DE NOVO CLASSIFICATION REQUEST FOR
IDX-DR

REGULATORY INFORMATION

FDA identifies this generic type of device as:

Retinal diagnostic software device. A retinal diagnostic software device is a prescription software device that incorporates an adaptive algorithm to evaluate ophthalmic images for diagnostic screening to identify retinal diseases or conditions.

NEW REGULATION NUMBER: 21 CFR 886.1100

CLASSIFICATION: Class II

PRODUCT CODE: PIB

BACKGROUND

DEVICE NAME: IDx-DR

SUBMISSION NUMBER: DEN180001

DATE OF DE NOVO: January 12, 2018

CONTACT: IDx, LLC
2300 Oakdale Blvd
Coralville, IA 52241

INDICATIONS FOR USE

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.

LIMITATIONS

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

Warnings

- IDx-DR is only designed to detect diabetic retinopathy. IDx-DR is not intended to detect concomitant diseases. Patients should not rely on IDx-DR for detection of any other disease.

- People with diabetes may be at elevated risk of glaucoma and should be seen by an eye care provider for glaucoma screening in accordance with recognized patient management recommendations. IDx-DR does not screen for glaucoma.

- Patients should be informed that IDx-DR does not treat retinopathy and that their images are analyzed to determine whether further examination is needed by an eye care provider. Physicians should review IDx-DR results and advise patients of recommended referrals to an eye care provider for evaluation and potential treatment.

- If IDx-DR is not able to generate a screening result on a patient who has been pharmacologically dilated, the patient may have vision threatening diabetic retinopathy, or other abnormalities including cataract. Such a patient should be seen by an eye care provider for evaluation.

- Patients with an IDx-DR output indicating diabetic retinopathy should be immediately referred to an eye-care provider for further screening and treatment. In cases where the IDx-DR test provides no result, the patient should always be immediately retested or referred to an eye care provider. In cases where the IDx-DR test does not detect the presence of referable disease, the patient should be strongly encouraged to test again at an appropriate point in the future.

- Do not use IDx-DR to screen for diabetes mellitus – IDx-DR is only for use in people already diagnosed with diabetes mellitus.

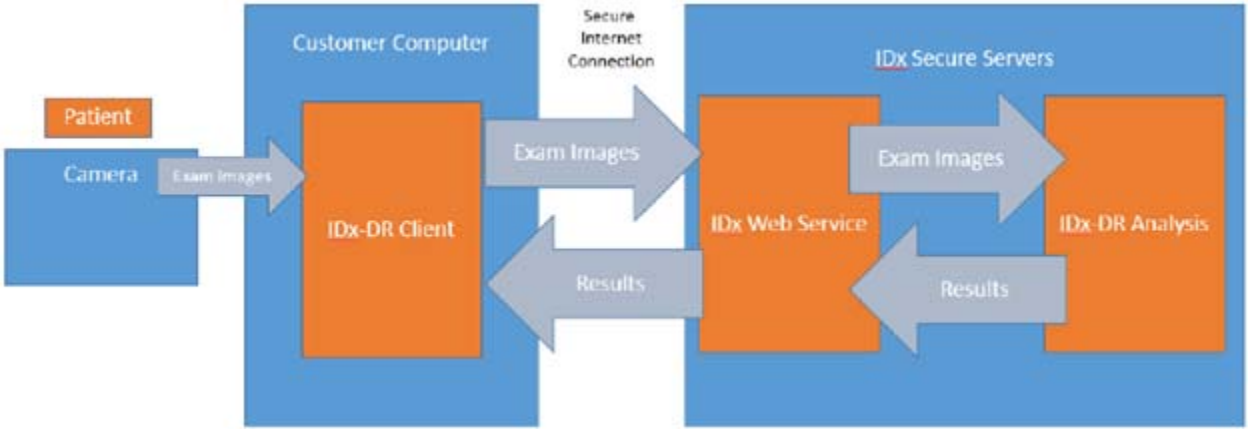
- IDx-DR is designed to work with good quality, in-focus, digital retinal color images of the fovea and disc. Do not submit retinal color images that are of poor quality, retinal color images that were not made with a digital fundus camera, retinal images that are not in color, images of other tissues or objects other than the retina, or color images that were obtained by scanning images.

