November 10, 2022

AEYE Health, Inc.
% John Smith MD, JD
Partner
Hogan Lovells US LLP
555 13th Street NW
Washington, District of Columbia 20004

Re: K221183
Trade/Device Name: Aeye-ds
Regulation Number: 21 CFR 886.1100
Regulation Name: Retinal Diagnostic Software Device
Regulatory Class: Class II
Product Code: PIB
Dated: October 7, 2022
Received: October 7, 2022

Dear Dr. Smith:

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
OHT1: Office of Ophthalmic, Anesthesia,
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)*

K221183

Device Name

AEYE-DS

Indications for Use *(Describe)*

The AEYE-DS device is indicated for use by health care providers to automatically detect more than mild diabetic retinopathy (mtmDR) in adults diagnosed with diabetes who have not been previously diagnosed with diabetic retinopathy. The AEYE-DS is indicated for use with the Topcon NW400.

Type of Use *(Select one or both, as applicable)*

X 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**

# AEYE-DS DEVICE

**510(k) Number K221183**


**Applicant Name:** AEYE Health Inc.

**Contact Person:** Zack Dvey-Aharon, Ph.D.

**Contact:** AEYE Health Inc.
200 Park Ave
New York, NY, 10166 USA
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**Date Prepared:** November 9, 2022

**Trade Name:** AEYE-DS

**Classification Name:** 21 CFR 886.1100; (Product Code PIB)
Retinal Diagnostic Software Device

**Classification:** Class II

**Predicate Device:**

The AEYE-DS device is substantially equivalent to the following predicate device:

| Predicate | Device | Manufacturer | 510(k) No. |
|---|---|---|---|
| Main | IDx-DR | IDx LLC | DEN180001 |

**Device Description:**

AEYE-DS is a retinal diagnostic software device that incorporates an algorithm to evaluate ophthalmic images for diagnostic screening to identify retinal diseases or conditions. Specifically, the AEYE-DS is designed to perform diagnostic screening for the condition of more-than-mild diabetic retinopathy (mtmDR).

The AEYE-DS is comprised of 5 software components: (1) Client; (2) Service; (3) Analytics; (4) Reporting and Archiving; and (5) System Security. The device configuration of these modules is presented in the figure below, indicating which components are local to the user and which are remotely located.

