Leica Biosystems Imaging, Inc.
April Komplin
Regulatory Affairs Manager
1360 Park Center Drive
Vista, California 92081

April 16, 2024

Re: K232202
Trade/Device Name: Aperio GT 450 DX
Regulation Number: 21 CFR 864.3700
Regulation Name: Whole slide imaging system
Regulatory Class: Class II
Product Code: PSY
Dated: July 25, 2023
Received: July 25, 2023

Dear April Komplin:

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 System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

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 and Part 809); 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 systems (QS) regulation (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.

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,

Shyam Kalavar -S

Shyam Kalavar
Deputy Branch Chief
Division of Molecular Genetics and Pathology 2
OHT7: Office of In Vitro Diagnostics
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)*
K232202

Device Name
Aperio GT 450 DX

Indications for Use *(Describe)*

The Aperio GT 450 DX is an automated digital slide creation and viewing system. The Aperio GT 450 DX is intended for in vitro diagnostic use as an aid to the pathologist to review and interpret digital images of surgical pathology slides prepared from formalin-fixed paraffin embedded (FFPE) tissue. The Aperio GT 450 DX is for creation and viewing of digital images of scanned glass slides that would otherwise be appropriate for manual visualization by conventional light microscopy.

Aperio GT 450 DX is comprised of the Aperio GT 450 DX scanner, which generates images in the Digital Imaging and Communications in Medicine (DICOM) and in the ScanScope Virtual Slide (SVS) file formats, the Aperio WebViewer DX viewer, and the displays. The Aperio GT450 DX is intended to be used with the interoperable components specified in Table 1.

Table 1: Interoperable components of Aperio GT 450 DX

Scanner Hardware	Scanner Output file format	Interoperable Viewing Software	Interoperable Displays
Aperio GT 450 DX scanner	SVS	Aperio WebViewer DX	Barco MDPC-8127 Dell UP3017 Dell U3023E Dell U3223QE
Aperio GT 450 DX scanner	SVS	Sectra Digital Pathology Module (3.3)	Dell U3223QE
Aperio GT 450 DX scanner	DICOM	Sectra Digital Pathology Module (3.3)	Dell U3223QE

The Aperio GT 450 DX is not intended for use with frozen section, cytology, or non-FFPE hematopathology specimens. It is the responsibility of a qualified pathologist to employ appropriate procedures and safeguards to assure the validity of the interpretation of images obtained using the Aperio GT 450 DX.

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
Aperio GT 450 DX, Leica Biosystems Imaging, Inc.

Date Prepared: April 16, 2024

Submitter

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Device Information

Subject Device

Proprietary Name:	Aperio GT 450 DX
Common Name:	Aperio GT 450 DX
Classification Name:	Whole Slide Imaging System
Regulation Section:	21 CFR 864.3700
Regulatory	Classification: Class II
Product Code:	PSY
Review Panel:	88 – Pathology
510(k) Number:	K232202

Predicate Device

Proprietary Name: Aperio AT2 DX System

Submission Number: K190332

I. Intended Use

The Aperio GT 450 DX is an automated digital slide creation and viewing system. The Aperio GT 450 DX is intended for in vitro diagnostic use as an aid to the pathologist to review and interpret digital images of surgical pathology slides prepared from formalin-fixed paraffin embedded (FFPE) tissue. The Aperio GT 450 DX is for creation and viewing of digital images of scanned glass slides that would otherwise be appropriate for manual visualization by conventional light microscopy.

Aperio GT 450 DX is comprised of the Aperio GT 450 DX scanner, which generates images in the Digital Imaging and Communications in Medicine (DICOM) and in the ScanScope Virtual Slide (SVS) file formats, the Aperio WebViewer DX viewer, and the displays. The Aperio GT450 DX is intended to be used with the interoperable components specified in Table 1.

