510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

I Background Information:

A 510(k) Number

K243391

B Applicant

PathAI, Inc.

C Proprietary and Established Names

AISight Dx

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
QKQ	Class II	21 CFR 864.3700 - Whole Slide Imaging System	88-Pathology

II Submission/Device Overview:

A Purpose for Submission:

1. New device
2. Establish a Pre-Determined Change Control Plan (PCCP) for qualifying and adding additional FDA-cleared [510(k) cleared] whole slide imaging scanners and image file formats from these scanners, FDA-cleared pathology displays as interoperable components to AISight Dx and additional web browsers for use with AISight Dx.

B Type of Test:

Digital pathology viewing software

III Intended Use/Indications for Use:

A Intended Use(s):

For In Vitro Diagnostic Use

AISight Dx is a software only device intended for viewing and management of digital images of scanned surgical pathology slides prepared from formalin-fixed paraffin embedded (FFPE) tissue. It is an aid to the pathologist to review, interpret, and manage digital images of these slides for primary diagnosis. AISight Dx is not intended for use with frozen sections, cytology, or non-FFPE hematopathology specimens.

It is the responsibility of a qualified pathologist to employ appropriate procedures and safeguards to assure the quality of the images obtained and, where necessary, use conventional light microscopy review when making a diagnostic decision. AISight DX is intended to be used with interoperable displays, scanners and file formats, and web browsers that have been 510(k) cleared for use with the AISight Dx or 510(k)-cleared displays, 510(k)-cleared scanners and file formats, and web browsers that have been assessed in accordance with the Predetermined Change Control Plan (PCCP) for qualifying interoperable devices.

B Indication(s) for Use:

Same as Intended Use.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

For In vitro diagnostic (IVD) use only

IV Device/System Characteristics:

A Device Description:

AISight Dx (Version 2.9) is a web-based, software-only device that is intended to aid pathology professionals in viewing, interpretation, and management of digital whole slide images (WSI) of scanned surgical pathology slides prepared from formalin-fixed, paraffin-embedded (FFPE) tissue obtained from Leica Aperio GT 450 DX scanner or Hamamatsu NanoZoomer S360MD Slide scanner. It aids the pathologist in the review, interpretation, and management of pathology slide digital images used to generate a primary diagnosis.

Table 1: Interoperable Devices of AISight Dx

Scanner	Scanner Output File format	Viewing Software	Display
Leica Aperio GT 450 DX	SVS, DICOM	AISight Dx	Barco MDPC8127 Dell UP3017 Dell U3023E Dell U3223QE JVC Kenwood JD-C24BN01A
Hamamatsu S360MD Slide scanner	NDPI		

AISight Dx is operated as follows:

1. The tissue slides are scanned with an FDA-cleared, interoperable WSI scanner in accordance with the WSI scanner's quality control process.
2. The scanned WSI files are transported from the WSI scanner to the subject device using the following methods:
    a. Bulk ingestion (automatic slide upload) by laboratory personnel
    b. Manual ingestion (manual slide upload) by a pathologist
3. Cases are assigned by creating accessions.
4. The pathologist selects a case and open the accessions to read slides with the following tools:
    a. Zooming and panning
    b. Measurement of distances and areas
    c. Annotation
    d. Annotation counter
    e. Viewing multiple slides side by side
5. The pathologist renders a diagnosis and submits the patient report.

Additional information about the interoperable components and system requirements are given in Tables 2-4 below.

