2 July, 2026

iHealthScreen, Inc.
Alauddin Bhuiyan
Chief Executive Officer
132-02 89th Ave. Suite 214
Richmond Hill, New York 11418

Re: K253704
Trade/Device Name: iPredict-DR
Regulation Number: 21 CFR 886.1100
Regulation Name: Retinal diagnostic software device
Regulatory Class: Class II
Product Code: PIB
Dated: November 15, 2025
Received: November 24, 2025

Dear Alauddin Bhuiyan:

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 (the 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 available 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.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device"

(https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality Management System Regulation (QMSR) (21 CFR Part 820), which includes, but is not limited to, ISO 13485 clause 7.3 (Design controls), ISO 13485 clause 8.3 (Nonconforming product), ISO 13485 clause 8.5.2 (Corrective action), and ISO 13485 clause 8.5.3 (Preventative action). Please note that regardless of whether a change requires premarket review, the QMSR requires device manufacturers to review and approve changes to device design and production (ISO 13485 clause 7.3 and ISO 13485 clause 7.5) and document changes and approvals in the Medical Device File (ISO 13485 clause 4.2.3).

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 Part 803) for devices or postmarketing safety reporting (21 CFR Part 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 Management System Regulation (QMSR) (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

All medical devices, including Class I and unclassified devices and combination product device constituent parts are required to be in compliance with the final Unique Device Identification System rule ("UDI Rule"). The UDI Rule requires, among other things, that a device bear a unique device identifier (UDI) on its label and package (21 CFR 801.20(a)) unless an exception or alternative applies (21 CFR 801.20(b)) and that the dates on the device label be formatted in accordance with 21 CFR 801.18. The UDI Rule (21 CFR 830.300(a) and 830.320(b)) also requires that certain information be submitted to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). For additional information on these requirements, please see the UDI System webpage at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-system-udi-system.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 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,

Alexander Beylin -S Date: 2026.07.02 11:09:19 -04'00'

for CAPT Bradley Cunningham, MSE, RAC
Acting 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

Indications for Use

Please type in the marketing application/submission number, if it is known. This textbox will be left blank for original applications/submissions.	K253704

Please provide the device trade name(s).

iPredict-DR

Please provide your Indications for Use below.

iPredict-DR is intended for use by healthcare providers to automatically detect more than mild diabetic retinopathy in adults diagnosed with diabetes who have not been previously diagnosed with diabetic retinopathy.

iPredict-DR is indicated for use with iCare's DRSPlus color fundus camera.

Please select the types of uses (select one or both, as applicable).

- ☒ Prescription Use (21 CFR 801 Subpart D)
- ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

510(k) Summary – iPredict-DR

K253704

Date Prepared	June 29, 2026
Official Contact (Owner)	iHealthScreen, Inc.
	132-02 89th Ave, Suite 214,
	Richmond Hill, New York 11418, USA
Contact person:	Alauddin Bhuiyan, Chief Executive Officer
Email:	bhuiyan@ihealthscreen.org
Phone:	+1-718 926 9000

Proprietary Name	iPredict-DR
Common/Usual Name	Retinal diagnostic software
Classification Name	Retinal diagnostic software device
Classification Reference	21 CFR 886.1100
Product Code	PIB
Regulatory Class	Class II

Predicate Device(s):

Trade name of the predicate device:	IDx-DR
510(k) Number:	K203629
Classification Reference	21 CFR 886.1100
Classification Name:	Retinal diagnostic software device
Product Code	PIB
510(k) submitter/holder:	Digital Diagnostics Inc.; 2300 Oakdale Blvd., Coralville, IA 52241

Intended Use / Indications for Use

iPredict-DR is intended for use by healthcare providers to automatically detect more than mild diabetic retinopathy in adults diagnosed with diabetes who have not been previously diagnosed with diabetic retinopathy.

iPredict-DR is indicated for use with iCare's DRSPlus color fundus camera.