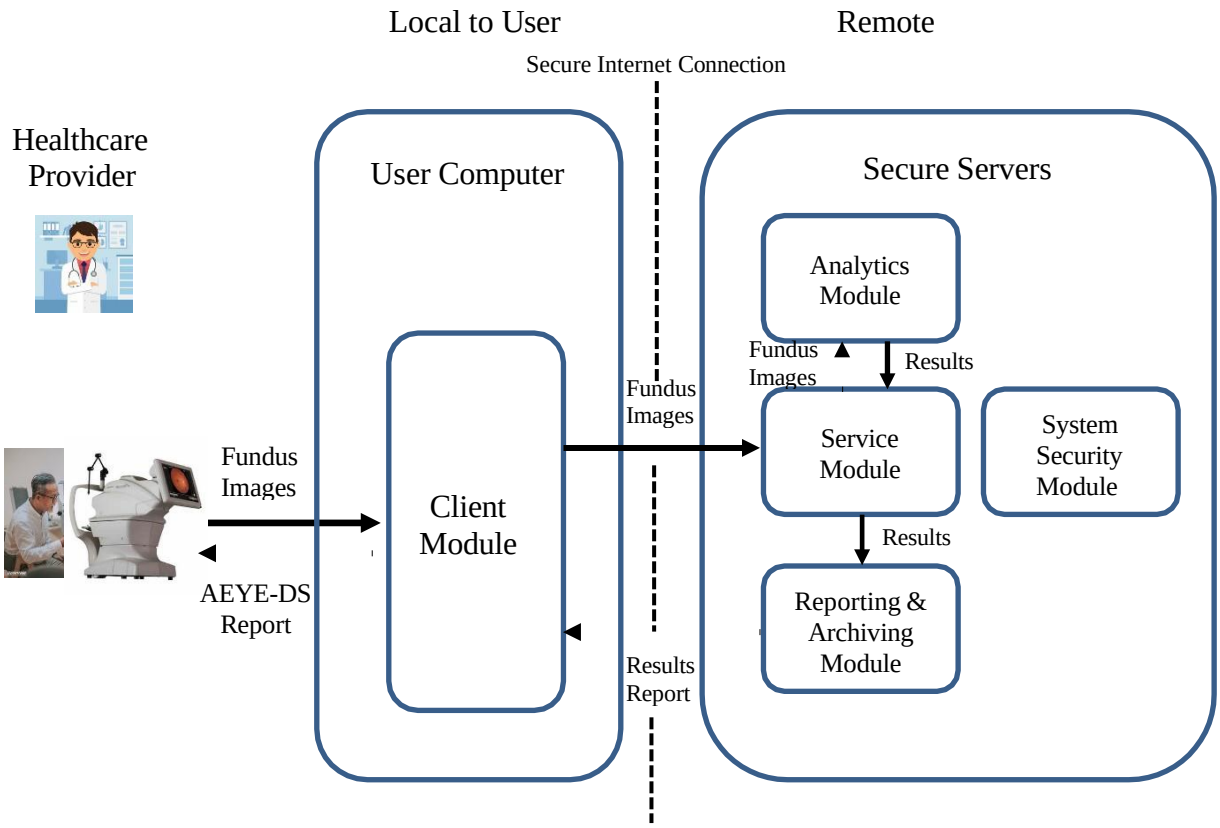


**Figure 1: Device Configuration**

The AEYE-DS device is based on the main technological principle of Artificial Intelligence (AI) software as a medical device. The software as a medical device uses artificial intelligence technology to analyze specific disease features from fundus retinal images for diagnostic screening of diabetic retinopathy.

The AEYE-DS device is based on the principle of operation, whereby a fundus camera is used to obtain retinal images. The fundus camera is attached to a computer, where the Client module/software is installed. The Client module/software guides the user to acquire the images and enables the user to interact with the server-based analysis software over a secure internet connection. Using the Client module/software, users identify the fundus images per eye to be dispatched to the Service module/software. The Service module/software is installed on a server hosted at a secure datacenter, receives the fundus images and transfers them to the Analytics module/software. The Analytics module/software, which runs alongside the Service module/software, processes the fundus images and returns information on the image quality and the presence or absence of mtmDR to the Service module/software. The Service module/software then returns the results to the Client module/software.

**Intended Use/Indication for Use:**

The AEYE-DS device is indicated for use by health care providers to automatically detect more than mild diabetic retinopathy (mtmDR) in adults diagnosed with diabetes who have not been previously diagnosed with diabetic retinopathy. The AEYE-DS is indicated for use with the Topcon NW400.

Prescription Use only: Federal law restricts this device for sale by or on the order of a physician.

**Performance Standards:**

The AEYE-DS device complies with the following FDA recognized consensus standards:

- Software Verification and Validation Testing Software verification and validation testing were conducted, and documentation was provided as recommended by FDA's Guidance for Industry and FDA Staff, "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices." The software for this device was considered as a "Major" level of concern, since a failure or latent flaw in the software could result in serious injury to the patient through incorrect or delayed information or through the action of a care provider.
- IEC 62304 Edition 1.1 2015-06 CONSOLIDATED VERSION Medical device software – Software life cycle processes
- ISO 14971 Medical devices – Application of risk management to medical devices

**Non-Clinical (Bench) Performance Data:**

Software validation testing in compliance with FDA guidelines for software validation and IEC 62304 standard requirements was also conducted.

The software hazard analysis was performed as part of the system hazard analysis. The hazards of the software influencing the operations of the system, the hardware problems impairing the software's integrity, and the incorrect operations of the system by the user that could affect the software's correct functioning, were handled as part of the system hazard analysis. The risks and the risk reductions are found in the Risk Analysis for the AEYE-DS device.

The cybersecurity requirements for the AEYE-DS device were identified according to the Content of Premarket Submissions for Management of Cybersecurity in Medical Devices. A threat analysis was performed and documented in the Cybersecurity Report. Updates to the software are also detailed in the Cybersecurity Report.

The results of the performance tests, including software validation, cybersecurity and hazard analysis demonstrated that the AEYE-DS device (version 5.00) is substantially equivalent to the predicate devices.

