component analyzes the images to determine exam quality and detect mtmDR and vtDR. It consists of an ensemble of clinically aligned machine learning (including deep learning) algorithms.

V. Intended Use / Indications for Use

The EyeArt v2.2.0 has the same intended use as the predicate device and all other devices regulated under 21 CFR 886.1100, which is "to evaluate ophthalmic images for diagnostic screening to identify retinal diseases or conditions." The Indication for Use (IFU) statement for EyeArt v2.2.0 is the following:

EyeArt is indicated for use by healthcare providers to automatically detect more than mild diabetic retinopathy and vision-threatening diabetic retinopathy (severe non-proliferative diabetic retinopathy or proliferative diabetic retinopathy and/or diabetic macular edema) in eyes of adults

diagnosed with diabetes who have not been previously diagnosed with diabetic retinopathy. EyeArt is indicated for use with Canon CR-2 AF, Canon CR-2 Plus AF, and Topcon NW400 cameras.

The IFU statement for EyeArt v2.2.0 is not substantially different from that of the predicate device and the differences do not alter the intended use. The main difference in the IFU statement for EyeArt v2.2.0 versus that of the predicate is the inclusion of an additional fundus camera, the Topcon NW400. This difference is supported with non-clinical and clinical performance testing.

VI. Purpose of this submission

The purpose of this 510(k) notification is to modify EyeArt (software version 2.1.0) and update it to software version 2.2.0. The technological differences between the subject and predicate device are summarized as follows:

- Updated image quality assessment module in the EyeArt Analysis Computation Engine;
- Support for additional Topcon NW400 camera model, in addition to previously cleared Canon CR-2 AF and CR-2 Plus AF;
- Live image quality feedback to provide quality feedback to the EyeArt operator as they capture images;
- Ability to save a patient encounter entry and retry imaging after pupil dilation.

VII. Comparison of the technological characteristics with the predicate

The main technological principle for the subject and predicate devices is artificial intelligence (AI)-based technology to analyze specific features from retinal images. Both include the same general components: the EyeArt Client installed on the computer used by the EyeArt operator to help capture good quality retinal images, transfer the images for analyses, and receive results; EyeArt Analysis Computation Engine to analyze images and determine exam quality and detect DR; and EyeArt Server to provide a secure interface between the Client and Analysis Computation Engine.

Table 1: Comparison of the IFU statements of the EyeArt subject device and the predicate device

EyeArt v2.2.0 (Subject device)	**EyeArt v2.1.0 (K200667, Predicate device)**	**Discussion**
EyeArt is indicated for use by healthcare providers to automatically detect more than mild diabetic retinopathy and vision-threatening diabetic retinopathy (severe non-proliferative diabetic retinopathy or proliferative diabetic retinopathy and/or diabetic macular edema) in eyes of adults diagnosed with diabetes who have not been previously diagnosed with diabetic retinopathy.	*EyeArt is indicated for use by healthcare providers to automatically detect more than mild diabetic retinopathy and vision-threatening diabetic retinopathy (severe non-proliferative diabetic retinopathy or proliferative diabetic retinopathy and/or diabetic macular edema) in eyes of adults diagnosed with diabetes who have not been previously diagnosed with more than mild diabetic retinopathy.*	Main difference is the addition of the Topcon NW400 fundus camera, supported by non-clinical and clinical

EyeArt v2.2.0 (Subject device)	**EyeArt v2.1.0 (K200667, Predicate device)**	**Discussion**
EyeArt is indicated for use with Canon CR-2 AF, Canon CR-2 Plus AF, and Topcon NW400 cameras.	*EyeArt is indicated for use with Canon CR-2 AF and Canon CR-2 Plus AF cameras in both primary care and eye care settings.*	performance testing.

Table 2: Comparison of other technological elements of the EyeArt device and the predicate device.