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

Device description

iPredict-DR software application is intended to perform computer-aided detection of more than mild diabetic retinopathy (mtmDR) in digital retinal images of diabetic patients 22 years or older, to be used by a healthcare provider (user) with basic training, in primary care or endocrinology settings. The Application hosts a software module developed using Deep-Learning algorithms to analyze digital retinal images of diagnosed diabetic patients for features suggestive of diabetic retinopathy (DR). iPredict-DR outputs a screening result of “more than mild DR detected” or “more than mild DR not detected” to the user. iPredict-DR software is designed and validated to perform at clinically acceptable sensitivity and specificity in the detection of diabetic retinopathy (DR).

iPredict-DR’s results and respective retinal images of a patient can be viewed in the form of a report made available through the application. iPredict-DR is limited to the analysis of retinal color imaging data and creating a screening result on the detection of diabetic retinopathy only.

Supported hardware (retinal camera)

iPredict-DR software application is indicated for use with iCare’s DRSPlus retinal camera (iCare Inc. K192113). DRSPlus is available commercially and was used to validate iPredict-DR as part of this regulatory clearance application. This retinal camera is intended to be used for taking digital images of the retina of the human eye. DRSPlus camera, its hardware, and its built-in imaging functionality is out of scope for the iPredict-DR software application.

iPredict-DR architecture and modes of operation

iPredict-DR software system is intended to be used with color fundus images obtained using DRSPlus retinal camera with 45 degrees field of view. The camera is connected to a computer where iPredict-DR client software is available for use. iPredict-DR client software is a web-based user interface (UI) module/component that is the user facing side of the application for data and image collection, which connects to the AI based processing modules in the server to process retinal images and evaluate the patient’s mtmDR disease status. The UI allows uploading of images by healthcare providers as drag/drop or using “upload image” option. Other information, including patient name and date of birth can be added as well. A computer with internet connection is required to access iPredict-DR. The components of iPredict-DR are described in Figure 1.

For each patient, iPredict-DR analyzes left and right eye’s retinal images and determines whether more than mild DR (mtmDR) in the individual eye is detected. If either of the eyes has mtmDR, the patient is considered at “referable DR” stage and recommended to be referred to an eye care professional. The mtmDR output is determined according to the Early Treatment Diabetic Retinopathy Study (ETDRS) grading protocol for no-DR, mild, moderate, and severe DR, from which iPredict-DR classifies the output of “mtmDR detected or referable DR (includes moderate or severe DR)” or “mtmDR not detected or non-referable DR (includes no or mild DR)”. A report is generated with the “mtmDR detected” or “mtmDR not detected” output and with the respective recommendation of “referable DR” or “non-referable DR”.