**Animal Performance Data / Histology Data:**

Not Applicable

**Clinical Performance Data:**

The AEYE-DS device performance for automated more than mild Diabetic Retinopathy (mtmDR) detection from digital funduscopic images was demonstrated in a pivotal clinical study. The study was a prospective, multi-center, single-arm, blinded study. The study was conducted at 8 study sites in the United States (7 sites) and Israel (1 site), with active enrollment from October 2020 through November 2021. A total of 531 subjects were screened and enrolled in the study. The study population represented the target population for the use of this device and consisted of stable, visually asymptomatic subjects who were previously diagnosed with diabetes and had no prior diagnosis of mtmDR. Subjects participated in a routine retinal screening test for diabetic retinopathy (DR) in hospitals, primary care clinics or medical research centers. Patients of both genders, all ethnicities and ≥22 years of age were recruited to the study. General patient demographics, medical history, concomitant medications, fundoscopy system used, OCT system used, etc., were obtained for each study subject.

Novice operators, who had not previously performed ocular imaging, obtained fundoscopy images from each eye of the patient, using the Topcon Model NW400 funduscopic camera. Upon submission of the fundoscopy images to the AEYE-DS client software, a diagnostic result (and PDF diagnostics report) of more than mild DR (mtmDR) detected or more than mild DR not detected was produced. A result of 'insufficient quality' was determined if the novice operator reached a maximum of 6 image submission attempts and one or more of the images was still of insufficient image quality. After the novice operator generated an AEYE-DS diagnostic output, each participant underwent additional retinal imaging captured by a professional ophthalmic photographer, to obtain dilated four widefield stereo color fundus images, lens photography for media opacity assessment and macular optical coherence tomography (OCT) imaging. The professional images were sent to an independent reading center where the severity of retinopathy and diabetic macular edema (DME) were determined according to the Early Treatment for Diabetic Retinopathy Study severity (ETDRS) scale. The Reading Center diagnostic results formed the reference standard (ground truth) for the study. As part of the final clinical assessment, each participant was categorized as mtmDR+ or mtmDR-, based on the worst of two eyes. The final clinical assessment based on the worst of two eyes was compared with the AEYE- DS output, at the participant level.

The baseline demographic data and characteristics analysis showed that the mean age was 55 years (range 21-88), 47% were male and 53% were female, 29% were African-American, 39% White

and 29% Hispanic or Latino, the remainder were of other racial/ethnic origins. Approximately 95% of the subjects in the study were diagnosed with type 2 diabetes while approximately 5% percent were diagnosed with type 1 diabetes. Duration of diabetes since diagnosis ranged from 1 day to approximately 44 years, with a mean of approximately 10 years (SD=7.9). Most recent HbA1c levels were reported for 446 (86.3%) subjects. HbA1c levels ranged from 5% to 15.6% with a mean of 8.26% (SD=2.15).

The primary efficacy objective of this study was the sensitivity and specificity of the AEYE-DS device to detect mtmDR on digital funduscopic images, acquired by the Topcon NW400 fundoscopy device, based on two macula-centered images (one image from each eye of the patient).

AEYE-DS correctly identified 53 of the 57 fully analyzable subjects with mtmDR+, thus the sensitivity was 92.98% [CI: 83.30%; 97.24%] with a lower one-sided 97.5% confidence bound of 83.3%, which is higher than the pre-defined performance goal of 82%. Sensitivity was identical when calculated for fundus-based mtmDR+ and for multi-modal mtmDR+. Of the 405 fully analyzable subjects who were mtmDR-, according to the Reading Center diagnosis, 370 subjects were correctly identified by AEYE-DS as mtmDR-, based on fundus images alone. Thus, the specificity is 91.36% [CI: 88.22%; 93.72%] with a lower one-sided 97.5% confidence bound of 88.22%, which is higher than the pre-defined performance goal of 87%. Specificity was almost identical when calculated for multi-modal mtmDR-. Therefore, the null hypotheses for sensitivity and specificity were rejected and it is concluded that the study is deemed successful. Positive Predictive Value (PPV) was 60.23% [CI: 49.78%; 69.82%] and the Negative Predictive Value (NPV) was 98.93% [CI: 97.28%; 99.58%]. The PPV was influenced by the actual prevalence of mtmDR+ patients in the pivotal study diabetic population (i.e., 12.3%), as this was not an enriched study.

Further sub-analyses showed that there were no significant effects of sex, race/ethnicity, HbA1c (<10% vs >10%), age (<55 years vs >55 years), diabetic duration since diagnosis (<10 years vs
>10 years, if available) and lens status on sensitivity and specificity. As sequential enrollment provided a sufficient number of mtmDR+ subjects, enrichment was not performed. Therefore, subset analysis by cohort (not enriched, enriched) was not performed.

