June 17, 2022

Digital Diagnostics Inc.
% Kelliann Payne
Partner
Hogan Lovells US LLP
1735 Market St., Floor 23
Philadelphia, Pennsylvania 19103

Re: K213037
Trade/Device Name: IDx-DR v2.3
Regulation Number: 21 CFR 886.1100
Regulation Name: Retinal Diagnostic Software Device
Regulatory Class: Class II
Product Code: PIB
Dated: September 21, 2021
Received: May 17, 2022

Dear Kelliann Payne:

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 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)*
K213037

Device Name
IDx-DR v2.3

Indications for Use *(Describe)*
IDx-DR is 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.

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

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

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(k) Summary
K213037

I. Submitter

Digital Diagnostics Inc.
2300 Oakdale Blvd.
Coralville, IA 52241
Phone: 319-248-5620

Contact Person: Ashley Miller
Date Prepared: June 14, 2022

II. Device

Name of Device: IDx-DR v2.3
Common or Usual Name: Diabetic Retinopathy Detection Device
Classification Name: Retinal diagnostic software device
Regulatory Class: II
Regulation: 21 CFR 886.1100
Product Code: PIB

III. Device Description

The IDx-DR device is an autonomous, artificial intelligence (AI)-based system for the automated detection of more than mild diabetic retinopathy (mtmDR). It consists of several component parts (see **Figure 1** below).

The component parts of IDx-DR are summarized as follows:

- IDx-DR Analysis: Software that analyzes the patient's images and determines exam quality and the presence/absence of mtmDR.
- IDx-DR Client: A software application component running on a computer, usually connected to the fundus camera, at the user site. Using this software, the user can transfer images to IDx-DR Analysis via IDx-DR Service and receive results back.
- IDx-DR Service: IDx-DR Service comprises a general exam analysis service delivery software package. IDx-DR Service contains a webserver front-end that securely handles incoming requests, a database that stores user information, and a logging system that records information about each transaction through IDx-DR Service. IDx-DR Service is also primarily responsible for device cybersecurity.

The Topcon NW400 fundus camera is attached to a computer, where IDx-DR Client is installed. Guided by the IDx-DR Client, end-users acquire two fundus images per eye to

be dispatched to IDx-DR Service. IDx-DR Service is installed on a server hosted at a secure datacenter. From IDx-DR Service, images are transferred to IDx-DR Analysis System. No information other than the fundus images is required to perform the analysis. IDx-DR Analysis System, which runs on dedicated servers hosted in the same secure datacenter as IDx-DR Service, processes the fundus images and returns information on the exam quality and the presence or absence of more than mild diabetic retinopathy (mtmDR) to IDx-DR Service. IDx-DR Service then transports the results to the IDx-DR Client that displays them to the user.

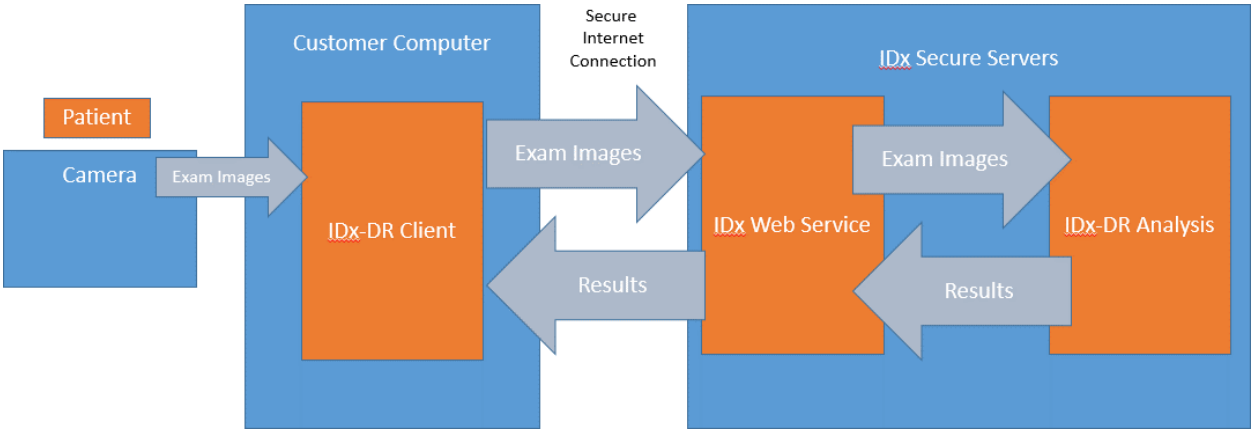

Figure 1: IDx-DR Components

IV. Indications for Use

IDx-DR is 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.