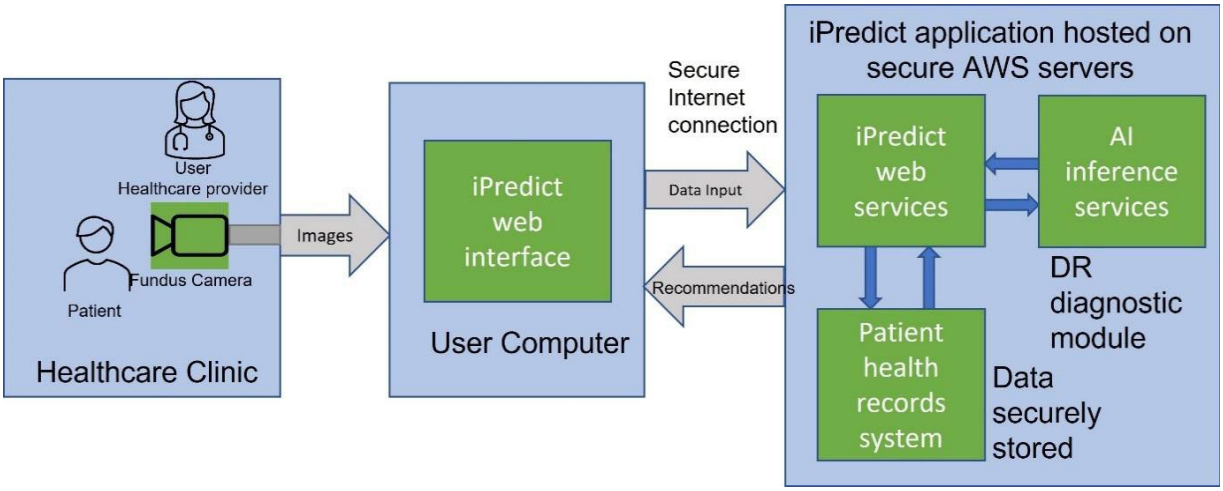

Figure 1. iPredict-DR system

iPredict-DR Client: It is a cloud-based software application's web/user interface (UI) running on a computer with internet connection, and connected to the fundus camera, located at the customer site. Using this UI, the patient's color retinal images and patient data are transferred to the DR diagnostic module or the AI server for DR diagnosis, and the UI receives the results back as a pdf report with a recommendation of referable or non-referable DR. The images and data are saved to the database server after processing. If images cannot be analyzed due to inadequate image quality, quality feedback is provided to help the operator acquire high quality images and successfully obtain a result after resubmission of images. If the image quality is poor and automatic evaluation is not feasible, the device provides an output that a referral to ophthalmologist is recommended "Refer to eye care professional due to insufficient quality image".

- iPredict-DR-server: iPredict-DR-server contains a webserver front-end that securely handles incoming requests, a database that stores customer information, and a logging system that records information about each transaction through iPredict-DR-service. iPredict-DR webserver is also responsible for device cybersecurity. The report generation module in the web server provides a pdf report of the patient's status of the disease and returns the report to user-interface with a recommendation of referable or non-referable DR status of the patient.

- iPredict-DR AI module: The AI module (deep learning algorithms and decision modules) processes the images in server and returns the results as "mtmDR detected or mtmDR not detected" and "referable or non-referable DR" to the webserver and to the report generation module.

Target Environment

The target environment for iPredict-DR is a primary care or endocrinology clinical setting with standard room, lighting, and other clinical environmental conditions. The targeted users are healthcare providers – clinician or healthcare assistant with self-training (maximum half an hour of training).

Predicate Device Description

Predicate Device(s): IDx-DR

IDx-DR (K203629) is an artificial intelligence-supported retinal image analysis system indicated for use by healthcare 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 retinal camera.

iPredict-DR has the same intended use and same indications for use (IFU) as the predicate IDx-DR device. A comprehensive summary of Substantial Equivalence in Table 1 below, details the similarities and differences between the subject device, iPredict-DR, and the predicate device, IDX-DR; and demonstrates the substantial equivalence between the subject device and predicate device in terms of the intended use and indications for use, technological characteristics, safety and effectiveness, clinical performance, non-clinical testing, and intended patient population.

An overview of the technological and functional characteristics between iPredict-DR and IDx-DR (K203629) is presented below. The subject device and predicate device have the same technological principle as AI-based technology utilized to analyze specific pathologic features from retinal fundus images. Specifically, both iPredict-DR and IDX-DR screen for DR in diabetic patients, and both devices are used for the screening of retinal diseases using a proprietary algorithm that was trained on extensive datasets and further validated based on prospective data. The proposed new device was evaluated using the same methods utilized for the cleared predicate (and consistent with the special controls for the device type), and the results demonstrate substantial equivalence to the predicate.