	EyeArt v2.2.0 (Subject device)	**EyeArt v2.1.0 (K200667, Predicate device)**	**Discussion**
Technological principle	Artificial Intelligence software as a medical device	Artificial Intelligence software as a medical device	Equivalent
Inputs	Macula and disc centered retinal fundus images with 45° field of view, 2 per eye	Macula and disc centered retinal fundus images with 45° field of view, 2 per eye	Equivalent
Main outputs	Detection of diabetic retinopathy in each eye: **More than mild diabetic retinopathy (mtmDR):** one of *negative*, *positive*, or *ungradable*. **Vision-threatening diabetic retinopathy (vtDR):** one of *negative*, *positive*, or *ungradable*.	Detection of diabetic retinopathy in each eye: **More than mild diabetic retinopathy (mtmDR):** one of *negative for mtmDR*, *mtmDR detected*, or *ungradable*. **Vision-threatening diabetic retinopathy (vtDR):** one of *negative for vtDR*, *vtDR detected*, or *ungradable*.	Equivalent
Architecture	Client software (user facing) transfers images to and receives results from Analysis Computation Engine through Server.	Client software (user facing) transfers images to and receives results from Analysis Computation Engine through Server.	Equivalent
Indicated Cameras	Canon CR-2 AF, Canon CR-2 Plus AF, and Topcon NW400	Canon CR-2 AF and Canon CR-2 Plus AF	The Canon CR-2 AF and Canon CR-2 Plus AF cameras are used to capture macula and disc centered retinal images with 45° field of view (2 per eye) for both the subject and the predicate device. The clinical performance data support the use of EyeArt with the additional indicated Topcon NW400 camera.

VIII. Performance data: non-clinical testing

EyeArt (software version v2.2.0) was identified as having a major level of concern as defined in the FDA guidance document "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices."

Verification and validation activities at unit, integration, and system level were performed. In all instances, EyeArt functioned as intended and results observed were as expected (i.e., all specifications were met).

Comprehensive risk analysis has been conducted for EyeArt with identification and detailed characterization of the hazards including their causes and severity. Adequate risk control measures have been designed and implemented to mitigate all identified hazards to acceptable levels. EyeArt also implements comprehensive cybersecurity measures for data confidentiality, data integrity, and data and service availability. Designed to meet industry standard cybersecurity best practices, EyeArt ensures that data remains secure (with encryption during transit and at rest) and private (with authentication and authorization protocols enabling access). EyeArt has been designed to provide results that are aligned with the clinical practice recommendations for the ophthalmic care of patients with diabetes and has been developed in a clinically aligned framework.

IX. Performance testing: clinical testing

A. Prospective clinical study

A prospective, multi-center clinical study (Protocol EN-01b) was conducted to evaluate the diagnostic accuracy and precision of EyeArt v2.2.0 with the Topcon NW400 and Canon CR-2 AF cameras. Eligible adults age 22 or older with known diagnosis of diabetes mellitus (DM) who provided informed consent were enrolled across six sites that did not contribute data used for training or development of EyeArt. Main exclusion criteria were persistent visual impairment in one or both eyes, contraindication to fundus photography or pharmacologic mydriasis, and/or history of retinal vascular occlusion, ocular injections, laser treatments to the retina, or prior intraocular surgery other than uncomplicated cataract extraction. Participants underwent EyeArt imaging with the study cameras. Multiple EyeArt imaging sessions were performed by multiple operators on multiple cameras to collect data for estimation of precision. Pupils were pharmacologically dilated as needed per instructions in the User Manual. Participants then underwent dilated 4-widefield stereo fundus imaging by a certified photographer. The clinical reference standard (CRS) was determined by experienced and certified graders at the University of Wisconsin Reading Center (WRC) per the Early Treatment for Diabetic Retinopathy Study (ETDRS) severity scale on the dilated 4-wide field stereo fundus images. Graders and WRC study staff were masked to participant history and EyeArt results. The WRC grading was used to determine the "ground truth" for study eyes, which was determined as follows:

- Clinical reference for more than mild DR (mtmDR):
  - ***positive*** if ETDRS level was 35 or greater (but not equal to 90) or DME grade was *present*
  - ***negative*** if ETDRS levels were 10-20 and DME grade was *absent*

- ***ungradable*** if ETDRS level was 90, or DME grade was *questionable* or *ungradable* with ETDRS level 10-20

- Clinical reference for vision-threatening DR (vtDR):
  - ***positive*** if ETDRS level was 53 or greater (but not equal to 90) or DME grade was *present*
  - ***negative*** if ETDRS levels were 10-47 and DME grade was *absent*
  - ***ungradable*** if ETDRS level was 90, or DME grade was *questionable* or *ungradable* with ETDRS level 10-47

246 participants were enrolled and four participants either withdrew consent (N=1) or did not meet eligibility criteria (N=3). Data from 336 eyes of 171 participants were included in the accuracy and agreement analyses and data from 264 eyes from 132 participants were included in the precision analyses. In the accuracy analysis population, the mean age was 58.8±13.7 years (range 23 – 83). 46.2% were women (79/171) and 53.8% (92/171) were men. 86% (147/171) of the cohort was White, 10.5% (18/171) Black, 0.6% (1/171) Asian, 2.3% (4/171) other race, 0.6% (1/171) Native Hawaiian or other Pacific Islander. 11.7% (20/171) were Hispanic/Latino. 70.8% (121/171) have type 2 DM and 29.2% (50/171) have type 1 DM. Mean DM duration was 16.4±11.8 years (range zero – 53 years) and mean hemoglobin A1c (HbA1c) level from the prior three months was 7.7%±1.5% (range 5.6% – 14.1%). 22.0% (74/336) and 9.2% (31/336) of study eyes were mtmDR+ and vtDR+ by CRS grading, respectively. 3.0% (10/336) and 3.6% (12/336) of study eyes were designated ungradable for mtmDR and vtDR (respectively) by CRS grading.

Canon CR-2 AF/Plus AF and Topcon NW400 images from 90.4% of participants received EyeArt analysis results without pupil dilation. After dilation as needed, 99.0% of participants with Canon CR-2 AF/Plus AF images and 98.9% with Topcon NW400 images yielded in EyeArt analysis results.

Table 3 provides the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (PPV) using EyeArt v2.2.0 with the Canon CR-2 AF/Plus AF and Topcon NW400 cameras. Best-case (images unanalyzable by EyeArt are imputed as being in agreement with the CRS determination) and worst-case (images unanalyzable by EyeArt are imputed as being in disagreement with the CRS determination) sensitivity and specificity are also shown.

Table 3: Key performance measures of EyeArt with Canon CR-2 AF/Plus AF and Topcon NW400 for mtmDR and vtDR detection.

EN-01b entire analysis population	mtmDR		vtDR	
	EyeArt v2.2.0 with Canon CR-2 AF /Plus AF	**EyeArt v2.2.0 with Topcon NW400**	**EyeArt v2.2.0 with Canon CR-2 AF /Plus AF**	**EyeArt v2.2.0 with Topcon NW400**
Sensitivity	95.9% [90.4% - 100%] (70/73)	94.4% [88.3% - 98.8%] (68/72)	96.8% [90.0% - 100%] (30/31)	96.8% [89.5% - 100%] (30/31)
Best-case sensitivity	95.9% [90.5% - 100.0%] (71/74)	94.6% [88.6% - 98.8%] (70/74)	96.8% [90.9% - 100.0%] (30/31)	96.8% [89.5% - 100.0%] (30/31)
Worst-case sensitivity	94.6% [88.9% - 98.8%] (70/74)	91.9% [84.8% - 97.3%] (68/74)	96.8% [90.0% - 100.0%] (30/31)	96.8% [89.5% - 100.0%] (30/31)