Table 2: Interoperable WSI Scanners and File Formats

Manufacturer	Model	File Format	Validation Method
Leica	Aperio GT 450 DX	SVS	Clinical study (see VII-B-a)
Leica	Aperio GT 450 DX	DICOM	Bench testing (see VII-B-b)
Hamamatsu	NanoZoomer S360MD Slide scanner	NDPI	Clinical study (see VII-B-a)

Table 3: Interoperable WSI Displays

Manufacturer	Model
JVC	Kenwood JD-C240BN01A
BARCO	MDPC-8127
Dell	UP3017
Dell	U3023E
Dell	U3223QE

Table 4: Computer Environment/System Requirements

Workstation Component	Specifications
Memory	4 GB RAM Capable of supporting at least one of the supported web browsers.
Network connectivity	Internet access Outbound traffic enabled on port 443 25 Mbps download and upload speed
Supported web browsers	Google Chrome version 111.0 or later Microsoft Edge version 111.0 or later

B Instrument Description Information:

1. Instrument Name:
   AISight Dx

2. Specimen Identification:
   Glass slides and scanned images are identified based on the previously assigned specimen identifiers such as patient identifiers, barcodes, etc. Digital images of surgical pathology slides prepared from FFPE tissue.

3. Specimen Sampling and Handling:
   Specimen sampling and handling are performed upstream and independent of the use of the subject device. Specimen sampling includes surgical pathology specimens such as biopsy or resection specimens which are processed using standard histology techniques. The FFPE tissue sections are stained using the Hematoxylin and Eosin (H&E) staining procedure. Then digital images are obtained from these glass slides using either the Aperio GT 450 DX scanner or the Hamamatsu S360MD Slide scanner.

4. Calibration:
   Not Applicable

5. Quality Control:
   Prior to using a WSI for diagnosis, it is the responsibility of the laboratory staff, while scanning glass slides and uploading WSIs, and the pathologist, while reviewing the WSIs, to ensure that all scanned slide images have been imported for every case and the images are of acceptable quality for diagnostic purposes per their laboratory standards. Additional details of the quality control procedures are provided in the device's user manual.

V Substantial Equivalence Information:

A Predicate Device Name(s):

Aperio GT 450 DX, NanoZoomer S360MD Slide scanner system

B Predicate 510(k) Number(s):

K232202, K233027

C Comparison with Predicate(s):

The subject device is similar to the predicate, having similar indications for use, intended use and technological characteristics as its predicate devices, with the exception of the implementation of a PCCP that specifies the protocols and acceptance criteria for validating and adding additional FDA cleared scanners and file formats, additional FDA cleared pathology displays and additional web browsers as interoperable components to the AISight Dx in a controlled manner, such that the

device is as safe and as effective as the predicate devices.

The description of the planned modifications, testing methods, validation activities, performance requirements, and communication to users are part of the device quality system and are summarized below.

Planned modifications by PCCP:

a. Additional Scanners and file formats: To include additional FDA cleared scanners (candidate) and associated file formats, the candidate scanners will be verified and validated in accordance with the requirements outlined in the PCCP protocol, including method comparison (clinical study) study, measurement and turnaround time testing. Original file formats associated with the candidate scanner will be verified and validated via a clinical study as specified in the PCCP protocol. Additional FDA cleared file formats of the scanner will be verified and validated through pixel-wise comparison testing which should demonstrate that the new FDA-cleared scanner and associated file format produce images that are identical to those generated by the predicate device. Two images will be considered to be identical if the 95th percentile of the pixel-wise color differences across all required screenshot image pairs is less than 3 CIEDE2000 units ($\Delta E00 < 3$). If the bench testing does not meet this acceptance criterion, a clinical study may be used. Upon successful validation, labeling will be updated in accordance with the authorized PCCP to provide users with current information regarding the device's compatible scanner hardware and file formats. Labeling will be updated in accordance with the authorized PCCP to provide users with current information regarding the device's compatible scanner hardware.

b. Additional Displays: When a new FDA-cleared display is identified as the candidate, it will be verified and validated in accordance with a system-level integration test which will also be conducted to confirm that the new display functions adequately with the complete WSI system, including the original scanner and viewer components. Following successful validation, the device labeling will be updated in accordance with the authorized PCCP to ensure that users are provided with accurate and current information regarding display compatibility. If the candidate display meets the criteria, the design change will be implemented according to the quality management system and the new display may be added as an interoperable component to the subject device without additional premarket review. The device labeling and company website will be revised to identify the new display according to the quality management system.

c. Additional Web Browsers: To include additional web browsers, the new browsers will be verified and validated in accordance with the requirements outlined in the PCCP Protocol, including pixel-to-pixel comparison and turnaround time testing. Upon successful validation, labeling will be updated in accordance with the authorized PCCP to provide users with current information regarding the device's compatible browsers.