V. Predicate Device

IDx-DR, Diabetic Retinopathy Detection Device, K203629
This predicate has not been subject to a design-related recall.

No reference devices were used in this submission.

VI. Purpose of Submission

The purpose of this 510(k) submission is to modify the following: the image quality classifier of the IDx-DR Analysis System, from version 2.1.1 to 2.3.0; update IDx-DR Service from version 1.1.2 to 1.2.0; and update IDx-DR Client from v3.3.0 to v3.5.0.

VII. Comparison of Technological Characteristics with the Predicate Device

The main technological principle for both the subject and predicate devices is AI-based technology to analyze specific pathologic features from fundus retinal images. The subject device has the same intended use and indications for use as those cleared under K203629.

The major technological differences that exist between each component of the subject and predicate devices are described below.

IDx-DR Service

- Updated to look up the IDx-DR Analysis System version and sends it to IDx-DR Client for display on the user interface.

IDx-DR Client

- Updated to provide clear language of "exam completed" after repeated imaging attempts have resulted in an insufficient image quality output. The result output and report will remain unchanged, indicating exam quality was insufficient and a diagnostic result is not provided.
- Updated to visually communicate image quality feedback by adding a green checkmark or a red "X" to images on the submission feedback screen.

IDx-DR Analysis System

- The image quality classifier of the subject device was replaced with a new image quality classifier.
- Updated to improve the speed of the device.

Table 1 provides a comparison between the technical characteristics and indications for use of the subject and predicate devices.

Table 1: Comparison of the Subject and Predicate Device

	Subject Device IDx-DR v2.3	**Predicate Device IDx-DR v2.0, K203629**	**Discussion**
Component Software Versions	IDx-DR Client v3.5.0 IDx-DR Analysis System v2.3.0 IDx-DR Service v1.2.0	IDx-DR Client v3.2.0 IDx-DR Analysis System v2.1.1 IDx-DR Service v1.1.2	See above for the major technological differences between each component of the subject and predicate device.
Technological Principle	Artificial intelligence software as a medical device.	Artificial intelligence software as a medical device.	Equivalent

	Subject Device IDx-DR v2.3	Predicate Device IDx-DR v2.0, K203629	Discussion
Indications for Use	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.	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.	Equivalent
Indicated Camera	Topcon NW400 fundus camera	Topcon NW400 fundus camera	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 and referral decision: • mtmDR detected: Refer to an eye care professional • mtmDR not detected: Rescreen in 12 months • Insufficient image quality	Detection of diabetic retinopathy and referral decision: • mtmDR detected: Refer to an eye care professional • mtmDR not detected: Rescreen in 12 months • Insufficient image quality	Equivalent
Architecture	User facing client software transfers images to and receives results from analysis software through a web server.	User facing client software transfers images to and receives results from analysis software through a web server.	Equivalent
Workflow	The graphical user interface includes on-screen prompts to guide the user through the image acquisition workflow one image at a time and submission of the exam.	The graphical user interface includes on-screen prompts to guide the user through the image acquisition workflow one image at a time and submission of the exam.	Equivalent

VIII. Performance Data

The following performance data were provided in support of the substantial equivalence determination.

A. Summary of Non-clinical Studies

IDx-DR 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 includes:

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. Verification and Validation Documentation
9. Revision Level History
10. Unresolved Anomalies
11. Cybersecurity

A comprehensive risk analysis was performed on IDx-DR with identification and detailed description of the hazards, their causes and severity, as well as acceptable methods for control of the identified hazards. A description of acceptable verification and validation activities, at the unit, integration, and system level, including test protocols with pass/fail criteria and a report of the results, was provided. 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 utilizing platform controls, application controls, and procedure controls, and evidence was provided for the intended performance of the controls. 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.