Table 1: Comparison with the predicate device

Features and Characteristics	IDx-DR (Predicate device) 510(k) K203629	iPredict-DR (Subject device)	Discussion of Differences and Comments
Regulation Number/Name	21 CFR 886.1100 / Retinal diagnostic software device	21 CFR 886.1100 / Retinal diagnostic software device	Equivalent
Product code	PIB, Class II	PIB, Class II	Equivalent

Intended Use / Indications for use	IDx-DR is intended for use by healthcare 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.	iPredict-DR is intended for use by healthcare providers to automatically detect more than mild diabetic retinopathy (mtmDR) in adults diagnosed with diabetes who have not been previously diagnosed with diabetic retinopathy. iPredict-DR is indicated for use with iCare's DRSPlus retinal camera.	Both devices have the same intended use per 21 CFR 886.1100 / Retinal diagnostic software device. They are substantially equivalent.
Prescription/ over-the-counter use	Prescription Use	Prescription Use	Equivalent
Technological principle	Artificial Intelligence software as a medical device that performs automated analysis of retinal images using Deep Learning neural network algorithms	Artificial Intelligence software as a medical device that performs automated analysis of retinal images using Deep Learning neural network algorithms	Equivalent
Mode of Action	Image processing software device intended to detect more than mild diabetic retinopathy in retinal images of patients diagnosed with diabetes	Image processing software device intended to detect more than mild diabetic retinopathy in retinal images of patients diagnosed with diabetes	Both devices are intended to detect DR-specific findings on acquired retinal images per 21 CFR 886.1100 / Retinal diagnostic software device. They are substantially equivalent.
Inputs	Macula and disc centered color fundus images with 45◦ field of view, 2 per eye	Macula and disc centered color fundus images with 45◦ field of view, 2 per eye	Equivalent
Outputs	Detection of diabetic retinopathy	Detection of diabetic retinopathy	

	More than mild diabetic retinopathy (mtmDR): mtmDR not detected, mtmDR detected, or insufficient quality	More than mild diabetic retinopathy (mtmDR): mtmDR not detected, mtmDR detected, or insufficient quality	They are substantially equivalent.
End Users	Healthcare providers	Healthcare providers	Equivalent
Location of use (primary)	Primary care settings, healthcare clinics, hospitals	Primary care settings, healthcare clinics, hospitals	Equivalent
Deployment	Computer-based Client software Application	Computer-based Client software Application	Equivalent
Architecture	Client software (user facing) transfers images to and receives results from Analysis through Web Server.	Client software (user facing) transfers images to and receives results from Analysis through Web Server.	Equivalent
Software Level of Concern	Major level of concern	Enhanced level of documentation to be submitted to the FDA	iPredict-DR software's level of concern is described as the "Enhanced level documentation" as per the latest FDA regulations and the Risk analysis performed. This does not present any additional risk and only indicates compliance with the updated regulatory language used by the FDA to translate the "level of concern" into "level of documentation". They are substantially equivalent.

Indicated Cameras	Topcon NW400	iCare's DRSPlus	The legally marketed cameras specified for use are being used to capture macula and disc centered with 45° field of view; for both subject device (iPredict-DR) and predicate device (IDX-DR). The clinical performance data supports the use of iPredict-DR with the indicated cameras. Both cameras produce retinal images. They are substantially equivalent.
Workflow	Labeling (the Quick Reference Guide) guides the user through the image acquisition workflow and submission of the exam. The graphical user interface includes onscreen prompts to guide the user through the image acquisition workflow one image at a time and submission of the exam.	Labeling (the Quick Reference Guide) guides the user through the image acquisition workflow and submission of the exam. The graphical user interface includes onscreen prompts to guide the user through the image acquisition workflow one image at a time and submission of the exam.	Equivalent

Conclusion on substantial equivalence:

Based upon the technical comparison information presented, it is concluded that iPredict-DR is substantially equivalent to the previously cleared predicate device, IDx-DR. Both devices have the same intended use with regard to retinal disease diagnosis based on the analysis of digital retinal images. The indications for use are the same in that both devices import images from ophthalmic devices for analysis, detect retinal features suggestive of retinal disease, and display disease diagnosis results.

Labeling

The User Manual or Instructions for Use (IFU) and the Installation Instructions for iPredict-DR are provided in the document intended to be used by healthcare providers at primary care or endocrinology clinics; for adult patients diagnosed with diabetes. A soft copy of the user manual is included with iPredict-DR web application. A user is eligible to request a paper/printed copy of the user manual/IFU at no additional cost, by contacting iHealthScreen. The user manual includes a description of the intended patient population, retinal imaging process, iPredict-DR functioning and processing steps, the factors that may impact iPredict-DR screening results, complete set of warnings, precautions, and contraindications. These warnings were found to be appropriate by other similar legally marketed devices, including the predicate device.