The similarities and differences between the AISight Dx and the predicate devices, NanoZoomer S360MD Slide scanner system and Aperio GT 450 DX are summarized in the Table 5 below.

Table 5: Comparison with Predicate

<table>
<tr><th>Specification</th><th>Predicate Device (K233027)</th><th>Predicate Device (K232202)</th><th>Subject Device (K243391)</th></tr>
<tr><td>Device Trade Name</td><td>NanoZoomer S360MD Slide scanner system</td><td>Aperio GT 450 DX</td><td>AISight Dx</td></tr>
<tr><td>Product Code</td><td>PSY</td><td>PSY</td><td>QKQ</td></tr>
<tr><td>Regulation</td><td>21 CFR 864.3700</td><td>21 CFR 864.3700</td><td>21 CFR 864.3700</td></tr>
<tr><td>Regulation Name</td><td>Whole Slide Imaging System</td><td>Whole Slide Imaging System</td><td>Whole Slide Imaging System</td></tr>
<tr><td>Classification</td><td>II</td><td>II</td><td>II</td></tr>
<tr><td colspan="4">General Device Characteristics - Similarities</td></tr>
<tr><td>Indications for Use</td><td>The NanoZoomer S360MD Slide scanner system (“NanoZoomer System”) is an automated digital slide creation, viewing, and management system. The NanoZoomer System 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 NanoZoomer System is not intended for use with frozen section, cytology, or non-FFPE hematopathology specimens. The NanoZoomer System comprises the NanoZoomer S360MD Slide scanner, the NZViewMD Software and a compatible display that has been 510(k) cleared for use with the NanoZoomer system or a 510(k)- cleared display that has been assessed in accordance with the Predetermined Change Control Plan (PCCP) for qualifying additional compatible displays.
The NanoZoomer System is for creation and viewing of digital images of scanned glass slides that would otherwise be appropriate for</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
<table>
<tr><th>Scanner Hardware</th><th>Scanner Output file format</th><th>Interoperable Viewing Software</th><th>Interoperable Displays</th></tr>
<tr><td>Aperio GT 450 DX scanner</td><td>SVS</td><td>Aperio WebViewer DX</td><td>Barco MDPC8127
Dell UP3017
Dell U3023E
Dell U3223QE</td></tr>
</table>
</td><td>AISight Dx is a software only device intended for viewing and management of digital images of scanned surgical pathology slides prepared from formalin-fixed paraffin embedded (FFPE) tissue. It is an aid to the pathologist to review, interpret, and manage digital images of these slides for primary diagnosis. AISight Dx is not intended for use with frozen sections, cytology, or non-FFPE hematopathology specimens.

It is the responsibility of a qualified pathologist to employ appropriate procedures and safeguards to assure the quality of the images obtained and, where necessary, use conventional light microscopy review when making a diagnostic decision. AISight DX is intended to be used with interoperable displays, scanners and file formats, and web browsers that have been 510(k) cleared for use with the AISight Dx or 510(k)-cleared displays, 510(k)-cleared scanners and file formats, and web browsers that have been assessed in accordance with the Predetermined Change Control Plan (PCCP) for qualifying interoperable devices.</td></tr>
</table>