The powered secondary endpoint of this study was the sensitivity and specificity of the AEYE-DS device to detect mtmDR from digital funduscopic images, acquired by the Topcon NW400 fundoscopy device, based on four images (one macula centered image and one optic disc centered image per eye). Diagnostic results and AEYE-DS device diagnostic results and showed a sensitivity and specificity of 94.74% [CI: 85.63%; 98.19%] and 88.64% [CI: 85.18%; 91.38%], respectively. The sensitivity is 94.74% with a lower one-sided 97.5% confidence bound of 85.63%, which is higher than the performance goal of 82%, therefore the null hypothesis is rejected in favor of the alternative hypothesis for the sensitivity. The specificity is 88.64% with a lower one-sided 97.5% confidence bound of 85.18%, which is slightly lower than the

performance goal of 87%, therefore the null hypothesis is not rejected in favor of the alternative hypothesis for the specificity. The Positive Predictive Value (PPV) was 54% [CI: 44.26%; 63.44%] and the Negative Predictive Value (NPV) was 99.17% [CI: 97.59%; 99.72%]. Sensitivity and specificity (and PPV and NPV) results were the same when calculated for fundus-based mtmDR+ and for multi-modal mtmDR+. The sensitivity of the AEYE-DS device based on 4 images passed the study performance goals, but the specificity was slightly lower. The implications of the slightly lower specificity mean that more subjects may be determined to be mtmDR+ and sent for follow-up ophthalmic examinations than necessary. As the sensitivity results were successful and even higher than the sensitivity with 2 images, and true-mtmDR+ subjects will not be missed by the AEYE-DS device, the price of a slightly lower specificity based on 4 images is not too high and does not involve any risks. In any case, as the use of two images is less complicated and time consuming than four images, it is more probable that AEYE-DS device users will rely on the use of 2 (macula-centered) images per eye. For this reason, the Instructions for Use will allow the use of 2 or 4 images per eye to obtain an EYE-DS diagnostic output.

Key results from the pivotal study are summarized in the table below.

| | **AEYE-DS Device** | |
|---|---|---|
| | 1 image per eye (Topcon NW400) | 2 images per eye (Topcon NW400) |
| Sensitivity: | 93% [CI: 83.3%; 97.2%] | 94.7% [CI: 85.6%; 98.2%] |
| Specificity: | 91.4% [CI: 88.2%; 93.7%] | 88.6% [CI: 85.2%; 91.4%] |
| Imageability: | 99.1% [CI: 97.8%; 99.7%] | 99.1% [CI: 97.8%; 99.7%] |
| PPV: | 60.2% [CI: 49.8%; 69.8%] | 54% [CI: 44.3%; 63.4%] |
| NPV: | 99% [CI: 97.3%; 99.6%] | 99.2% [CI: 97.6%; 99.7%] |

The imageability results from the pivotal study, reflecting data on the usability in the hands of the study novice operators, reported >99% imageability for the AEYE-DS device using the Topcon NW400 fundoscopy camera. In obtaining 2 sufficient quality images per eye, the vast majority of the study subjects (413 (88%)) did not require pupil dilation in the study, resulting in 91.67% sensitivity and 91.78% specificity, based on 1 image per eye. The endpoint analyses results show that the sensitivity and specificity for non-mydriatic (non-dilated subjects) are almost identical to the pivotal study efficacy results presented for the device. Moreover, it is apparent that only a small percent (~12%) of subjects required pupil dilation in order to obtain a diagnostic output. In this small percent of mydriatic (dilated) subjects, the results showed 100% sensitivity and 87.50% specificity, based on 1 image per eye.

**Precision Study**

Overall, twenty two (22) participants were included in the final statistical analysis. All 22 participants completed the entire AEYE-DS device imaging protocol and diagnostic output

twelve consecutive times, imaged by three different novice operators, using two different Topcon NW400 fundoscopy devices. Overall, 12 image sets/diagnoses were obtained for each participant, for a total of 264 image sets/diagnoses in total. Per protocol, operators allowed subjects at least 8 minutes between successive imaging. The results are presented in the following tables.