- IDx-DR is only intended to be used with images acquired with a Topcon TRC-NW400. Refer to the FDA approved label of the Topcon TRC-NW400 for relevant contraindications, warnings, and precautions.

  PLEASE REFER TO THE LABELING FOR A COMPLETE LIST OF WARNINGS, PRECAUTIONS AND CONTRAINDICATIONS.

DEVICE DESCRIPTION

The IDx-DR consists of several components. A fundus camera is attached to a computer, where the IDx-DR Client is installed. The Client allows the user to interact with the server-based analysis software over a secure internet connection. Using the Client, 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.



The component parts of IDx-DR illustrated above are summarized here and further described in the following sections:

- IDx-DR Analysis: the analysis software that analyzes the patient's images and determines exam quality and the presence/absence of diabetic retinopathy. Additional information about IDx-DR Analysis is provided below.

- IDx-DR Client: a software application component running on a computer, usually connected to the fundus camera, at the customer site. Using this software, the customer can transfer images to IDx-DR Analysis via IDx-Service and receive results back. IDx-DR Client does not require installation and runs on all Windows computers locally. It requires an internet connection to work. In a case where an exam could not be analyzed due to image quality or an image acquisition protocol error, quality feedback is provided to help the operator acquire high quality exams and successfully obtain a result after resubmission.

- IDx-Service: a general exam analysis service delivery software package, managed in a separate software project with its own set of product and software requirements. IDx-Service 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 IDx-Service. IDx-Service is also primarily responsible for device cybersecurity.

SUMMARY OF NONCLINICAL/BENCH STUDIES

SOFTWARE

Software version IDx-DR 2.0.0 US 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." The software documentation included:

1. Software/Firmware Description
2. Device Hazard Analysis

3. Software Requirement Specifications
4. Architecture Design Chart
5. Software Design Specifications
6. Traceability
7. Software Development Environment Description
8. Revision Level History
9. Unresolved Anomalies
10. Cybersecurity

A comprehensive risk analysis was provided for the software with detailed description of the hazards, their causes and severity as well as acceptable methods for control of the identified hazards. IDx provided a description, with test protocols including pass/fail criteria and report of results, of acceptable verification and validation activities at the unit, integration and system level. The expected impact of various hardware features on performance was assessed and minimum specifications for acceptable images for analysis were specified.

The cybersecurity considerations of data confidentiality, data integrity, data availability, denial of service attacks and malware were adequately addressed using platform controls, application controls and procedure controls and evidence was provided for the controls performance as intended. Risks related to failure of various software components and their potential impact on patient reports and operator failures were also adequately addressed in the risk analysis. This software documentation information provided sufficient evidence of safe and effective software performance.

IDx has provided a full characterization of the technical parameters of all the components of the software, including a description of the algorithms that analyzes the patient's images, determines exam quality and the diagnostic screening of diabetic retinopathy. IDx-DR requires one optic disc centered image and 1 macula centered image from a fundus camera with at least 1000 by 1000 pixels per image. The impact of the applicable image quality characteristics are described in the Image Quality and Human Factors Validation Testing sections below.

The IDx-DR artificial intelligence device design has the ability to perform analysis on the specific disease features that are important to a retina specialist for diagnostic screening of DR. IDx will make future algorithm improvements under a consistent medically relevant framework. A protocol was provided to mitigate the risk of algorithm changes leading to changes in the device's technical specifications, which would lead to changes in false positive or false negative results. These changes could significantly affect clinical functionality or performance specifications directly associated with the intended use of the device. The protocol specifies the level of change in device specifications that could significantly affect the safety or effectiveness of the device, triggering the requirement for a 510(k) premarket notification submission before commercial introduction. This protocol implements the recommendations provided in the FDA guidance document "Deciding When to Submit a 510(k) for a Software Change to an Existing Device: Guidance for Industry and FDA Staff."