Specification	Predicate Device (K233027)	Predicate Device (K232202)	Subject Device (K243391)
	manual visualization by conventional light microscopy. 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 NanoZoomer System	<table><tr><td>Aperio GT 450 DX scanner</td><td>SVS</td><td>Sectra Digital Pathology Module (3.3)</td><td>Dell U3223QE</td></tr><tr><td>Aperio GT 450 DX scanner</td><td>DICOM</td><td>Sectra Digital Pathology Module (3.3)</td><td>Dell U3223QE</td></tr></table> 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.	
Scanner	Hamamatsu NanoZoomer S360MD Slide scanner	Aperio Leica GT 450 DX	Hamamatsu NanoZoomer S360MD Slide scanner, Aperio Leica GT 450 DX, or FDA-cleared scanning hardware validated per the PCCP to ensure performance requirements are met prior to modifications being implemented.
Compatible Display	JVC Kenwood JD-C24BN01A, BARCO MDPC-8127, or FDA-cleared display validated per the PCCP to ensure performance requirements are met prior to modifications being implemented.	BARCO MDPC-8127, Dell UP3017, Dell U3023E, Dell U3223QE	JVC Kenwood JD-C24BN01A, BARCO MDPC- 8127, Dell UP3017, Dell U3023E, Dell U3223QE, or FDA-cleared display validated per the PCCP to ensure performance requirements are met prior to modifications being implemented.
Specimen Type	Surgical pathology slides prepared from FFPE tissue	Surgical pathology slides prepared from FFPE tissue	Surgical pathology slides prepared from FFPE tissue
Image File Format	NDPI	SVS, DICOM	NDPI, SVS, DICOM
Image Manipulation Functions	Panning, zooming, image adjustments, annotations, and distance/area measurements	Panning, zooming, gamma function, annotations, and measurements (distance)	Panning, zooming, image adjustments, annotations, and distance/area measurements
General Device Characteristics – Differences			
Type of Software Application	Windows based	Internet browser based	Internet browser based

Specification	Predicate Device (K233027)	Predicate Device (K232202)	Subject Device (K243391)
Device Components	Scanner, Image Management Software and Display	Scanner, Image Management Software and Display	Image Management Software
Principle of Operation	After WSI are acquired by using NanoZoomer S360MD Slide scanner, the WSI are automatically saved to the hard disk during scanning and may be viewed later by using the included viewing software. During review, the pathologist opens WSI from the image storage attached to local network, performs further QC, and reads WSI of the slides to make a diagnosis.	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.	After the WSIs are acquired using the NanoZoomer S360MD Slide scanner or Aperio GT450 DX, the WSIs are stored in customer provided image storage. Images are then ingested into AISight Dx image storage. During image review, the pathologist opens the WSI from AISight Dx image storage; performs further QC and then reads the WSI to make a diagnosis.
User Interface	NZViewMD	Aperio WebViewer DX	AISight Dx

VI Standards/Guidance Documents Referenced:

1. Technical Performance Assessment of Digital Pathology Whole Slide Imaging Devices: Guidance for Industry and Food and Drug Administration Staff, April 20, 2016.
2. Applying Human Factors and Usability Engineering to Medical Devices: Guidance for Industry and Food and Drug Administration Staff February 3, 2016.
3. EN ISO 13485:2016 Medical devices — Quality management systems — Requirements for regulatory purposes.
4. EN ISO 14971:2019-12 – Medical devices - Application of risk management to medical devices (same as ISO 14971:2007, Corrected version 2007-10-01), Recognition Number: 5-40.
5. EN 62304:2006- AMD1:2015 – Medical device software - software life-cycle processes, Recognition Number: 13-32.
6. EN ISO 62366-1:2015 - AMD1:2015 – Application of usability engineering to medical devices, Recognition Number: 5-114.
7. ISO/IEC 27001:2013 – Information technology — Security techniques - Information security management systems — Requirements.
8. Recommended Content and Format of Non-Clinical Bench Performance Testing Information in Premarket Submissions: Guidance for Industry and Food and Drug Administration Staff, December 20, 2019. |
9. ISO/CIE 11664-4:2014 Colorimetry – Part 4: CIE 1976 L*a*b* colour space
10. ISO/CIE 11664-6:2019 Colorimetry – Part 6: CIEDE2000 colour-difference formula