Table 1: Interoperable components of Aperio GT 450 DX

Scanner Hardware	Scanner Output file format	Interoperable Viewing Software	Interoperable Displays
Aperio GT 450 DX scanner	SVS	Aperio WebViewer DX	Barco MDPC-8127 Dell UP3017 Dell U3023E Dell U3223QE
Aperio GT 450 DX scanner	SVS	Sectra Digital Pathology Module (3.3)	Dell U3223QE
Aperio GT 450 DX scanner	DICOM	Sectra Digital Pathology Module (3.3)	Dell U3223QE

The Aperio GT 450 DX is not intended for use with frozen section, cytology, or non-FFPE hematopathology specimens. It is the responsibility of a qualified pathologist to employ appropriate procedures and safeguards to assure the validity of the interpretation of images obtained using the Aperio GT 450 DX.

II. Device Description

The Aperio GT 450 DX is a Whole Slide Imaging (WSI) system, including image acquisition and image viewing components.

Aperio GT 450 DX is a WSI system comprised of an image acquisition subsystem known as the Aperio GT 450 DX scanner and Aperio WebViewer DX image viewing software which is accessed from a workstation and a display.

1) Image Acquisition Subsystem

The image acquisition subsystem of the Aperio GT 450 DX captures the information from surgical pathology glass slides prepared from FFPE tissue and saves it as a high-resolution digital image file. This subsystem is comprised of the Aperio GT 450 DX scanner and corresponding scanner configuration software, Aperio GT 450 Scanner Administration Manager DX (SAM DX).

The Aperio GT 450 DX scanner is a semi-automated benchtop brightfield WSI scanner that can achieve a scan speed of 32 seconds at the 40x scanning magnification for a 15 mm x 15 mm area. The scanner supports continuous glass-slide loading (Up to 15 racks with a total of 450-slide capacity), priority rack scanning, and automated image quality checks during image acquisition. The Aperio GT 450 DX scanner can be used with Leica Biosystems Imaging, Inc.--manufactured slide racks (Product No. 23RACKGT450) and other supported slide racks (e.g., Prisma® 20-slide basket from Sakura Finetek USA, Inc). The Aperio GT 450 DX scanner detects the racks once loaded in the scanner and scans the slides automatically. Users operate the scanner via a touchscreen interface.

The Aperio GT 450 DX scanner can save digital images in a unique Aperio ScanScope Virtual Slide (SVS) image format or Digital Imaging and Communications in Medicine (DICOM) image format. The digital images are sent to end-user-provided image storage attached to the scanner's local network, where they can be cataloged in image storage software (non-medical device, external to the WSI), including Image Management System (IMS), such as Aperio eSlide Manager, or a Picture Archiving and Communication System (PACS), such as Sectra PACS software.

Aperio GT 450 SAM DX is centralized scanner management software external to the connected scanner(s). This software application enables IT implementation, including configuration, monitoring, and service access of multiple scanners from a single desktop client location. Aperio GT 450 SAM DX is installed on a customer-provided server that resides on the same network as the scanner(s) for image management.

2) Image Viewing Subsystem

The image viewing subsystem of the WSI device displays the digital images to the human reader. This subsystem comprises Aperio WebViewer DX image viewing software, a workstation PC, and monitor(s). Both the workstation and display are procured by the customer

from commercial distributors and qualified for *in vitro* diagnostic use by Leica Biosystems Imaging, Inc. The Aperio WebViewer DX software is a web-based image viewer that enables users to perform Quality Control of images and to review and annotate digital images for routine diagnosis. The Aperio WebViewer DX also incorporates monitor display image validation checks, which provide the user with the ability to ensure the digital slide images are displayed as intended on their monitor, and that browser updates have not inadvertently affected the image display quality. Aperio WebViewer DX is installed on a server and accessed from an IMS (e.g., Aperio eSlide Manager) or a customer's Laboratory Information System (LIS) using compatible browsers.