Precision Tables based on 1 image per eye:

| Intra-Operator Repeatability | Repeat 2 - mtmDR | | |
|---|---|---|---|
| Repeat 1 - mtmDR | mtmDR + | mtmDR - | Insufficient quality |
| mtmDR + | 49 | 0 | 0 |
| mtmDR - | 2 | 81 | 0 |
| Insufficient quality | 0 | 0 | 0 |
| OA | 98.48% (130/132) [94.64% ;99.58% ] | | |
| APA | 98.00% [93.00% ;99.45% ] | | |
| ANA | 98.78% [95.66% ;99.66% ] | | |
| AUA | Not presented as all cases were of sufficient quality | | |

| Between – Operator Reproducibility | Operator 3 | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Operator 1 | mtmDR + Operator 2 | | | mtmDR - Operator 2 | | | Insufficient quality Operator 2 | | |
| | mtmDR+ | mtmDR - | IQ | mtmDR + | mtmDR - | IQ | mtmDR + | mtmDR - | IQ |
| mtmDR + | 16 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| mtmDR - | 0 | 1 | 0 | 0 | 27 | 0 | 0 | 0 | 0 |
| Insufficient quality | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| OA | 97.73% (43/44) [88.19% ;99.60% ] | | | | | | | | |
| APA | 97.96% [89.31% ;99.64% ] | | | | | | | | |
| ANA | 98.80% [93.49% ;99.79% ] | | | | | | | | |
| AUA | Not presented as all cases were of sufficient quality | | | | | | | | |

| Between-Device Reproducibility | Device 2 mtmDR | | |
|---|---|---|---|
| Device 1 - mtmDR | mtmDR + | mtmDR - | Insufficient quality |
| mtmDR + | 24 | 1 | 0 |
| mtmDR - | 0 | 41 | 0 |
| Insufficient quality | 0 | 0 | 0 |
| OA | 98.48% (65/66) [91.90% ;99.73% ] | | |
| APA | 97.96% [89.31% ;99.64% ] | | |
| ANA | 98.80% [93.49% ;99.79% ] | | |
| AUA | Not presented as all cases were of sufficient quality | | |

Precision Tables based on 2 images per eye:

| Intra-Operator Repeatability | Repeat 2 - mtmDR | | |
|---|---|---|---|
| Repeat 1 - mtmDR | mtmDR + | mtmDR - | Insufficient quality |
| mtmDR + | 56 | 1 | 0 |
| mtmDR - | 3 | 72 | 0 |
| Insufficient quality | 0 | 0 | 0 |
| OA | 96.97% (128/132) [92.47% ;98.82% ] | | |
| APA | 96.55% [91.47% ;98.65% ] | | |
| ANA | 97.30% [93.26% ;98.94% ] | | |
| AUA | Not presented as all cases were of sufficient quality | | |

| Between – Operator Reproducibility | Operator 3 | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Operator 1 | mtmDR + Operator 2 | | | mtmDR - Operator 2 | | | Insufficient quality Operator 2 | | |
| | mtmDR+ | mtmDR - | IQ | mtmDR + | mtmDR - | IQ | mtmDR + | mtmDR - | IQ |
| mtmDR + | 18 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| mtmDR - | 0 | 1 | 0 | 0 | 24 | 0 | 0 | 0 | 0 |
| Insufficient quality | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| OA | 95.45% (42/44) [84.87% ;98.74% ] | | | | | | | | |
| APA | 96.49% [88.08% ;99.03% ] | | | | | | | | |
| ANA | 97.33% [90.79% ;99.27% ] | | | | | | | | |
| AUA | Not presented as all cases were of sufficient quality | | | | | | | | |

| Between-Device Reproducibility | Device 2 mtmDR | | |
|---|---|---|---|
| Device 1 - mtmDR | mtmDR + | mtmDR - | Insufficient quality |
| mtmDR + | 27 | 1 | 0 |
| mtmDR - | 2 | 36 | 0 |
| Insufficient quality | 0 | 0 | 0 |
| OA | 95.45% (63/66) [87.47% ;98.44% ] | | |
| APA | 94.74% [85.63% ;98.19% ] | | |
| ANA | 96.00% [88.89% ;98.63% ] | | |
| AUA | Not presented as all cases were of sufficient quality | | |

**Human Factors Validation Study**

Usability of the AEYE-DS device was also assessed in a human factors validation study, including User Manual comprehension and usability of the device in the hands of potential users. Once the users underwent initial, one-time training and practice, all users stated that the device was easy and straightforward and all were successful in submitting images for diagnosis and obtaining a diagnosis output result and PDF report. All users stated that the user manual was clear and easy to use.