11. IEC 61966-2-1:1999 Multimedia systems and equipment – Colour measurement and management – Part 2-1: Colour management – Default RBG colour space – sRGB

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:
   Not applicable

2. Linearity:
   Not applicable

3. Analytical Specificity/Interference:
   Not applicable

4. Accuracy (Instrument):
   Not applicable

5. Carry-Over:
   Not applicable

B Other Supportive Instrument Performance Characteristics Data:

a. Clinical Validation Study

Two separate clinical studies were conducted to support the performance of the AlSight Dx system for reading WSIs for the pathology primary diagnosis indication when WSIs are created by Leica Aperio GT 450 DX scanner (Leica scanner) or Hamamatsu NanoZoomer S360MD (Hamamatsu scanner).

The imaging pipeline/configuration in the clinical studies used were as follows:

- Aperio GT 450 DX scanner images/SVS image format/AlSight Dx/Edge web browser/Barco MDPC-8127 display, and
- Hamamatsu S360MD Slide Scanner images/NDPI image format/AlSight Dx/Chrome web browser/Barco MDPC-8127 display.

The objective of the two clinical studies was to demonstrate that viewing, reviewing, and diagnosing WSIs of H&E stained FFPE tissue slides using AISight Dx [manual digital read (MD)] is non-inferior to glass slide reads using optical (light) microscopy [manual optical (MO)]. The primary endpoint of the study was the difference in major discordance rates between MD and MO when compared to the reference (main) diagnosis, which was the original sign-out pathologic diagnosis using MO [ground truth, (GT)] rendered at the institution. The studies were conducted at one site with 3 reader pathologists at each site. The study pathologists were the same for both the clinical studies (Leica scanner and Hamamatsu scanner) with a minimum 2-week washout period between the studies.

For primary analysis, each mismatch between the GT diagnosis and study read (glass slides or WSI) was assessed for clinical severity of the error by 2 different adjudicating pathologists. These independent pathologists were provided a table with both diagnoses to make the decision on minor, major, or no discordance, but were blinded to GT diagnosis or study diagnosis and glass slides or WSI reads. If the 2 pathologists disagreed on their assessment, the case were sent to a third pathologist. If all 3 pathologists disagreed on their assessments, a consensus meeting was held. Only major discordances were included in the analysis. Similarly, for secondary analysis, each mismatch between the glass slides and WSI read from each individual pathologist was assessed for clinical severity of the error by an adjudicating pathologist following the same criteria.

A major discordance was defined as a difference in diagnosis that resulted in a clinically important difference in patient management, whereas a minor discordance would not be associated with a clinically important difference in patient management. The adjudicators' concordance scores for the same case were compared to determine a consensus score for major discordance status [no major discordance (concordant or minor discordance) or major discordance]. The diagnosis consensus scores were used to estimate WSIR diagnosis major discordance rate.

Study Acceptance Criteria**:** The endpoint of the study was the difference in overall major discordance rates between the 2 modalities when compared to the reference diagnosis (original sign-out pathologic diagnosis) which was defined as the GT diagnosis. The acceptance criteria associated with each study endpoint were as follows: The upper bound of the 2-sided 95% CI of the difference between the overall major discordance rates of MD diagnosis and MO diagnosis when compared to the reference diagnosis shall be ≤4%.

Study with Leica GT 450 DX Scanner SVS file format:
The study included 258 randomly selected cases that represented a diverse mixture of pathologic diagnoses and tissue/organ types. Case slides were scanned on the Leica GT 450 DX scanner, producing WSIs in the SVS format at 40x magnification. Three study pathologists (the same pathologists who determined MO diagnosis) at a single site reviewed all study cases twice, once as MO using traditional light microscope and once as MD using AISight Dx on the Microsoft Edge web browser and a Barco MDPC-8127 display.

