



510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION DECISION SUMMARY

I Background Information:

A 510(k) Number

K252762

B Applicant

Indica Labs, LLC

C Proprietary and Established Names

HALO AP Dx

D Regulatory Information

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

II Submission/Device Overview:

A Purpose for Submission:

New device

B Type of Test:

Software only device

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

HALO AP Dx is a software only device intended as an aid to the pathologist to review, interpret and manage digital images of scanned surgical pathology slides prepared from formalin-fixed paraffin embedded (FFPE) tissue for the purposes of pathology primary diagnosis. HALO AP 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 quality of the images obtained and, where necessary, use conventional light microscopy review when making a diagnostic decision. HALO AP Dx is intended for use with the interoperable components specified in the Table below.

Table: Interoperable Components of HALO AP Dx

Scanner Hardware	Scanner Output File Format	Interoperable Displays
Leica Aperio GT 450 DX scanner	SVS	Dell U3223QE Barco MDPC-8127
	DICOM	Dell U3223QE
Hamamatsu NanoZoomer S360MD Slide scanner	NDPI	Barco MDPC-8127

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

IV Device/System Characteristics:

A Device Description:

HALO AP Dx, version 2.4 (abbreviated as v2.4), is a browser-based software-only device intended to aid pathology professionals in viewing, manipulating, management, and interpretation of digital pathology whole slide images (WSI) of glass slides obtained from the Hamamatsu Photonics K.K. NanoZoomer S360MD scanner or the Leica Biosystems Imaging, Inc. Aperio GT 450 DX. HALO AP Dx is operated as follows:

1. Image acquisition is performed using the NanoZoomer S360MD scanner or the Aperio GT 450 DX scanner. The operator performs quality control of the digital slides per the instructions of the scanners and additional laboratory specifications to determine if re-scans are necessary.
2. Once image acquisition is complete, the unaltered image is saved in an external image storage location. HALO AP Dx ingests the image, and a copy of image metadata is stored in the subject device's database to improve viewing response times.
3. Depending upon a laboratory's workflow, the scanned images may first be reviewed by histotechnicians to confirm image quality and initiate any re-scans. After review, the histotechnician may modify the case status and make it available to the pathologist.
4. The reading pathologist selects a patient case from a selected worklist within HALO AP Dx whereby the subject device fetches the associated images from external image storage.
5. The reading pathologist uses the subject device to view the images and can perform the following actions, as needed:
 - a. Zoom and pan the image.
 - b. Measure distances and areas in the image.
 - c. Annotate images.

- d. View multiple images side by side in a synchronized fashion.
6. The above steps are repeated as necessary.

After viewing all images belonging to a particular case (patient), the pathologist will make a diagnosis which is documented in another system, such as a Laboratory Information System.

The system specifications for HALO AP Dx are provided in tables 1 – 3 below.

Table 1: Computer Environment / System for Use with HALO AP Dx

Component	Requirement
Operating System	Windows 11
Memory	16 GB or more
Processor	Intel Core i7 CPU
Supported Browsers	Google Chrome version 138 and above Microsoft Edge version 138 and above

Table 2: Server System Requirements

Server	Operating System	Memory	Processor
Component Server, Processing Node Server, File Monitor Server	Windows Server 2022 Only x64 (64 bit) operating systems are supported	16 GB or more	8 CPU cores or more
Traefik Reverse Proxy	Windows Server 2022 Ubuntu 22.04	2GB, per 150 concurrent users	2 CPU Cores, per 150 concurrent users
MySQL Server	Windows Server 2022 Ubuntu 22.04 Only x64 (64 bit) operating systems are supported	16 GB or more	4 CPU Cores or more

Table 3: Server Configurations

Component	Specifications
Network Connectivity	1 Gbps (10 Gbps recommended) LAN connection between services
Antivirus Software	The following antivirus software has been validated for use with Windows Server: <ul style="list-style-type: none"> - Microsoft Windows Defender - Trend Micro - Webroot

B Instrument Description Information:

1. Instrument Name:
HALO AP Dx
2. Specimen Identification:
HALO AP Dx uses digital pathology images obtained from the interoperable scanners of Hematoxylin and Eosin (H&E) stained glass slides. The reading pathologist selects a case (patient) from a worklist (within the device or external to the device) whereby the subject device fetches the associated images from the external image storage. The scanned images are identified based on the previously assigned specimen identifier.
3. Specimen Sampling and Handling:
Specimen sampling and handling are performed upstream and independent of the use of the subject device. Specimen sampling includes biopsy or resection specimens which are processed using histology techniques. The FFPE tissue section is H&E stained. Digital images are then obtained from these glass slides using the interoperable scanners.
4. Calibration:
Not applicable.
5. Quality Control:
The scanning technician should perform quality control of all glass slides following the instructions for the specific staining protocol. Upon scanning, quality control should be performed on all digital slide images following procedures defined by the scanner manufacturer prior to import into HALO AP Dx.

The pathologist should review all images to ensure that all expected slides have been imported by viewing the thumbnails and labels, and manually verifying the tissue specimen, tissue block, and staining information is present. Additional details of the quality control procedures are provided in the device User's Guide and the Implementation Guide.

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):

Device & Predicate Device(s):	<u>K241273</u>	<u>K232202</u>	<u>K233027</u>																											
Device Trade Name	HALO AP Dx	Aperio GT450X	NanoZoomer S360MD Slide scanner system																											
General Device Characteristic Similarities																														
Intended Use /Indications For Use	<p>HALO AP Dx is a software only device intended as an aid to the pathologist to review, interpret and manage digital images of scanned surgical pathology slides prepared from formalin-fixed paraffin embedded (FFPE) tissue for the purposes of pathology primary diagnosis. HALO AP Dx is not intended for use with frozen section, cytology, or non-FFPE hematopathology specimens.</p> <p>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. HALO AP Dx is intended for use with the interoperable components specified in the Table below.</p> <p>Table: Interoperable components of HALO AP Dx</p> <table><tr><th>Scanner Hardware</th><th>Scanner Output file format</th><th>Interoperable Displays</th></tr><tr><td rowspan="2">Leica Aperio GT 450 DX scanner</td><td>SVS</td><td>Dell U3223QE Barco MDPC-8127</td></tr><tr><td>DICOM</td><td>Dell U3223QE</td></tr><tr><td>Hamamatsu NanoZoomer S360MD Slide scanner</td><td>NDPI</td><td>Barco MDPC-8127</td></tr></table>	Scanner Hardware	Scanner Output file format	Interoperable Displays	Leica Aperio GT 450 DX scanner	SVS	Dell U3223QE Barco MDPC-8127	DICOM	Dell U3223QE	Hamamatsu NanoZoomer S360MD Slide scanner	NDPI	Barco MDPC-8127	<p>The Aperio GT 450 DX is an automated digital slide creation and viewing system. The Aperio GT450 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.</p> <p>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.</p> <p>Table 1: Interoperable components of Aperio GT 450 DX</p> <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 MDPC-8127 Dell UP3017 Dell U3023E Dell U3223QE</td></tr><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> <p>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</p>	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	<p>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 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</p>
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		appropriate procedures and safeguards to assure the validity of the interpretation of images obtained using the Aperio GT 450 DX.	
Principle of Operation	During review, the pathologist opens the WSI images acquired with the scanner from the network storage, performs further QC, and reviews and interprets the WSI images 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.	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 system’s embedded image processing software is responsible for image acquisition and the processing of individual tiles prior to image composition or stitching. Hamamatsu’s NZAcquireMD software organizes all WSI tiles into a single NDPi file, which is a proprietary file format. During the review, the pathologist opens the WSI on the NZViewMD software to render a diagnosis.
Specimen Type	Digitized surgical pathology slides prepared from FFPE tissue	Same	Same
Type of Software Application	Internet browser-based application	Same	PC-based installed application
Image Manipulation and Review Functions	Functions for continuous panning and zooming, annotations, distance/area measurements, track visited areas, and image adjustments.	Same	Functions for continuous panning and zooming, annotations, distance/area measurements, track visited areas, export images, discrete Z-axis displacement, and display of diagnostic status of images.
General Device Characteristic Differences			
Device Components	HALO AP Dx viewing software	WSI scanner (Aperio GT450 DX scanner), Image Management System (Aperio WebViewer DX image viewing software), Display	WSI scanner (NanoZoomer S360MD Slide scanner), Image Management System (NZViewMD), Display
Diagnostic Image File Format	Leica SVS and DICOM, Hamamatsu NDPi	Leica SVS and DICOM	Hamamatsu NDPi
End User’s Interface	HALO AP Dx	Aperio WebViewer DX for Leica SVS, Sectra Digital Pathology Module (3.3) for Leica SVS and DICOM	NZViewMD