III. Comparison of technological characteristics with the predicate device

Table 1. Similarities between the Subject Device and the Predicate Device

<table>
<tr><th>Item</th><th>Subject Device</th><th>Predicate Device</th></tr>
<tr><td>Product Name</td><td>Aperio GT 450 DX</td><td>Aperio AT2 DX System</td></tr>
<tr><td>510(k) No.</td><td>K232202</td><td>K190332</td></tr>
<tr><td>Manufacturer</td><td>Leica Biosystems Imaging, Inc.</td><td>Leica Biosystems Imaging, Inc.</td></tr>
<tr><td>Intended Use</td><td>The Aperio GT 450 DX is an automated digital slide creation and viewing system. The Aperio GT 450 DX is intended for in vitro diagnostic use as an aid to the pathologist to review and interpret digital images of surgical pathology slides prepared from formalin-fixed paraffin embedded (FFPE) tissue. The Aperio GT 450 DX is for creation and viewing of digital images of scanned glass slides that would otherwise be appropriate for manual visualization by conventional light microscopy.

Aperio GT 450 DX is comprised of the Aperio GT 450 DX scanner, which generates images in the Digital Imaging and Communications in Medicine (DICOM) and in the ScanScope Virtual Slide (SVS) file formats, the Aperio WebViewer DX viewer, and the displays. The Aperio GT 450 DX is intended to be used with the interoperable components specified in Table 1.

Table 1: Interoperable components of Aperio GT 450 DX
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The Aperio AT2 DX System is composed of the Aperio AT2 DX scanner, the ImageScope DX review application and Display. The Aperio AT2 DX System is for creation and viewing of digital images</td></tr>
</table>

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Classification Regulation	21 CFR 864.3700				21 CFR 864.3700
Product Code	PSY – Whole Slide Imaging System				PSY – Whole Slide Imaging System
Classification Panel	(88) Pathology				(88) Pathology
Intended Users	Trained pathologists and clinical pathology histotechnicians				Trained pathologists and clinical pathology histotechnicians
Principle of Operation	The Aperio GT 450 DX is a WSI system. The technician places the slides into the Aperio GT 450 DX scanner. The Aperio GT 450 DX scanner automatically loads the slides, takes the micro images, finds the tissues, and scans the slides. The scanner also automatically performs quality control (QC) and notifies the user of any image quality issue during the image acquisition. The image data is sent to end-user-provided image storage attached to the local network. During the review, the pathologist opens WSI images acquired with the WSI scanner from the image storage, performs further QC, and reads WSI images of the slides to make a diagnosis.				The technician loads the slides into the WSI scanner. The scanner scans the slides and generates WSI image for each slide. The acquired WSI images are stored in an end user provided image storage attached to the local network. During review, the pathologist opens WSI images acquired with the WSI scanner from the image storage, performs further QC and reads WSI images of the slides to make a diagnosis.
Prescription Use	Prescription Use Only				Prescription Use Only

Use Environment	Clinical laboratory	Clinical laboratory
Specimen Type	Formalin-Fixed Paraffin-Embedded (FFPE) Specimen	Formalin-Fixed Paraffin-Embedded (FFPE) Specimen
Tissue Finding	Automatic	Automatic, manual
Focusing System	Automatic	Automatic, manual
Slide Storage/loading Capacity	450 slides, 1x 3-inch slide	400 slides, 1x 3-inch slide
Supported slide size	1 x 3 inch	1 x 3 inch
Scanning Resolution at 40x	0.26 µm/pixel	0.25 µm/pixel
Scanning Region	≤ 23.6 mm x 58 mm for 1x 3 inch slide	≤ 22.9 mm x 54.9 mm for 1x 3-inch slide
Focusing Resolution at 40x	+/- 0.125 micron	+/- 0.125 micron
Focusing error at 40x	+/- 0.5 micron	+/- 0.5 micron
Color Reproducibility	Max ΔE< 10	Max ΔE< 10
Image Storage	Images are stored in the end-user-provided image storage attached to the local network.	Images are stored in an end user-provided image storage attached to the local network.