Study Results:
The overall major discordance rate was determined as a ratio between total number of major discordances and the total number of cases assessed across the 3 pathologists. The major discordance rate between MO and GT was 9.50% (72/758) and between MD and GT was 9.23% (70/758; Table 8). The difference in major discordance rate between MO and MD was -0.26% (95% CI, -2.71, 2.52; $p<0.0001$). The upper limit of the CI was 2.52% which was less than the prespecified noninferiority threshold of 4%, therefore meeting the primary objective of the study.

Table 6: Clinical Study Results Based on Major Discordance Rates

Modality	(n/N)	Discordance Rate (%)	95% CI (%)
MO vs GT	72 / 758	9.50	6.20,13.18
MD vs GT	70 / 758	9.23	6.07,13.17
Difference		-0.26	-2.71, 2.52

Overall concordance rate between MO and MD was calculated. The proportion of concordances for each modality was computed as a ratio between total number of cases with complete agreement along with minor discordances and the total number of cases assessed across the three (3) pathologists. The secondary endpoint was met as the overall concordance was 96.57% (95% CI, 93.39, 98.97).

The major discordance rates for MD and MO diagnoses (relative to the reference diagnosis), and the difference between the two modalities, by each organ type is shown in the table below. The clinical study was not powered to analyze the results by individual organ site or diagnosis.

Table 7: Major Discordance Rates for MD and MO Diagnoses by Organ Type

Organ Type	Major Discordance Rate		
	Manual Digital (MD) % (n/N)	Manual Optical (MO) % (n/N)	Difference % (MD-MO)
Anus/Perianal	11.11 (6/54)	11.11 (6/54)	0.00
Appendix	16.67(2/12)	16.67 (2/12)	0
Bladder	33.33 (14/42)	23.81 (10/42)	9.52
Brain	5.26 (1/19)	5.26 (1/19)	0
Endocrine	3.70 (1/27)	7.41 (2/27)	-3.70
Gallbladder	0.00 (0/3)	0.00 (0/3)	0.00
GE Junction	3.51 (2/57)	5.26 (3/57)	-1.75
Gynecological	15.87 (10/63)	14.29 (9/63)	1.59
Hernial/Peritoneal	0 (0/6)	0 (0/6)	0
Kidney/Neoplastic	0 (0/3)	0 (0/3)	0
Liver/BD, Neoplasm	0 (0/21)	4.76 (1/21)	-4.76
Lung	3.45 (1/29)	13.79 (4/29)	-10.34
Lymph Node	9.09 (4/44)	4.55 (2/44)	4.55
Salivary Gland	11.11 (1/9)	22.22 (2/9)	-11.11
Skin	17.74 (11/62)	12.90 (8/62)	4.84
Soft Tissue Tumors	13.33(2/15)	0.00 (0/15)	13.33
Stomach	0.00 (0/24)	4.17 (1/24)	-4.17

Study with Hamamatsu NanoZoomer S360MD Scanner NDPI file format:

The study included 258 randomly selected cases that represented a diverse mixture of pathologic diagnoses and tissue/organ types. Case slides were scanned on the Hamamatsu NanoZoomer S360MD scanner, producing WSIs in the NDPI format at 40x magnification. Three study pathologists (the same pathologists who determined MO diagnosis) at a single site reviewed all study cases twice, once as MO using traditional light microscope and once as MD using AISight Dx on the Microsoft Chrome web browser and a Barco MDPC-8127 display.

Study Results:
The overall major discordance rate was determined as a ratio between total number of major discordances and the total number of cases assessed across the 3 pathologists. The major discordance rate between MO and GT was 9.58% (73/762) and between MD and GT was 8.40% (64/762; Table 5). The difference in major discordance rate between MO and MD was -1.18% (95% CI, -3.49, 1.16; p<0.0001). The upper limit of the CI was 1.16 % which was less than the prespecified noninferiority threshold of 4%, therefore meeting the primary objective of the study.