EN-01b entire analysis population	mtmDR		vtDR	
	EyeArt v2.2.0 with Canon CR-2 AF /Plus AF	**EyeArt v2.2.0 with Topcon NW400**	**EyeArt v2.2.0 with Canon CR-2 AF /Plus AF**	**EyeArt v2.2.0 with Topcon NW400**
Specificity	86.4% [81.2% - 91.1%] (216/250)	91.1% [86.8% - 94.8%] (226/248)	91.7% [87.7% - 95.2%] (266/290)	91.6% [87.5% - 95.1%] (263/287)
Best-case specificity	86.5% [81.3% – 91.2%] (218/252)	91.3% [87.1% - 94.9%] (230/252)	91.8% [87.9% - 95.3%] (269/293)	91.8% [87.8% - 95.1%] (269/293)
Worst-case specificity	85.7% [80.6% - 90.3%] (216/252)	89.7% [85.05% - 93/3%] (226/252)	90.8% [86.7% - 94.7%] (266/293)	89.8% [85.7% - 93.6%] (263/293)
PPV – Positive Predictive Value	67.3% [55.9% - 77.4%] (70/104)	75.6% [64.6% - 85.4%] (68/90)	55.6% [39.2% - 72.0%] (30/54)	55.6% [38.0% - 72.1%] (30/54)
NPV – Negative Predictive Value	98.6% [96.9% - 100%] (216/219)	98.3% [96.4% - 99.6%] (226/230)	99.6% [98.8% - 100%] (266/267)	99.6% [98.5% - 100%] (263/264)
All the 95% confidence intervals (95%CI, [xx.x% - xx.x%]) are computed using the clustered bootstrap method that takes into consideration the correlation between eyes of the same participant.				

Agreement between cameras – For mtmDR detection, the average positive agreement (APA) between EyeArt results with the Topcon NW400 camera and those with the Canon CR-2 AF/Plus AF cameras was 97.1% [95% CI: 93.8% - 99.7%] among reference standard positives and the average negative agreement (ANA) was 95.0% [95% CI: 92.7% - 97.1%] among reference standard negatives. For vtDR detection, APA was 100.0% [95% CI: 94.0% - 100.0%] among reference standard positives and ANA was 96.4% [95% CI: 94.6% - 98.0%] among reference standard negatives.

Estimates of precision – Intra-operator repeatability data was collected from multiple sites by having each participant in the repeatability cohorts undergo at least three EyeArt operations performed by the same EyeArt operator with the same Topcon NW400 camera unit. The inter-operator reproducibility data was collected by having each participant in the reproducibility cohorts undergo at least one EyeArt operation performed by three distinct operators each operating a distinct Topcon NW400 camera unit. The precision results of EyeArt with the Topcon NW400 cameras is provided in **Table 4** for mtmDR and vtDR detection.

Table 4: Key precision measures of EyeArt with the Topcon NW400 camera for mtmDR and vtDR detection

EyeArt with Topcon NW400	mtmDR		vtDR	
	Intra-operator Repeatability	**Inter-operator Reproducibility**	**Intra-operator Repeatability**	**Inter-operator Reproducibility**
APA among reference standard positives	100.0% [98.2% - 100.0%]	100.0% [96.4% - 100.0%]	100.0% [94.9% - 100.0%]	100.0% [75.8% - 100.0%]
ANA among reference standard negatives	98.9% [97.6% - 99.7%]	97.2% [92.3% - 100.0%]	99.5% [98.8% - 100.0%]	93.3% [87.3% - 97.7%]
All the 95% confidence intervals (95%CI, [xx.x% - xx.x%]) are computed using the clustered bootstrap method that takes into consideration the correlation between eyes of the same participant. For cases with proportion of 100%, the 95% CIs using clustered bootstrap are [100% - 100%], hence the Wilson method is used, which however is not designed to consider eye correlation.				

The results of this prospective study support a determination of substantial equivalence between EyeArt v2.2.0 and EyeArt v2.1.0 and support the addition of the Topcon NW400 camera to the IFU statement.