SUMMARY OF CLINICAL INFORMATION

IDx conducted a pivotal clinical study with 900 patients who were enrolled at 10 primary care sites. The target population was asymptomatic persons, ages 22 and older, who had been diagnosed with diabetes and had not been previously diagnosed with diabetic retinopathy (DR). The study population was enriched by targeting enrollment of subjects with elevated Hemoglobin A1c (HbA1C) levels for a portion of the study in order to increase the likelihood of enrolling patients with more serious DR. Before any participant was recruited, IDx-DR operator trainees had to attest that they had not previously performed ocular imaging. They then underwent a one-time standardized four hour training program on how to acquire images, how to improve image quality if IDx-DR gave an insufficient quality output, and how to submit images for analysis to IDx-DR. No additional training was provided to any of the IDx-DR operators for the duration of the study. A diagnosis of diabetes was defined as meeting the criteria established by either the World Health Organization (WHO) or the American Diabetes Association (ADA); Hemoglobin A1c (HbA1c $\geq$ 6.5% based on repeated assessments; Fasting Plasma Glucose (FPG) $\geq$ 126 mg/dL (7.0 mmol/L) based on repeated assessments; Oral Glucose Tolerance Test (OGTT) with two-hour plasma glucose (2-hr PG) $\geq$ 200 mg/dL (11.1 mmol/L) using the equivalent of an oral 75g anhydrous glucose dose dissolved in water; or symptoms of hyperglycemia or hyperglycemic crisis with a random plasma glucose (RPG) $\geq$ 200 mg/dL (11.1 mmol/L). During the study, the IDx-DR operator made sure that for every participant, a final IDx-DR output of more than mild DR (mtmDR) detected (defined below), more than mild DR not detected, or insufficient quality, was obtained. After the novice operator had generated an IDx-DR result, but during the same visit, each participant underwent additional retinal imaging captured by a professional ophthalmic photographer who had been certified by the Fundus Photography Reading Center (FPRC). The professional ophthalmic photographer remained masked at all times to the IDx-DR output and used a different, FDA-cleared camera system (Topcon 3D OCT-1 Maestro) to obtain dilated four widefield stereo color fundus photography, lens photography for media opacity assessment, and macular optical coherence tomography (OCT) imaging.

Fundus Photography Reading Center – Reference Standard

These images were all sent to the FPRC, where the severity of retinopathy and diabetic macular edema (DME) were determined according to the Early Treatment for Diabetic Retinopathy Study severity (ETDRS) scale. These readings formed the reference standard for the study. The FPRC grading protocol consisted of the following: the four widefield stereo image pairs were read by three experienced and validated readers according to the well-established ETDRS scale, using a majority voting paradigm. The macular OCT images were read by the same readers for the presence of center involved DME according to the Diabetic Retinopathy Clinical Research Network (DRCR) grading paradigm. Each participant was categorized as mtmDR+ (ETDRS level 35 or higher and /or DME present), or mtmDR- (ETDRS level 10-20 and DME absent). The worst of two eyes were compared with the IDx-DR output at the participant level. Because DME can be identified on the basis of retinal thickening on stereoscopic fundus photographs, as well as on the basis of retinal thickening on OCT, performance using both definitions was

analyzed. Stereoscopic fundus-based Clinically Significant DME (CSDME) was identified if there was either retinal thickening or adjacent hard exudates < 600μm from the foveal center, or a zone of retinal thickening > 1 disc area, part of which is less than 1 disc diameter from the foveal center, according to the FPRC, in any eye. OCT based center involved DME was identified if a participant had central subfield (a 1.0mm circle centered on the fovea) thickness that was >300μm according to the FPRC, in any eye. Accordingly, the definition of mtmDR+: fundus mtmDR+ is defined as:

- ETDRS level ≥ 35 (determined from fundus photographs) and/or
- CSDME (determined from fundus photographs) and multimodal mtmDR+ is defined as:
  - ETDRS level ≥ 35 (determined from fundus photographs), and / or
  - CSDME (determined from fundus photographs) and / or
  - center-involved DME (determined from OCT).