In summary, the AEYE-DS device using 2 or 4 images acquired from the Topcon NW400 fundoscopy device demonstrates successful performance, in terms of sensitivity, specificity, PPV and NPV, as well as imageability, usability, and precision.

**Substantial Equivalence:**

The subject AEYE-DS device, manufactured by AEYE Health Inc., is substantially equivalent to the cleared IDx-DR device (manufactured by IDx LLC and the subject of De Novo DEN180001).

**Table 1: Comparison of the AEYE-DS Device to the predicate IDx-DR Device (DEN180001)**

| Technological Characteristic | AEYE-DS Device | IDx-DR Device (DEN180001) |
|---|---|---|
| **Product Code, Class** | PIB<br>Class II | PIB<br>Class II |
| **Indications for Use** | The AEYE-DS is indicated for use by health care providers to automatically detect more than mild diabetic retinopathy (mtmDR) in adults diagnosed with diabetes who have not been previously diagnosed with diabetic retinopathy. The AEYE-DS is indicated for use with the Topcon NW400. | IDx-DR is indicated for use by health care providers to automatically detect more than mild diabetic retinopathy (mtmDR) in adults diagnosed with diabetes who have not been previously diagnosed with diabetic retinopathy. IDx-DR is indicated for use with the Topcon NW400. |
| **Target Population** | Adult subjects diagnosed with Diabetes | Adult subjects diagnosed with Diabetes |
| **Anatomical Sites** | Eye examination | Eye examination |
| **Environment Used** | Hospitals, Clinics | Hospitals, Clinics |
| **Energy Used / Delivered** | Not Applicable | Not Applicable |
| **Design:** | A fundus camera is attached to a computer, where the AEYE-DS Client module is installed. The Client module allows the user to interact with the server-based analysis software over a secure internet connection. Using the Client module, users identify one (macular) or two (macular and disc) fundus images per eye to be dispatched to the Service module. The Service is installed on a server hosted at a secure datacenter. The Analytics module, which runs alongside the Service module, processes the fundus images and returns information on the image quality and the presence or absence of mtmDR to the Service module. The Service then returns the results to the Client module. | A fundus camera is attached to a computer, where the Idx-DR Client software is installed. The Client software allows the user to interact with the server-based analysis software over a secure internet connection. Using the Client software, users identify two fundus images per eye to be dispatched to Idx-Service. Idx-Service is installed on a server hosted at a secure datacenter. Idx-DR Analysis, which runs inside Idx-Service, processes the fundus images and returns information on the image quality and the presence or absence of mtmDR to Idx-Service. Idx-Service then returns the results to the Idx-DR Client. |

| Technological Characteristic | AEYE-DS Device | IDx-DR Device (DEN180001) |
|---|---|---|
| -Mechanism of Action | Artificial Intelligence software as a medical device | Artificial Intelligence software as a medical device |
| - Components | The AEYE-DS device consists of the following components:<br>- Client software on computer connected to fundoscopy camera<br>- Server including Service software and Analytics software | The Idx-DR device consists of the following components:<br>- Client software on computer connected to fundoscopy camera<br>- Server including Service software and Analytics software |
| - Inputs | Macula and disc centered color fundus images with at least 45º field of view, 2 images per eye; Or<br>Macula centered color fundus images with at least 45º field of view, 1 image per eye. | Macula and disc centered color fundus images with 45º field of view, 2 images per eye |
| - Outputs | More than mild diabetic retinopathy (mtmDR) detected, not detected or insufficient quality | More than mild diabetic retinopathy (mtmDR) detected, not detected or insufficient quality |
| - Indicated Cameras | Topcon NW400 camera | Topcon NW400 camera |
| - Minimum image size | 1000 x 1000 pixels per image | 1000 x 1000 pixels per image |
| **Performance** | 1 image per eye (Topcon NW400)<br>Sensitivity: 93% [CI: 83.3%; 97.2%]<br>Specificity: 91.4% [CI: 88.2%; 93.7%]<br>Imageability: 99.1% [CI: 97.8%; 99.7%]<br>PPV: 60.2% [CI: 49.8%; 69.8%]<br>NPV: 99% [CI: 97.3%; 99.6%] | 1 image per eye (Topcon NW400)<br><br>NOT APPLICABLE |
| | 2 images per eye (Topcon NW400)<br>Sensitivity: 94.7% [CI: 85.6%; 98.2%]<br>Specificity: 88.6% [CI: 85.2%; 91.4%]<br>Imageability: 99.1% [CI: 97.8%; 99.7%]<br>PPV: 54% [CI: 44.3%; 63.4%]<br>NPV: 99.2% [CI: 97.6%; 99.7%] | 2 images per eye (Topcon NW400)<br>Sensitivity: 87.4% (95%CI, 81.9% - 92.9%).<br>Specificity: 89.5% (95% CI, 86.9%-93.1%)<br>Imageability: 96%<br>PPV (Positive Predictive Value): 73%<br>NPV (Negative Predictive Value): 96% |