Software

The iPredict-DR software version 4.0 was determined to require an Enhanced Level Documentation; as defined in the FDA guidance document "Content of Premarket Submissions for Device Software Functions, JUNE 2023". Software validation testing was performed as per the FDA guidelines for software validation and IEC 62304 standard requirements which showed compliance. The software verification and validation were performed for unit, integration, and system level testing. iPredict-DR passed the tests as intended (i.e. met all specifications).

The software hazard analysis was performed as part of system risk and safety analysis. The hazards of the software and the incorrect operations of the system by the user that could affect the software's appropriate functioning, were handled as part of the system hazard analysis. iPredict-DR risk control measures have been designed and implemented adequately to mitigate all identified hazards to acceptable levels. iPredict-DR analyzed and implemented the cybersecurity requirements to be compliant according to the Content of Premarket Submissions for Management of Cybersecurity in Medical Devices.

Clinical testing

Study design and methods

In a pivotal prospective clinical trial, 922 participants were enrolled, of whom 905 were eligible for recruitment, and 886 subjects completed the study procedures. For the primary sensitivity/specificity/PPV/NPV analysis, the number of subjects was **871**.

After enrollment of subjects meeting the inclusion criteria and obtaining informed consent, retinal photos of subjects' non-dilated eyes (both eyes) were taken with the DRSPlus Digital Retinography System (CenterVue, Inc), at each of the investigational sites. For ground truth imaging, dilated 4 W-D stereoscopic and OCT imaging fundus photos were taken with the Topcon Maestro2.

All images were graded by three certified, masked expert graders at the Wisconsin Reading Center (WRC). Each eye was independently evaluated (i.e., graders were blinded to each other's gradings) using ETDRS severity levels. The final ground truth was determined by a majority vote

(2 of 3 graders). If all three grades differed, adjudication was performed.

The WRC grading was used to determine the clinical reference standard for subject eyes as follows:

Clinical reference standard for more than mild DR not detected or non-referable DR

- ETDRS level 10 and 20
- Center-involving diabetic macular edema (CI-DME) absent

Clinical reference standard for more than mild DR (mtmDR) or referable DR

- ETDRS Level 20 or above (excluding subjects with ETDRS level 60 with prior panretinal photocoagulation)
- CI-DME present

If a subjects clinical reference standard images were graded ETDRS level 90 (ungradable) there were three possible outcomes in the primary outcome analysis:

1. ETDRS 90 (considered positive for analysis) and device output positive: Agreement
2. ETDRS 90 (considered positive for analysis) and device output negative: Disagreement
3. ETDRS 90 and device output ungradable: Exclude image from full analysis set/ungradable

Study demographics

Table 2. Demographic and baseline characteristics of the study population, N = 886 (Note that binary performance endpoints use N=871)

SL. No.	Characteristic	Category / statistic	All subjects (N = 886)
1	Age (years)	Mean ± SD	62.9 ± 12.18
		Median	64
		Range	22 – 92
		22-44 years, n (%)	70 (7.9%)
		45-60 years, n (%)	269 (30.4%)
		61-75 years, n (%)	424 (47.9%)
		76-92 years, n (%)	123 (13.9%)
2	Sex / Gender	Female, n (%)	421 (47.5%)
		Male, n (%)	465 (52.5%)
		Asian	72 (8.1%)
		Black or African American	192 (21.7%)
		White	610 (68.8%)