FPRC readers were masked to the IDx-DR system outputs at all times, masked to the fundus photograph reading when evaluating the OCT images, and masked to OCT readings when evaluating fundus photographs. A total of 900 participants were enrolled at 10 sites, of which 892 participants completed all procedures. A subset of 819 of these participants could be fully analyzed, giving an analyzable fraction of 92% (95% CI, 90%-93%). Median age was 59 years (range, 22-84 years); 47.5% of participants were male. For the entire group of participants, 16.1% were Hispanic, 83.3% were not Hispanic, and 0.6% were unknown. Also, 63.4% were white, 28.6% African American, and 1.6% Asian. 7.1% had type 1 diabetes and 92.9% had type 2 diabetes. Overall mean HbA1C ± std was 9.4 ± 2.3mmol/l. Mean duration of diabetes was 12.7 ± 8.9 years, with a median of 11.0 and a range of 0.0 - 57.0 years. The 819 participants whose results could be fully evaluated and the 73 participants whose results could not be analyzed differed significantly with respect to lens status, while mean age, ethnicity, race, and HbA1C level were not significantly different.

Study Endpoint Results

A total of 900 participants were enrolled at 10 sites, of which 892 participants completed all procedures. Of the 892 participants completing all procedures, 40 had exams that could not be analyzed by the FPRC and 33 received an IDx-DR insufficient quality result or had a missing IDx-DR output. Thus, a subset of 819 of participants could be fully analyzed by the IDx-DR device to produce an IDx-DR disease output, giving an analyzable fraction of 92% (95% CI, 90%-93%). The primary outcomes were the sensitivity and specificity of IDx-DR. Performance thresholds were defined at 85.0% for sensitivity and 82.5% for specificity, reflecting anticipated enrollment numbers and pre-specified regulatory requirements. In addition to observed sensitivity and specificity, enrichment corrected sensitivity and specificity were calculated using logistic regression to evaluate whether performance would have been different if the study population had not been enriched with subjects with higher HbA1C levels. Analyses were based on the data from all participants who had valid results on both IDx-DR and the FPRC imaging

and reading protocol, except where indicated; reported subgroup analyses were prespecified. A total of 198 mtmDR+ participants were fully analyzable according to the FPRC reading protocol, thus prevalence was 23.8% (198/819). Of these, 29 had CSDME according to fundus photography; 19 participants had center-involved DME according to OCT; and 42 participants had either CSDME and/or center involved DME, with corresponding prevalence of 3.5% for CSDME, 2.3% for center-involved DME, and 5.1% for any DME according to both of these assessments. Average centerfield thickness was 239μm (+-0.05 μm) in the participants with CSDME (from fundus photographs only), and 304μm (+-0.06 μm) in the participants with center-involved OCT DME. IDx-DR correctly identified 173 of the 198 fully analyzable participants with fundus mtmDR+, thus observed sensitivity was at 87.4% (95%CI, 81.9% - 92.9%). Sensitivity corrected for enrichment was also high, at 87.2% (95% CI, 81.8% - 91.2%) to fundus mtmDR+, and 85.9% (95% CI, 82.5%-88.7%) to multimodal mtmDR+, i.e. including participants with either CSDME or center involved DME. There were no significant effects for age, sex, race, ethnicity, HbA1C, lens status or site, on sensitivity. The retrospective power was 93%. IDx-DR correctly identified, with an mtmDR positive output, 28 of 29 (96%; 95% CI, 83%-99%) participants with CSDME (fundus photographs only), 16 of 19 participants (84%; 95% CI, 62% - 94%) with center-involved DME (OCT only), and identified all participants with ETDRS level 43 or higher. Among the 621 fully analyzable participants who did not have fundus mtmDR according to FPRC grading, there were 556 participants with an mtmDR not detected output, thus observed specificity was 89.5% (95% CI, 86.9%-93.1%). Specificity corrected for enrichment was also high at 90.7% (95% CI, 88.3% - 92.7%) for fundus mtmDR- participants, and 90.7% (95% CI, 86.8%-93.5%) for multimodal mtmDR- participants. There were no significant effects of sex, ethnicity, race, HbA1C, lens status, or site, on specificity, while increased specificity was observed in subjects over 65 years of age ($p = 0.030$). The retrospective power was 87%. Positive predictive value was 72.7% (173/238) and negative predictive value was 95.7% (556/581). In the 38 participants with AI system insufficient image quality, the prevalence of mtmDR was 10/38 (26%), comparable to the mtmDR prevalence in the fully analyzable dataset. Among the 73/892 non-analyzable participants, 35 (4%) lacked a completed FPRC grading. In the worst case scenario, assuming all of these 35 participants had mtmDR, the sensitivity and specificity would have been 80.7% (two-sided 95% CI, 76.7%-84.2%) and 89.8% (two-sided 95% CI, 85.9% - 92.7%) respectively.