Table 2. Differences between the Subject Device and the Predicate Device

Item	Subject Device	Predicate Device
Product Name	Aperio GT 450 DX	Aperio AT2 DX System
510(k) No.	K232202	K190332
Scanning Magnification	40x	40x 20x
Slide Loading Method	Automatic	Automatic and Manual
Continuous Loading	Yes	No
Throughput (includes slide handling) at 40x	81 slides per hour	20 slides per hour
Scan Speed at 40x	< 32 sec/slide, 15 x 15 mm	≤ 2 min 35 sec/slide, 15 x 15mm
Scan Output Image Format	SVS and DICOM	SVS

Auto QC during scanning	Yes	No
Focusing method	Real-Time focus and point focus	Point focus
Objective lens	40x/0.65 Plan Apo wide field	20x/0.75 NA Plan Apo (40x scanning with 2x optical magnification changer)
Type of viewer Software Application	Web-based application	Native MS Windows
Turnaround Time	Within 3 seconds until the image is fully loaded.	No longer than 7 seconds until the image is fully loaded.
Compatible Display (Monitor)	DELL UP3017 Dell U3023E Dell U3223QE Barco MDPC-8127	Dell MR2416
Image Manipulation Functions	Panning, zooming, gamma function, annotations, and measurements (distance)	Panning, zooming, gamma function, annotations, and measurements (distance and area)

The Aperio GT 450 DX and the predicate device have similar Indications for Use and Principle of Operation. Compared to the predicate device, the Aperio GT 450 DX generates images in both SVS and DICOM formats and also supports additional FDA-cleared third-party viewing software and displays. The Aperio GT 450 DX can continuously load slides and perform auto quality control during the scan process. The Aperio GT 450 DX viewer is a web-based software.

The differences between the Aperio GT 450 DX and the predicate device do not raise any safety and effectiveness concerns. The Aperio WebViewer DX is as safe and effective as the predicate device.

IV. Performance Data

1. Technical Studies

Multiple studies were conducted to evaluate the performance of the Aperio GT 450 DX as recommended in FDA's guidance, *Technical Performance Assessment of Digital Pathology Whole Slide Imaging Devices.*

1) Slide Feeder

Information was provided on the configuration of the slide feed mechanism, including a physical description of the slide, the number of slides in the queue (carrier), and the class of

automation. Information was provided on the user interaction with the slide feeder, including hardware, software, feedback mechanisms, and Failure Mode and Effects Analysis (FMEA).

2) Light source

Descriptive information associated with the lamp and the condenser was provided. Testing information was provided to verify the spectral distribution of the light source as part of the color reproduction capability of the Aperio GT 450 DX scanner.

3) Imaging optics

An optical schematic with all optical elements identified from the slide (object plane) to the digital image sensor (image plane) was provided. Descriptive information regarding the microscope objective, the auxiliary lenses, and the magnification of imaging optics was provided. Testing information regarding the relative irradiance, optical distortions, and lateral chromatics aberrations was provided.

4) Mechanical scanner movement

Information and specifications on the configuration of the stage, method of movement, control of movement of the stage, and FMEA were provided. Test data to verify the repeatability of the stage movement and verify the mechanism that the stage movement stays within limits during operations was provided.

5) Digital imaging sensor

Information and specifications on the sensor type, pixel information, responsivity specifications, noise specifications, readout rate, and digital output format were provided. Test data to determine the correct functioning of the digital image sensor was provided. The digital image sensor converts slides' optical signals to digital signals. The digital signals consist of a set of numerical values corresponding to the brightness and color at each point in the optical image.

6) Image processing software

Information and specifications on exposure control, white balance, color correction, sub-sampling, pixel-offset correction, pixel-gain or flat-field correction, and pixel-defect correction were provided.

7) Image composition

Information and specifications on the scanning method, the scanning speed, and the number of planes at the Z-axis to be digitized were provided. Test data to analyze the image composition performance was provided.

8) Image files format

Information and specifications on the compression method, compression ratio, file format, and file organization were provided.