3	**Race, n (%)**	**Other (incl. American Indian / Alaska Native and Native Hawaiian / Pacific Islander)**	**12 (1.4%)**
4	**Ethnicity, n (%)**	**Hispanic or Latino**	**272 (30.7%)**
		Not Hispanic / Latino	**614 (69.3%)**
5	**HbA1c (%)**	**Mean ± SD**	**7.81 ± 1.62**
		Median	**7.2**
		Range	**6.5 – 15.5**
		< 10%, n (%)	**794 (89.6%)**
		≥ 10%, n (%)	**92 (10.4%)**
6	**Duration of diabetes (years)**	**Mean ± SD**	**13.1 ± 10.20**
		Median	**10**
		Range	**0 – 55**
		< 10 years, n (%)	**369 (41.6%)**
		≥ 10 years, n (%)	**517 (58.4%)**
7	**Diabetes type**	**Type 2 – 843 subjects Type 1 – 42 subjects Type 3c - 1 subject**	**886 (100%)**

Summary of clinical study results: Table 3 below describes the validation study results for primary endpoints.

Table 3: Primary-analysis performance (subject-level, N = 871)

Metric	Estimate (x / n)	95% Wilson CI
Sensitivity	85.58% (184 / 215)	[80.26%, 89.65%]
Specificity	91.77% (602 / 656)	[89.41%, 93.64%]
Positive predictive value (PPV) [1]	77.31% (184 / 238)	[71.58%, 82.17%]
Negative predictive value (NPV)	95.10% (602 / 633)	[93.13%, 96.53%]
Imageability (1 − IIQ rate)	99.08% (863 / 871)	[98.20%, 99.53%]
Prevalence (mtmDR+ in ITS)	24.68% (215 / 871)	[21.94%, 27.65%]

IIQ - Insufficient Image Quality.

Clinical validation results summary:

The iPredict-DR algorithm performed with sensitivity of 85.58% and specificity of 91.77%. Considering that CRS ungradable images were considered CRS positive in the iPredict-DR primary analysis, the results of this clinical study support a determination of substantial equivalence between iPredict-DR and IDx-DR.

Precision Study (Repeatability and Reproducibility)

iHealthScreen conducted a precision study (repeatability and reproducibility) using data from a cohort comprised of pivotal study subjects. A total of 50 subjects were recruited, with 24 subjects with "mtmDR detected" and 26 subjects with "mtmDR not detected." The "mtmDR not detected" category included normal and mild DR cases, while the "mtmDR detected" category encompassed moderate, severe, and proliferative DR cases, as well as DME. The precision study evaluated the iPredict-DR results when retinal photography was repeated using the DRSPlus camera with different operator-camera pairs. There were 3 operator-camera pairings consisting of 3 different operators using 2 different camera units of the same model (each operator operated a given camera unit). The study objective was to demonstrate that the results are repeatable and reliable. Study success required at least 80% overall agreement for both inter- and intra-operator use.

- **Repeatability (Intra-operator variability) analysis:** Repeatability was assessed to determine whether the same operator produced consistent iPredict-DR results when imaging the same eye twice using the same operator-camera pairing. Each operator-camera pairing consisted of one operator assigned to one of two identical DRSplus camera units. For every eye, each operator-camera pairing acquired two repeat image sets (Attempt 1 and Attempt 2). Each image set consisted of a macula-centered image and a disc-centered image, which together form a single iPredict-DR result for that eye. Across the study, this produced a total of 600 repeatability pairs (3 operators × 50 subjects × 2 eyes × 2 cameras). The observed intra-operator overall agreement was 94.67%, therefore meeting the 80% criterion for success. Additionally, average agreement for positive results (mtmDR detected) was 94.55%, and average agreement for negative results (mtmDR not detected) was 95.48%.

- **Reproducibility (Inter-operator variability) analysis:** Reproducibility was assessed to determine whether different operators, using different but identical DRSplus camera units, produced consistent iPredict-DR results for the same eye under routine imaging conditions. Each operator-camera pairing acquired one image set (Attempt 1) for every eye. Each image set consisted of a macula-centered and a disc-centered image, which together form a single combined iPredict-DR result per eye. Inter-operator reproducibility was evaluated by comparing the three iPredict-DR outputs (one from each operator-camera pairing) for the same eye using only the first attempt from each operator. Agreement was quantified using pairwise 3×3 tables (two-operator reproducibility) and using the full three-rater 3×3×3 agreement table (three-operator reproducibility). Overall agreement was 91%, therefore meeting the 80% criterion for success. In addition, average agreement for positive results (mtmDR detected) was 94.22% %, and average agreement for negative results (mtmDR not detected) was 94.65%.