The following summarizes the key performance results of the IDx-DR study:
Sensitivity – 87%
Specificity – 90%
Imageability – 96%
PPV (Positive Predictive Value) – 73%
NPV (Negative Predictive Value) – 96%

Image Quality Results
Of the 857 participants that received a completed FPRC grading, 38 participants (4%) received an insufficient image quality output from IDx-DR after completion of IDx-DR imaging protocol. Thus image-ability, defined as the percentage of participants with a

completed FPRC grading and a disease level output was high (819/852) or 96.1% (95.0% CI, 94.0-96.8%). For the IDx-DR imaging protocol, 76.4% of participants did not require pharmacologic dilation, while 23.6% did require dilation to obtain an IDx-DR disease level output. The majority of participants, 64.7%, completed the IDx-DR imaging protocol of four photographs the first time; 8.5% were able to complete the protocol after a single retry; 3.2% needed two retries; 19.7% needed three, 3.4% needed four; and 0.5% needed five retries. In this clinical study, the IDx-DR System was able to achieve sufficient performance when compared to the highest quality reference standard as determined by the FPRC, met predetermined sensitivity and specificity standards for the autonomous detection of more than mild DR or DME in people with diabetes but no history of DR in primary care settings.

Precision Study

A separate reproducibility and repeatability (precision) study was conducted involving 24 participants. Participants in the substudy had already participated in the IDx-DR protocol: 12 participants had mtmDR- based on the original FPRC grading and 12 had mtmDR+. Each participant in the sub-study completed the entire IDx-DR imaging protocol 10 times, imaged by three different NW400 Operators on two different Topcon NW400 fundus cameras. NW400 operators were instructed to give participants at least 15 minutes between exams. Each subject underwent the entire IDx-DR imaging protocol 10 times, i.e., 10 image sets per subject, 240 image sets in total. Five images from a single subject were determined to be of insufficient quality according to the IDx-DR and thus were omitted from analysis, the remaining 235 (97.9%) image sets were used for analysis. The binary output of IDx-DR was used to assess repeatability and reproducibility. For 23 out of 24 participants, the IDx-DR outputs were identical on all 10 imaging protocols for each of them, irrespective of camera, operator, or repeat. For one of the 24 subjects, 9 out of 10 IDx-DR outputs were identical as mild or more DR not detected, while 1 out of these 10 outputs was mild or more DR detected. Thus, there is almost complete agreement (99.6%) of IDx-DR outputs across repeats, operators and cameras.

Human Factors Validation Testing Study

Human Factors Validation Testing Study was performed to assess the user interface (IDx-DR Client). IDx's human factors testing validated the setting in which the device is intended to be used. The IDx-DR workflow, training materials, and instructions were developed through a series pre-trial human factors testing. The standardized workflow, training program, and operator materials developed by this process were then implemented and tested during the IDx-DR clinical trial, which took place in the primary care setting. Final human factors validation results were successful in the IDx-DR clinical trial, as reflected by the data on subject imageability. This IDx-DR Human Factors Validation Test Plan empirically tested, improved upon, and validated the IDx-DR System (i.e. the camera, camera operation, the IDx-DR imaging protocol, and the standardized training and operational materials) in a real-world environment in order to mitigate the residual usability.