9) Image review manipulation software

Information and specifications on continuous panning and pre-fetching, continuous zooming, discrete Z-axis displacement, the ability to compare multiple slides simultaneously on multiple windows, image enhancement and sharpening functions, color manipulation, annotation tools, and digital bookmarks were provided.

10) Computer environment

Information and specifications on the computer hardware, operating system, graphics card, graphics card driver, color management settings, color profile, and display interface were provided.

11) Display

Information and specifications on the technological characteristics of the display device, the physical size of the viewable area and aspect ratio, backlight type and properties, frame rate and refresh rate, a pixel array, pitch, pixel aperture ratio, and subpixel matrix scheme, subpixel driving to improve grayscale resolution, supported color spaces, display interface, user controls of brightness, contrast, gamma, color space, power-saving options, etc., via the on-screen display menu, ambient light adaptation, touchscreen technology, color calibration tools, and frequency and nature of quality-control tests were provided. Test data to verify the performance of the display was provided.

12) Color reproducibility

Test data to evaluate the color reproducibility of the system was provided.

13) Spatial resolution

Test data to evaluate the composite optical performance of all components in the image acquisition phase was provided.

14) Focusing test

Test data to evaluate the technical focus quality of the system was provided.

15) Whole slide tissue coverage

Test data to demonstrate that the entire tissue specimen on the glass slide is detected by the tissue detection algorithms and that all the tissue specimens are included in the digital image file was provided.

16) Stitching error

Test data to evaluate the stitching errors and artifacts in the reconstructed image was provided.

17) Turnaround time

Test data to evaluate the turnaround time of the system was provided.

2. User Interface/Human Factors Validation

Human factors studies for Aperio GT 450 DX were conducted. The studies were designed around critical user tasks and use scenarios performed by representative users from histotechnicians and pathologists. The information included a list of all critical user tasks and a description of the followed process to identify them. A systematic evaluation involving simulated use by representative users performing all tasks (including critical tasks) required for the operation of the device and a subjective assessment of failure was provided. All participants were able to perform all tasks (including the critical tasks), and no critical task failures were observed. There were several occasional difficulties, which was expected with any new software and instrument. The learnability and ease of use were considerably high. All difficulties observed had little influence on the perception of usability, and no difficulties or failures were observed on tasks that could lead to patient harm. In all instances, both pathologists and histotechnicians were able to identify cases easily and ensure that everything was complete.

3. Electromagnetic Compatibility (EMC) Testing

The Aperio GT 450 DX scanner meets the technical requirements of IEC/EN 61010-1:2010/AMD1: 2016, *Safety requirements for electrical equipment for measurement, control, and laboratory use - Part 1: General requirements* and IEC/EN 61010-2-101: 2018,

Safety requirements for electrical equipment for measurement, control, and laboratory use - Part 2-101: Particular requirements for in vitro diagnostic (IVD) medical equipment.

The Aperio GT 450 DX scanner meets the technical requirements of IEC/EN 61326-2-6:2013 *Electrical equipment for measurement, control and laboratory use - EMC requirements - Part 2-6: Particular requirements - In vitro diagnostic (IVD) medical equipment,* and the EMC Immunity requirements in the FDA Guidance, *Electromagnetic Compatibility (EMC) of Medical Devices* (June 6, 2022). It is important to note that in accordance with the FDA Guidance Document on EMC, and the FDA's partial recognition of the IEC 61326 series of EMC immunity standards as a consensus standard, a subset of higher EMC immunity test level (including Electrostatic discharge (ESD), Radio frequency interference (RFI), Electrical Fast Transient (EFT), Conducted RFI, and magnetic field) provided in IEC 60601-1-2:2014+A1:2020, *Amendment 1 - Medical electrical equipment - Part 1-2: General requirements for basic safety and essential performance - Collateral Standard: Electromagnetic disturbances - Requirements and tests,* have been deemed appropriate and were applied during the course of this testing.