Non-clinical (Bench) testing

1. **Verification and Validation:** The verification and validation testing reports summarize the evaluation of the iPredict-DR Diabetic Retinopathy Screening Software. The verification and validation testing concluded that the iPredict-DR Software meets the requirements, is suitable for its intended use, and can be released. The testing report demonstrates that the algorithm developed to determine the quality of retinal images and to detect the presence or absence of diabetic retinopathy (DR) in retinal images, meets or exceeds the sensitivity and specificity requirements.

   All testing demonstrated that the software met the predetermined pass/fail criteria. All reported issues were minor with no adverse impact to the safety and efficacy of this application. The test failures reported do not impact safety or efficacy based on the rationale provided for each test failure. All protocol deviations were evaluated in accordance with the iPredict-DR Software Development Plan, and it was determined that the intent of the modified test steps was not affected by the changes. The protocol deviations did not exclude any aspect of the requirements being verified and the functional requirements traced to each protocol are still valid.

2. **Risk analysis and management:** We reviewed the risk management outputs and have concluded that the risk management effort complies with the iPredict-DR Risk Management Plan, and in doing so, has complied with the requirements of ISO 14971:2019. Based on review of the relevant documentation, we have concluded that the overall residual risk posed by iPredict-DR is acceptable. The likelihood of harm is considered generally low, and the controls for usability are believed to support safe, proper, and effective use. Adequate risk control measures were designed and implemented to mitigate all identified hazards to acceptable levels.

3. **Cybersecurity assessment report:** This document summarizes the results of the cybersecurity assessment and mitigation efforts undertaken for the iPredict-DR system and aligns with the FDA's 2023 Guidance titled "Cybersecurity in Medical Devices: Quality System Considerations and Content of Premarket Submissions, Guidance for Industry and Food and Drug Administration Staff" and UL 2900-1:2017 (Updated in year 2025). This document addresses cybersecurity within the iPredict-DR application and the cloud server to which it communicates, considering data security, data confidentiality, data integrity, denial of service attacks, and malware. It provides a complete assessment of the system design and threat model, requirements verification, malformed input testing, structured penetration testing, vulnerability testing, data/attack targets, system interfaces/ attack vectors, system weaknesses, risk mitigations, and post-market management.

   This cybersecurity analysis provides sufficient evidence of safe and effective software performance and ensures that the data security and privacy is maintained according to the industry standards. The "Software Maintenance Plan" lists the procedures involved with maintaining the software and managing cybersecurity vulnerabilities following the release, as part of the lifecycle management.

4. **Human factors testing:** T The human factors data support the safety and effectiveness of the iPredict-DR. The usability of iPredict-DR was analyzed through a human factor validation study, for the understanding and implementation of the instructions in the user manual, as well as the usability of iPredict-DR's user interface in submitting the retinal images for processing and receiving the diagnostic results and reports. The study was

conducted in the setting in which the device is intended to be used, to validate that the iPredict-DR application is safe and effective for the intended users and uses, in the intended use environment.

Conclusion on non-clinical testing: The performance data for the non-clinical or bench tests, including software validation, risk analysis, cybersecurity, and human factor validation (summative testing), demonstrate that the iPredict-DR device is safe and effective for use, and substantially equivalent to the predicate device.

Conclusion: iPredict-DR is substantially equivalent to the predicate device, IDx-DR. iPredict-DR has the same intended use and equivalent indications for use. The technological characteristics are similar. The technological differences between iPredict-DR and its predicate device raise no new issues of safety or effectiveness. Performance data support the substantial equivalence of iPredict-DR to the predicate device.