The Human Factors Validation Test Plan occurred across two stages. The empirical testing first collected feedback in three "Phases" to improve usability of the IDx-DR

Client, derive standardized training materials, and develop the validation test plan. Final testing was carried out as a part of the IDx-DX clinical trial, which validated the camera use, the imaging protocol, and the standardized system materials that enable the capture of four medical-grade retinal images by previously untrained camera operators for at least 80% of the subjects imaged. The three Phases of initial empirical testing were carried out as follows: the camera and imaging protocol were tested and improved in Phase I and II. Training content and product image feedback controls were tested and improved in Phase III. To create consistent, scalable training, the training and operational materials were standardized prior to the IDx-DR1 clinical trial. The development of standardized training materials was tested by bringing in previously untrained photographers and training them under the Phase III consent and protocol. The critical task for the IDx-DR system is the ability to capture 4 images of sufficient quality. The purpose of the system validation test plan was to demonstrate that IDx's intended image capture workflow and training methodology can successfully be used by previously untrained camera operators to capture four medical-grade retinal images from 80% or more of subjects who complete the full imaging protocol on a camera intended for use with IDx-DR IDx-DR System. The Human Factors Validation Plan was designed to validate the camera, imaging protocol, and standardized materials developed from empirical data gathered during Phases I, II, and III. Operators underwent training prior to the clinical trial as described below. As a part of training prior to the IDx-DR clinical trial, operators completed a trainee self-certification form, which includes documentation that they have successfully imaged 10 subjects.

Clinical trial results indicating that previously untrained camera operators can capture four medical grade retinal images from the vast majority of subjects who complete the protocol using the IDx-DR System valid Camera, IDx-DR Imaging Protocol, and Standardized training and operational materials. Finally, the IDx-DR validation testing results show an image quality sufficient rate of 96%.

Pediatric Extrapolation

In this De Novo request, existing clinical data were not leveraged to support the use of the device in a pediatric patient population.

LABELING

The device labeling is for primary care clinics and stable visually asymptomatic patients diagnosed with diabetes that have not been previously diagnosed with diabetic retinopathy. Several product warnings are included in the labeling that carefully specify the intended patient population, image acquisition factors that may impact IDx-DR results, and provide guidance for patient referral based on the IDx-DR screening result. These warnings were found to be appropriate. The labeling also provided a complete summary of the clinical trial procedures, patient population, and results. This summary includes prominent instructions regarding interpretation of the output as well as a representation of average variability observed in the device performance for various device outputs. Labeling intended for internal consideration was also provided which adequately described detailed steps and features that could affect accuracy of results.

RISKS TO HEALTH

The table below identifies the risks to health that may be associated with use of a retinal diagnostic software device and the measures necessary to mitigate these risks.

Identified Risk	Mitigation Measures
False positive results leading to additional unnecessary medical procedures • Diagnostic algorithm failure • Software failure	Clinical performance testing; Software verification, validation, and hazard analysis; and Protocol for technical specification changes
False negative results leading to delay of further evaluation or treatment • Diagnostic algorithm failure • Software failure	Clinical performance testing; Software verification, validation, and hazard analysis; Protocol for technical specification changes; and Labeling
Operator failure to provide images that meet input quality specifications	Labeling, Training, and Human factors validation testing

SPECIAL CONTROLS:

In combination with the general controls of the FD&C Act, the retinal diagnostic software device is subject to the following special controls:

1. Software verification and validation documentation, based on a comprehensive hazard analysis, must fulfill the following:

    a. Software documentation must provide a full characterization of technical parameters of the software, including algorithm(s).

    b. Software documentation must describe the expected impact of applicable image acquisition hardware characteristics on performance and associated minimum specifications.

    c. Software documentation must include a cybersecurity vulnerability and management process to assure software functionality.

    d. Software documentation must include mitigation measures to manage failure of any subsystem components with respect to incorrect patient reports and operator failures.

2. Clinical performance data supporting the indications for use must be provided, including the following:

    a. Clinical performance testing must evaluate sensitivity, specificity, positive predictive value, and negative predictive value for each endpoint reported for the indicated disease or condition across the range of available device outcomes.

b. Clinical performance testing must evaluate performance under anticipated conditions of use.

c. Statistical methods must include the following:

   i. Where multiple samples from the same patient are used, statistical analysis must not assume statistical independence without adequate justification.
   ii. Statistical analysis must provide confidence intervals for each performance metric.

d. Clinical data must evaluate the variability in output performance due to both the user and the image acquisition device used.