B. Retrospective study

The clinical performance of EyeArt v2.2.0 was evaluated in a retrospective clinical study utilizing the data already collected in the EyeArt pivotal multi-center clinical study (Protocol EN-01). The primary endpoints were sensitivity and specificity, and the secondary endpoints were imageability (the proportion of evaluated participant eyes that received EyeArt disease detection results), positive predictive value (PPV), and negative predictive value (NPV). The modified version of EyeArt (v2.2.0) was evaluated on data from 1310 eyes of 655 participants that were enrolled in the pivotal study.

88.4% of undilated eyes received EyeArt results with EyeArt v2.2.0 vs. 86.6% with EyeArt v2.1.0. ("first-submission imageability," Table 5). "Final-submission imageability" after dilation as needed was 99.1% with EyeArt v2.2.0 and 97.3% with EyeArt v2.1.0.

Table 5: Imageability of EyeArt for mtmDR and vtDR detection for undilated (first submission) and dilate-if-needed (final submission) images.

EN-01 entire analysis population	**mtmDR**		**vtDR**	
	EyeArt v2.1.0 (predicate device)	**EyeArt v2.2.0** (subject device)	**EyeArt v2.1.0** (predicate device)	**EyeArt v2.2.0** (subject device)
Imageability (dilate-if-needed, final submissions)	97.3% [96.2% - 98.4%] (1246/1281)	99.1% [98.4% - 99.5%] (1269/1281)	97.3% [96.0% - 98.4%] (1230/1264)	99.1% [98.4% - 99.6%] (1252/1264)
Imageability (undilated, first submissions)	86.6% [83.7% - 89.1%] (1109/1281)	88.4% [86.2% - 90.6%] (1132/1281)	86.9% [84.1% - 89.4%] (1098/1264)	88.6% [86.4% - 90.8%] (1120/1264)
All the 95% confidence intervals (95%CI, [xx.x% - xx.x%]) are computed using the clustered bootstrap method that takes into consideration the correlation between eyes of the same participant.				

The main results are summarized in Tables 6 and 7.

Table 6: Key EyeArt performance measures for mtmDR and vtDR detection using "first-submission" images (undilated submissions)

EN-01 entire analysis population	**mtmDR**		**vtDR**	
	EyeArt v2.1.0 (predicate device)	**EyeArt v2.2.0** (subject device)	**EyeArt v2.1.0** (predicate device)	**EyeArt v2.2.0** (subject device)
Sensitivity	94.4% [90.6% - 97.5%] (151/160)	94.6% [91.0% - 97.9%] (159/168)	92.3% [83.6% - 100.0%] (36/39)	92.7% [83.7% - 100%] (38/41)
Specificity	86.1% [83.7% - 88.9%] (817/949)	85.9% [83.5% - 88.1%] (828/964)	92.4% [90.3% - 94.4%] (979/1059)	92.4% [90.7% - 94.2%] (997/1079)
PPV – Positive Predictive Value	53.4% [46.0% - 60.2%] (151/283)	53.9% [47.3% - 59.9%] (159/295)	31.0% [21.2% - 40.3%] (36/116)	31.7% [22.2% - 40.5%] (38/120)
NPV – Negative Predictive Value	98.9% [98.2% - 99.5%] (817/826)	98.9% [98.1% - 99.6%] (828/837)	99.7% [99.4% - 100.0%] (979/982)	99.7% [99.3% - 100%] (997/1000)
All the 95% confidence intervals (95%CI, [xx.x% - xx.x%]) are computed using the clustered bootstrap method that takes into consideration the correlation between eyes of the same participant.				