Table 8: Clinical Study Results Based on Major Discordance Rates

Modality	(n/N)	Discordance Rate (%)	95% CI (%)
MO vs GT	73/762	9.58	(6.20, 13.44)
MD vs GT	64/762	8.40	(5.50, 11.62)
Difference		-1.18	(-3.49, 1.16)

Overall concordance rate between MO and MD was calculated. The proportion of concordances for each modality was computed as a ratio between total number of cases with complete agreement along with minor discordances and the total number of cases assessed across the 3 pathologists. The overall concordance was 97.90% (95% CI, 96.45, 99.21). The acceptance criterion for secondary endpoint was met.

The major discordance rates for MD and MO diagnoses (relative to the reference diagnosis), and the difference between the two modalities, by each organ type is shown in the table below. The clinical study was not powered to analyze the results by individual organ site or diagnosis.

Table 9: Major Discordance Rates for MD and MO Diagnoses by Organ Type

Organ Type	Major Discordance Rate		
	Manual Digital (MD) % (n/N)	Manual Optical (MO) % (n/N)	Difference % (MD-MO)
Anus/Perianal	9.26 (5/54)	12.96 (7/54)	-3.70
Appendix	16.67 (2/12)	8.33 (1/12)	8.33
Bladder	21.42 (9/42)	26.19 (11/42)	-4.76
Brain	5.26 (1/19)	5.26 (1/19)	0
Endocrine	3.70 (1/27)	7.41 (2/27)	-3.70
Gallbladder	0 (0/3)	0 (0/3)	0
GE Junction	8.77 (5/57)	5.26 (3/57)	3.51
Gynecological	12.70 (8/63)	12.70(8/63)	0
Hernial/Peritoneal	0 (0/6)	0 (0/6)	0
Kidney/Neoplastic	0 (0/3)	0 (0/3)	0
Liver/BD, Neoplasm	0 (1/24)	4.17 (1/24)	-4.17
Lung	6.90 (2/29)	13.79 (4/29)	-6.90
Lymph Node	4.55 (2/44)	4.55 (2/44)	0
Salivary Gland	22.22 (2/9)	22.22 (2/9)	0
Skin	15.87(10/63)	14.29 (9/63)	1.59
Soft Tissue Tumors	0 (0/15)	0 (0/15)	0

Stomach	0 (0/24)	4.17 (1/24)	-4.17

The differences in the numbers (n/N) for modality (MO vs GT, Tables 6 and 8 above) in the two clinical studies are due to differences in the number of diagnostic deferrals by a study pathologist in the digital modality (MD), which, per protocol, required the corresponding glass (MO) comparisons to be excluded from the major discordance analysis. As a result, the total number of evaluable MO-GT comparisons varied between the Leica and Hamamatsu studies (758 in Table 6 and 762 in Table 8). Similarly, these diagnostic deferrals by one study pathologist for each of the two studies affected the total N of comparisons being analyzed per organ (Tables 7 and 9 above).

b. Bench Testing for the Leica GT 450 DX Scanner DICOM file format:

To validate the Leica GT 450 DX scanner's DICOM file format, a pixel-wise comparison study was performed using the Leica GT 450 DX scanner's SVS file output, which was validated by a clinical study (see Section VII-B-a), as the comparator by comparing the 2 file formats, i.e., SVS and DICOM from the Leica Aperio GT 450 DX scanner. The DICOM/AISight Dx/Chrome browser configuration was compared to the SVS/AISight Dx/Chrome browser configuration. A total of 30 glass slides were scanned with a validated Leica GT 450 DX scanner to generate 30 SVS files and 30 DICOM files. Three regions of interest (ROI) from each slide were identified by a qualified pathologist. For each ROI, the screenshots were captured at two magnification levels (10x and 40x) and saved as PNG files. For each image-pair, the pixelwise differences between two images were calculated using the CIEDE2000 color difference metric. The OpenCV library cv2 was used to calculate the CIEDE2000 color difference between two pixels. The Python library scikit was used to calculate the 95th-percentile of the CIEDE2000 values for each image-pair. Two images were considered to be identical if the 95th percentile of the pixelwise color differences is less than 3 CIEDE2000. The test results are shown in Table 10.