| Technological Characteristic | AEYE-DS Device | IDx-DR Device (DEN180001) |
|---|---|---|
| **Human Factors** | The AEYE-DS device uses the Client module as the user interface. The safe and efficient use of the device was established in a Usability study with novice operators. | The IDx-DR device uses the Client software as the user interface. The safe and efficient use of the device was established in a Usability study with novice operators. |
| **Standards Met** | IEC 62304 and<br>FDA Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices<br>ISO 14971<br>FDA Guidance - Content of Premarket Submissions for Management of Cybersecurity in Medical Devices | FDA Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices<br>ISO 14971<br>FDA Guidance - Content of Premarket Submissions for Management of Cybersecurity in Medical Devices |
| **Materials** | No patient contacting materials | No patient contacting materials |
| **Biocompatibility** | Not Applicable | Not Applicable |
| **Compatibility With the Environment and Other Devices** | The AEYE-DS device is compatible for use with the Topcon NW400 device. Compatibility with the environment is not applicable. | The IDx-DR device is compatible for use with the Topcon NW400 device. Compatibility with the environment is not applicable. |
| **Sterility** | Not Applicable | Not Applicable |
| **Electrical Safety** | Not Applicable | Not Applicable |
| **Mechanical Safety** | Not Applicable | Not Applicable |
| **Chemical Safety** | Not Applicable | Not Applicable |
| **Thermal Safety** | Not Applicable | Not Applicable |
| **Radiation Safety** | Not Applicable | Not Applicable |

**Conclusions:**

The subject AEYE-DS device, manufactured by AEYE Health Inc., is substantially equivalent to the cleared IDx-DR device (manufactured by IDx LLC and the subject of De Novo DEN180001).

The subject AEYE-DS device has the same intended use and indications for use as the cleared IDx-DR device. The subject device and the cleared IDx-DR device are similar in terms of their intended prescription use only, suitable for the adult population diagnosed with diabetes, indicated for use in the same anatomical site (i.e., for eye examinations) and to be used in hospital or clinic settings..

The subject AEYE-DS and cleared IDx-DR devices are composed of the same components,

including a Client module, and a Server including the Service and Analytics modules. The AEYE- DS and the IDx-DR devices are both compatible for use with the Topcon NW400 device. The subject AEYE-DS device has the same mechanism of operation and uses the same underlying technology as the predicate IDx-DR device. That is, a user interface Client module communicates with the Server, where the fundus images (one macular and one disc centered image per eye) are received and analyzed in the Analytics module to provide information regarding the presence or absence of mtmDR, which is returned to the Client module. The only difference in the mechanism of action is the additional ability of the AEYE-DS device to receive only one (macular) fundus image per eye and process these images to return similar information on the presence or absence of mtmDR. Both the AEYE-DS (whether based on 1 or 2 images per eye) and the IDx-DR device are based on Artificial Intelligence (AI) software as a medical device.

The performance characteristics, including the sensitivity, specificity, imageability, PPV and NPV of the AEYE-DS device are substantially equivalent to the cleared IDx-DR device, whether based on 1 or 2 images per eye, as demonstrated in the clinical studies performed with the AEYE-DS device. The human factors incorporated into the subject AEYE-DS device and the cleared IDx- DR device are similar. Both devices use the Client module as the user interface and the safe and efficient use of the device was established in a Usability study with novice operators for both devices. The subject device, as the cleared device, complies with same relevant consensus standards and FDA guidance document requirements, including software validation, cybersecurity and risk analysis.

Consequently, it can be concluded that the subject AEYE-DS device is substantially equivalent to the predicate IDx-DR device, approved in De Novo DEN18001 and therefore, the AEYE-DS device may be legally marketed in the USA.