3. A training program with instructions on how to acquire and process quality images must be provided.

4. Human factors validation testing that evaluates the effect of the training program on user performance must be provided.

5. A protocol must be developed that describes the level of change in device technical specifications that could significantly affect the safety or effectiveness of the device.

6. Labeling must include:

   a. Instructions for use, including a description of how to obtain quality images and how device performance is affected by user interaction and user training.

   b. The type of imaging data used, what the device outputs to the user, and whether the output is qualitative or quantitative.

   c. Warnings regarding image acquisition factors that affect image quality.

   d. Warnings regarding interpretation of the provided outcomes, including:

      i. A warning that the device is not to be used to screen for the presence of diseases or conditions beyond its indicated uses.
      ii. A warning that the device provides a screening diagnosis only and that it is critical that the patient be advised to receive follow-up care.
      iii. A warning that the device does not treat the screened disease.

   e. A summary of the clinical performance of the device for each output, with confidence intervals.

   f. A summary of the clinical performance testing conducted with the device, including a description of the patient population and clinical environment under which it was evaluated.

BENEFIT/RISK DETERMINATION

The substantial benefits of early detection of mtmDR, including potential prevention of significant vision loss with the potential timely treatment of DR, are highly valuable to the intended population. Moreover, the high accuracy of the IDx-DR makes the potential risk of false negatives low. Accordingly, the probable benefits of the IDx-DR outweigh the probable risks.

Summary of Benefits
IDx-DR offers the important benefits of potential increased access to diabetic retinopathy screening for people with diabetes in a primary care setting. Earlier detection of mtmDR among these patients can help to enable the timely delivery of potentially sight saving interventions. The pivotal clinical study, which enrolled a total of 900 participants, demonstrated observed sensitivity for mtmDR 87.4%, with observed specificity of 89.5%. The device performed well across the range of study participant characteristics enrolled in the study. The vast majority of study participants had a screening diagnosis result. Among study participants who also had fundus photo reading center results (needed for study analysis), 96.1% (819/852) produced an IDx-DR output of mtmDR or negative for mtmDR. Thus, the clinical study successfully and robustly demonstrated safe and effective clinical performance of IDx-DR when used to automatically (without physician assistance) detect mtmDR.

Summary of Risks
The IDx-DR system, which makes use of a standard fundus camera, presents minimal physical harm risks to patients. As with most diagnostic tools, the principal risks are those of false negative results. A false negative result for mtmDR may result in delayed diagnosis and treatment if the patient is not referred to an eye care professional by the health care provider. This risk is mitigated by the health care provider's recommendation for follow-up screenings. DR is understood to progress slowly and, thus, repeat screenings would provide additional opportunities to correctly identify the existence of mtmDR. In addition, all patients are recommended to see their eye care professional as usual to evaluate for other ophthalmic conditions not addressed by IDx-DR. Thus, some percentage of false negative subjects will be additionally screened for DR during their annual eye care exam. Other risks associated with the device are expected to be rare. A false positive result, for example, would mean an indication of disease in a patient who does not have clinical signs of diabetic retinopathy. This would result in a referral for further examination by an eye care professional which might lead to alarm fatigue. Given that examination by an eye care professional once per year is the recommended standard of care, this would not introduce any significant risk for the patient.

Summary of Other Factors
Device errors can arise from failure to operate the instrument correctly, or more broadly, failure to correctly interpret test results. These are mitigated by appropriate end user device training and a comprehensive user manual. Device labeling, which has been developed in accordance with 21 CFR 809.10(b)(9), provides a detailed explanation of the interpretation of results.

Patient Perspectives
This submission did not include specific information on patient perspectives for this device.

Benefit/Risk Conclusion

In conclusion, given the available information above, the data support that for the screening of diabetic retinopathy in patients with diabetes, the probable benefits outweigh the probable risks for the IDx-DR. The device provides substantial benefits and the risks can be mitigated by the use of general controls and the identified special controls.

CONCLUSION

The De Novo request for the IDx-DR is granted and the device is classified under the following:

Product Code: PIB
Device Type: Retinal diagnostic software device
Class: II
Regulation: 21 CFR 886.1100