A full characterization of the technical parameters of all of the components of the software, including a description of the algorithms that analyzes the patient's images to determine exam quality and the diagnostic screening of diabetic retinopathy, has been provided. IDx-DR requires one optic disc-centered image and one macula centered image from a fundus camera with at least 22 pixels per degree on the retina. So, a 1000 pixel field of view diameter for a 45 degree field of view image.

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 diabetic retinopathy. Future algorithm improvements will be made under a consistent medically relevant framework. A protocol was provided to mitigate the risk of algorithm changes leading to changes in the device 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 new 510(k) premarket notification submission before commercial introduction. The protocol incorporates a risk management approach and other approaches 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* in development, validation, and execution of the device changes.

Usability

Usability validation testing was performed under simulated-use to assess the user interface (IDx-DR Client) of the subject device. The testing was performed in an environment equivalent to the intended use environment of IDx-DR with subjects that had no prior experience using the IDx-DR Client. The critical task for the IDx-DR system is the ability to capture four images of sufficient quality. The purpose of the usability validation test plan was to demonstrate that the intended image capture workflow and training methodology can successfully be used by the intended operators to capture four retinal images. The results of the usability validation study indicated that no existing critical tasks were impacted by the modification and no new critical tasks were introduced, and demonstrated that previously untrained camera operators could capture four retinal images of sufficient quality following the imaging protocol and using the indicated camera system and standardized training and operating materials.

B. Summary of Clinical Performance Testing

A retrospective study was conducted to validate the clinical performance of the modified IDx-DR ("IDx-DR v2.3). Data previously collected from the pivotal study of the predicate ("IDx-DR v2.0"; Abràmoff et al. Digital Medicine 2018;1:39) was analyzed to evaluate the performance of the upgraded Analysis component. The three co-primary endpoints are sensitivity, specificity, and "diagnosability" (the proportion of evaluated participants for whom IDx-DR returns a diagnostic result). The secondary endpoints are positive predictive value (PPV) and negative predictive value (NPV).

Data from the 892 participants evaluated during the pivotal study were used to evaluate the modified algorithm; of these, images from 850 participants were available for analysis and diagnosable by the clinical reference standard, thus were evaluable for performance. Of the "first submission" images (i.e., first images taken and without pharmacologic pupil dilation), IDx-DR v2.3 was able to analyze images from 552 of the 850 participants (64.9%) and IDx-DR v2.0 was able to analyze images from 533 of the 850 subjects (62.7%). Of the "final submission" images (after following the as-needed pharmacologic pupil dilation image acquisition protocol), IDx-DR v2.3 was able to analyze images from 809 of the 850 participants (95.2%) and IDx-DR v2.0 was able to analyze images from 819 of the 850 participants (96.4%).

Table 2 presents the diagnosability for participants who were diagnosable by both the subject and predicate devices based on images from the "first" and "final submission" for each participant from the pivotal study.

Table 2: Diagnosability Results for the Subject and Predicate Devices Based on First and Final Submissions

Characteristic	Pivotal Study Device (IDx-DR v2.0)	Subject Device (IDx-DR v2.3)
Diagnosability of first submission images		
Point Estimate	62.71% (533/850)	64.94% (552/850)
95% Confidence Interval[1]	(59.40%, 65.89%)	(61.67%, 68.08%)
Diagnosability of final submission images		
Point Estimate	96.35% (819/850)	95.18% (809/850)
95% Confidence Interval[2]	(94.86%, 97.51%)	(93.51%, 96.52%)

[1]*Calculated using the modified Wald method*
[2]*Calculated using an exact binomial model*

Table 3 presents the sensitivity and specificity for participants who were diagnosable by both the subject and predicate devices based on images from the "final submission" for each participant from the pivotal study.