4. Clinical testing

Two clinical studies were conducted with the Aperio GT 450 DX: Clinical accuracy and precision.

1) Clinical accuracy study

Clinical accuracy was evaluated by analyzing the concordance (concordant, minor discrepancy, major discrepancy) of the diagnoses made using the Aperio GT 450 DX (referred to as whole slide image review [WSIR] diagnosis) with the reference diagnoses (original sign-out pathologic diagnosis), and the concordance of traditional light microscope slide review (MSR) diagnoses with the reference diagnoses. For WSIR, concordance was evaluated for cases accessed from the local server (local cohort) and the Leica Biosystems web-hosting site (remote cohort). Accuracy was assessed by analyzing the major discrepancy rates for WSIR and MSR diagnoses versus the reference diagnoses and calculating the difference in major discrepancy rates between the two modalities. A major discrepancy was defined as a difference in diagnoses that resulted in a clinically important difference in patient management.

For the primary study endpoint, the difference in overall major discrepancy rates (WSIR diagnosis minus MSR diagnosis) for the full cohort (local and remote cohorts combined)

when compared to the reference diagnosis, along with 95% confidence intervals (CIs), were calculated. Secondary study endpoints included the determination of the major discrepancy rate of WSIR diagnosis relative to the reference diagnosis, along with the 95% CIs. Additionally, the difference in the major discrepancy rates (WSIR diagnosis minus MSR diagnosis) when compared to the reference diagnosis, along with 95% CIs, were calculated for local and remote cohorts, respectively. The acceptance criteria associated with each study endpoint were as follows:

Primary Endpoint:

- The upper bound of the 2-sided 95% confidence interval (CI) of the difference between the overall major discrepancy rates of WSIR diagnosis and MSR diagnosis when compared to the reference diagnosis shall be ≤4%.

Secondary Endpoints:

- The upper bound of the 2-sided 95% CI of the major discrepancy rate between the WSIR diagnosis and the reference diagnosis shall be ≤7%.
- The upper bound of the 2-sided 95% CI of the difference between the major discrepancy rates of the WSIR diagnosis and MSR diagnosis when compared to the reference diagnosis shall be ≤4% for local WSI access.
- The upper bound of the 2-sided 95% CI of the difference between the major discrepancy rates of the WSIR diagnosis and MSR diagnosis when compared to the reference diagnosis shall be ≤4% for remote WSI access.

Table 3. Overall Major Discrepancy Rates for the 2 Modalities and the Difference Between the Overall Major Discrepancy Rates for the Full Cohort, Local Cohort, and Remote Cohort

		Whole Slide Image Review Diagnosis (WSIRD)				Light Microscope Slide Review Diagnosis (MSRD)				Difference in Major Discrepancy Rates (WSIRD minus MSRD)	
Cohort		Major Discrepancy	Total	Major Discrepancy Rate (%)	Model 95% CI	Major Discrepancy	Total	Major Discrepancy Rate (%)	Model 95% CI	%	Model 95% CI
Full	Observed	218	3549	6.14%	-	133	3631	3.66%	-	-	-
	Model			5.84%	(5.01%, 6.80%)			3.44%	(2.84%, 4.17%)	2.40%	(1.40%, 3.39%)
Local	Observed	119	1806	6.59%	-	71	1844	3.85%	-	-	-
	Model			6.13%	(4.99%, 7.51%)			3.52%	(2.71%, 4.57%)	2.61%	(1.23%, 3.99%)
Remote	Observed	99	1743	5.68%	-	62	1787	3.47%	-	-	-
	Model			5.51%	(4.40%, 6.88%)			3.34%	(2.52%, 4.40%)	2.17%	(0.78%, 3.57%)

Note:
Full cohort includes both local and remote cohorts.

2) Precision Study

The precision of the Aperio GT 450 DX was assessed in 3 substudies:

- For intra-system precision, the objectives were to assess precision within each of the three independent systems and overall within-system.
- For inter-system/site precision, the objectives were to assess precision between systems/sites (3 independent systems at three different sites) and overall between systems/sites.
- For intra- and inter-pathologist precision, the objectives were to assess precision within and between pathologists (using images generated from a single system), overall within pathologists, and overall between pathologists.