Table 7: Key EyeArt performance measures for mtmDR and vtDR detection using "final-submission" images (dilate-if-needed submissions)

EN-01 entire analysis population	mtmDR		vtDR	
	EyeArt v2.1.0 (predicate device)	**EyeArt v2.2.0** (subject device)	**EyeArt v2.1.0** (predicate device)	**EyeArt v2.2.0** (subject device)
Sensitivity	94.4% [90.8% - 97.6%] (168/178)	95.1% [91.7% - 98.2%] (174/183)	92.7% [85.1% - 100.0%] (38/41)	95.5% [89.8% - 100.0%] (42/44)
Specificity	86.3% [83.8% - 88.7%] (922/1068)	86.1% [83.8% - 88.5%] (920/1068)	92.7% [90.9% - 94.5%] (1102/1189)	92.4% [90.7% - 94.2%] (1100/1190)
PPV – Positive Predictive Value	53.5% [46.0% - 60.2%] (168/314)	54.0% [47.4% - 60.3%] (174/322)	30.4% [22.0% - 40.0%] (38/125)	31.8% [22.5% - 40.2%] (42/132)
NPV – Negative Predictive Value	98.9% [98.3% - 99.6%] (922/932)	99.0% [98.4% - 99.7%] (920/929)	99.7% [99.4% - 100.0%] (1102/1105)	99.8% [99.5% - 100.0%] (1100/1102)
All the 95% confidence intervals (95%CI, [xx.x% - xx.x%]) are computed using the clustered bootstrap method that takes into consideration the correlation between eyes of the same participant.				

Worst-case and best-case performance is shown in Table 8. The worst-case imputation assumes that EyeArt ungradable submissions all disagree with the clinical reference standard, and the best-case imputation assumes that the EyeArt ungradable submissions all agree with the clinical reference standard.

Table 8: Worst-case and best-case EyeArt v2.2.0 performance for mtmDR and vtDR detection.

EN-01 entire analysis population	mtmDR		vtDR	
	EyeArt v2.2.0 (worst-case)	**EyeArt v2.2.0 (best-case)**	**EyeArt v2.2.0 (worst-case)**	**EyeArt v2.2.0 (best-case)**
Sensitivity	94.7% [91.3% - 97.6%] (178/188)	95.2% [91.7% - 98.0%] (179/188)	95.6% [89.5% - 100.0%] (43/45)	95.6% [89.5% - 100.0%] (43/45)
Specificity	85.4% [82.7% - 87.7%] (933/1093)	86.4% [83.8% - 88.7%] (944/1093)	91.5% [89.6% - 93.2%] (1115/1219)	92.5% [90.8% - 94.3%] (1127/1219)
PPV – Positive Predictive Value	52.7% [46.0% - 58.9%] (178/338)	54.6% [48.2% - 60.8%] (179/328)	29.3% [20.3% - 37.5%] (43/147)	31.9% [23.2% - 41.2%] (43/135)
NPV – Negative Predictive Value	98.9% [98.2% - 99.5%] (933/943)	99.1% [98.4% - 99.6%] (944/953)	99.8% [99.5% - 100.0%] (1115/1117)	99.8% [99.6% - 100.0%] (1127/1129)
All the 95% confidence intervals (95%CI, [xx.x% - xx.x%]) are computed using the clustered bootstrap method that takes into consideration the correlation between eyes of the same participant.				

The results of this retrospective study support a determination of substantial equivalence between EyeArt v2.2.0 and EyeArt v2.1.0.

X. Human Factors Validation Testing

The human factors data support the safety and effectiveness of the use of the EyeArt Client user interface and the indicated camera models. The human factors validation testing for EyeArt v2.2.0 was conducted as per the current human factors guidance document. The critical task for using EyeArt is the ability to capture four images of sufficient quality to produce EyeArt gradable results.

XI. Conclusions

EyeArt v2.2.0 with the Canon CR-2 AF, Canon CR-2 Plus AF, and Topcon NW400 cameras is substantially equivalent to the predicate device, EyeArt v2.1.0. They have the same intended use. The technological differences between EyeArt v2.2.0 and the predicate device do not raise new types of questions of safety or effectiveness. Performance data support the substantial equivalence of EyeArt to the predicate device.