Table 3: Performance Results for the Subject and Predicate Devices Based on Final Submissions

Characteristic	Pivotal Study Device (IDx-DR v2.0)	Subject Device (IDx-DR v2.3)
Sensitivity*		
Point Estimate	87.37% (173/198)	87.69% (171/195)
95% Confidence Interval[1]	(81.93%, 91.66%)	(82.24%, 91.95%)
Specificity*		
Point Estimate	89.53% (556/621)	90.07% (553/614)
95% Confidence Interval[1]	(86.85%, 91.83%)	(87.42%, 92.32%)

[1]*Calculated using an exact binomial model*
[*]*Excludes exam quality insufficient images, 31 for IDx-DR v2.0, 41 for IDx-DR v2.3*

Table 4 presents the PPV and NPV for participants who were diagnosable by both the subject and predicate devices based on images from the "final submission" for each subject from the pivotal study.

Table 4: Secondary Performance for the Subject and Predicate Devices Based on Final Submissions

Characteristic	Pivotal Study Device (IDx-DR v2.0)	Subject Device (IDx-DR v2.3)
Positive Predictive Value		
Point Estimate	72.69% (173/238)	73.71% (171/232)
95% Confidence Interval[1]	(66.56%, 78.25%)	(67.55%, 79.25%)
Negative Predictive Value		
Point Estimate	95.70% (556/581)	95.84% (553/577)
95% Confidence Interval[1]	(93.71%, 97.20%)	(93.87%, 97.32%)

[1]*Calculated using an exact binomial model*

Additional analyses were performed to include submissions that were non-diagnosable by the respective version of IDx-DR but were diagnosable by the reference standard.

Table 5 presents the worst-case imputations for IDx-DR v2.0 and IDx-DR v2.3 based on images from the final submission for each participant from the pivotal study, wherein the non-diagnosable submissions are assumed to have IDx-DR results disagreeing with the reference standard.

Table 5: Worst-Case Final Submission Performance by IDx-DR Device Version

Characteristic	Pivotal Study Device (IDx-DR v2.0)	Subject Device (IDx-DR v2.3)
Sensitivity		
Point Estimate	85.22% (173/203)	84.24% (171/203)
95% Confidence Interval[1]	(79.58%, 89.80%)	(78.48%, 88.96%)
Specificity		
Point Estimate	85.94% (556/647)	85.47% (553/647)
95% Confidence Interval[1]	(83.02%, 88.52%)	(82.52%, 88.10%)
Positive Predictive Value		
Point Estimate	65.53% (173/264)	64.53% (171/265)
95% Confidence Interval[1]	(59.46%, 71.25%)	(58.44%, 70.29%)
Negative Predictive Value		
Point Estimate	94.88% (556/586)	94.53% (553/585)
95% Confidence Interval[1]	(92.77%, 96.52%)	(92.37%, 96.23%)

[1]*Calculated using an exact binomial model*

Table 6 presents the best-case imputations for IDx-DR v2.0 and IDx-DR v2.3 based on images from the final submission for each participant from the pivotal study, wherein the non-diagnosable submissions are assumed to have IDx-DR results agreeing with the reference standard.

Table 6: Best-Case Final Submission Performance by IDx-DR Device Version

Characteristic	Pivotal Trial Device (IDx-DR v2.0)	Subject Device (IDx-DR v2.3)
Sensitivity		
Point Estimate	87.68% (178/203)	88.18% (179/203)
95% Confidence Interval[1]	(82.36%, 91.87%)	(82.92%, 92.28%)
Specificity		
Point Estimate	89.95% (582/647)	90.57% (586/647)
95% Confidence Interval[1]	(87.37%, 92.16%)	(88.05%, 92.71%)
Positive Predictive Value		
Point Estimate	73.25% (178/243)	74.58% (179/240)
95% Confidence Interval[1]	(67.22%, 78.71%)	(68.58%, 79.97%)
Negative Predictive Value		
Point Estimate	95.88% (582/607)	96.07% (586/610)
95% Confidence Interval[1]	(93.98%, 97.32%)	(94.20%, 97.46%)

[1]*Calculated using an exact binomial model*

The results of the clinical study support a determination of substantial equivalence between IDx-DR v2.3 and IDx-DR v2.0.

IX. Conclusions

The modified IDx-DR device is substantially equivalent to the predicate IDx-DR device cleared under K203629. The modifications do not raise new questions of safety and effectiveness of the device. The subject and predicate devices have the same indications for use, technological characteristics, and performance specifications.