The precision was considered acceptable if the lower bounds of the 2-sided 95% CI of the overall agreements for each precision component (intra-system, inter-system/site, intra-pathologist, and inter-pathologist) were ≥ 85%.

Table 4. Intra-System Precision Substudy: Agreement Within Systems

			Agreement Rate and 95% CI		
System	**Number of Pairwise Agreements**	**Number of Comparison Pairs**	**% Agreement**	**Lower**	**Upper**
System 1	255	261	97.7	95.7%	99.3%
System 2	270	276	97.8	95.9%	99.3%
System 3	212	222	95.5	92.5%	98.1%
Overall	**737**	**759**	**97.1**	**95.8%**	**98.3%**

Note:
1. 95% CI was produced using the percentile bootstrapping approach on 5000 bootstrap samples.
2. System 1 is at Site 1, System 2 is at Site 2, and System 3 is at Site 3.

Table 5. Inter-System/Site Precision Substudy: Agreement Between Systems

			Agreement Rate and 95% CI		
System	**Number of Pairwise Agreements**	**Number of Comparison Pairs**	**% Agreement**	**Lower**	**Upper**
System 1 vs System 2	241	253	95.3	92.5%	97.7%
System 1 vs System 3	246	253	97.2	95.0%	99.2%
System 2 vs System 3	244	253	96.4	94.0%	98.5%
Overall	**731**	**759**	**96.3**	**94.9%**	**97.6%**

Note:
1. 95% CI was produced using the percentile bootstrapping approach on 5000 bootstrap samples.
2. System 1 is at Site 1, System 2 is at Site 2, and System 3 is at Site 3

Table 6. Intra- and Inter-Pathologist Precision Substudy: Agreement Within Pathologists

			Agreement Rate and 95% CI		
Pathologist	**Number of Pairwise Agreements**	**Number of Comparison Pairs**	**% Agreement**	**Lower**	**Upper**
Pathologist 1	729	759	96.0	94.7%	97.3%
Pathologist 2	677	759	89.2	86.8%	91.3%
Pathologist 3	723	759	95.3	93.7%	96.7%
Overall	**2129**	**2277**	**93.5**	**92.4%**	**94.5%**

Note:
95% CI was produced using the percentile bootstrapping approach on 5000 bootstrap samples.

Table 7. Intra- and Inter-Pathologist Precision Substudy: Agreement Between Pathologists

			Agreement Rate and 95% CI		
Pathologist	**Number of Pairwise Agreements**	**Number of Comparison Pairs**	**% Agreement**	**Lower**	**Upper**
Pathologist 1 vs Pathologist 2	686	759	90.4	88.2%	92.4%
Pathologist 1 vs Pathologist 3	727	759	95.8	94.3%	97.2%

			Agreement Rate and 95% CI		
Pathologist	**Number of Pairwise Agreements**	**Number of Comparison Pairs**	**% Agreement**	**Lower**	**Upper**
Pathologist 2 vs Pathologist 3	676	759	89.1	86.9%	91.2%
Overall	**2089**	**2277**	**91.7**	**90.6%**	**92.8%**

Note:
95% CI was produced using the percentile bootstrapping approach on 5000 bootstrap samples.

The acceptance criteria were met for all endpoints for the clinical accuracy study. These results indicate that diagnoses made using the Aperio GT 450 DX, using both local and remote accessed image data, are accurate and comparable to diagnoses made using a light microscope. Additionally, all endpoints were met for the precision study. These results indicate that the Aperio GT 450 DX has an acceptable level of precision and validates the intended use.

The clinical study results demonstrate that Aperio GT 450 DX is substantially equivalent to the predicate device.

V. Conclusions

The study results demonstrate that Aperio GT 450 DX is substantially equivalent to the predicate device.