Table 10: Pixelwise Testing Results

Scanner	Subject File format	Comparator File Format	Viewer/Browser	Results (95th percentile CIEDE2000)
Leica Aperio GT450DX	SVS	DICOM	AISight/Chrome	Maximum: 0 Mean: 0

c. Turnaround Time Testing

The purpose of this test was to demonstrate that the turnaround time for rendering of images is acceptable. Turnaround times for image processing, image loading, panning, and zooming were tested using Google Chrome and Microsoft Edge web browsers using WSIs over a range of sizes. Test results showed these to be adequate for the intended use of the subject device.

Table 11. AISight Dx Turnaround Time Testing Results

Scanner	File Format	Subject Device/ Browser	Turnaround Time Results (Mean value for median file size

			(~1.5 GB) in seconds)
Leica Aperio GT 450 DX scanner	SVS	AISight Dx/ Edge	WSI Loading: 4.99 WSI zooming: 1.08 WSI panning: 0.93
		AISight Dx/ Chrome	WSI Loading: 5.04 WSI zooming: 1.05 WSI panning: 0.98
	DICOM	AISight Dx/ Edge	WSI Loading: 4.89 WSI zooming: 1.00 WSI panning: 1.00
		AISight Dx/ Chrome	WSI Loading: 4.97 WSI zooming: 1.01 WSI panning: 0.97
Hamamatsu NanoZoomer S360MD Slide scanner	NDPI	AISight Dx/ Edge	WSI Loading: 3.80 WSI zooming: 1.03 WSI panning: 0.97
		AISight Dx/ Chrome	WSI Loading: 3.62 WSI zooming: 0.98 WSI panning: 1.04

d. Measurement (area and distance) Testing

A linear and area measurement verification study was conducted to assess the measurement accuracy of AISight Dx. Measurement accuracy was verified using a NIST-calibrated test image containing objects with known sizes scanned on the Hamamatsu Nanozoomer S360MD. Additional functional testing was performed on a DICOM-formatted H&E tissue slide scanned with the Aperio GT450 DX to confirm that users can create, edit, and delete linear and area measurements at multiple magnifications. The tool functioned as expected.
The measurement tool accuracy verification results are provided in the table below:

Table 12. Measurement tool testing results

Description	Sample Size	Acceptance Criteria	Results
Straight Line Measurement Chromium-engine	1 NIST traceable Calibration Slide	< 0.01% difference in distance measurement	All measurements compared to the

based browsers (Chrome and Edge)		generated against reference screenshot	reference were exact match with no error
Area Measurement (polygon, rectangle, ellipse, circular and square fields) Chromium-engine based browsers (Chrome and Edge)	1 NIST traceable Calibration Slide	< 0.01% difference in area measurement generated against reference screenshot	All measurements compared to the reference were exact match with no error
Scale Bar Measurement Chromium-engine based browsers (Chrome and Edge)	1 NIST traceable Calibration Slide	< 0.01% difference in distance measurement generated against reference screenshot	All measurements compared to the reference were exact match with no error
Slide Stage Area Measurement Chromium-engine based browsers (Chrome and Edge)	1 NIST traceable Calibration Slide	< 0.01% difference in distance measurement generated against reference screenshot	All measurements compared to the reference were exact match with no error

e. Human Factors (Usability) Testing

Human Factors (HF) validation test was conducted to demonstrate that the AISight Dx Viewer can be used by pathologists under the expected use conditions. A systematic evaluation of task-based usability including critical tasks required for operation of the device were evaluated via a Use-Related Risk Analysis (URRA). The HF validation test was performed by representative users (board-certified pathologists) and conducted per FDA's Guidance on Applying Human Factors and Usability Engineering to Medical Devices (2016). Validation results confirmed that critical tasks were performed accurately and without any use-related errors that could result in patient harm or diagnostic inaccuracies.

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.