VI Standards/Guidance Documents Referenced:

1. FDA Guidance “Technical Performance Assessment of Digital Pathology Whole Slide Imaging Devices”. April 20, 2016.
2. FDA Guidance “Applying Human Factors and Usability Engineering to Medical Devices”. February 3, 2016.
3. FDA Guidance “Content of Premarket Submissions for Device Software Functions”. June 14, 2023.
4. FDA Guidance “Cybersecurity in Medical Devices: Quality System Considerations and Content of Premarket Submissions”. September 27, 2023.
5. IEC 62304 Edition 1.1 2015-06: Medical device software - Software life cycle processes
6. ISO 14971 Third Edition 2019-12: Medical devices - Application of risk management to medical devices
7. IEC 62366-1 Edition 1.1 2020-06: Medical devices - Part 1: Application of usability engineering to medical devices
8. AAMI TIR45:2012: Guidance on the use of AGILE practices in the development of medical device software

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:

Technical performance testing was conducted with the subject device, HALO AP Dx as specified below.

1. **Bench Testing - Pixelwise comparison test**
HALO AP Dx supports multiple file formats, multiple browsers, and multiple displays, constituting various configurations to be tested. Pixel-wise comparison testing to demonstrate

identical image reproduction was conducted to compare WSIs reproduced by the subject device and the comparators as listed in Table 4 below. The subject device was compared to the predicate device's image review manipulation software (IRMS), as defined in FDA guidance document, "Technical Performance Assessment of Digital Pathology Whole Slide Imaging Devices" dated April 20, 2016) using the quantitative pixel-wise comparison method. The basis for the comparison was the CIEDE2000 color difference equation, ΔE_{00} . The devices were tested as operating with the intended components, including the scanner, specific file format, image management systems (subject device with the intended browsers, comparator [predicate device IRMS]) and displays, as specified in the Table 4 below.

For each of the 6 configurations in Table 4 below, the device was tested with multiple slides across multiple regions of interest (ROI) at multiple magnification levels, on multiple displays. A total of 30 H&E-stained, FFPE glass slides of normal and tumor tissues from various human anatomical organs were used in the testing. For each configuration, the glass slides were scanned on a corresponding intended scanner to obtain 30 WSIs. For each of the 30 WSIs, 3 ROIs from different locations were selected by qualified personnel to represent various features in the tissue samples. Each ROI was captured at 2 magnification levels (10x, 40x).

The screenshots were captured for each of the intended display while viewing with the subject device and predicate device IRMS. The screenshots were cropped and registered to be pixelwise comparable. The cropped image included most of the pixels in the image except for those in the viewer-specific user interface areas.

For each configuration and each intended display, two sets of images were collected: comparator (predicate device IRMS) and the subject device (HALO AP Dx with the intended browser). Each image set included 180 images that covered all combinations of 30 slides, 3 ROIs and 2 magnification levels. The testing data, including the overview images of the 30 glass slides with annotations of the ROIs, registration/cropping information, and captured images, were provided in the FDA specific format. The above procedure was repeated for each corresponding intended display.

The comparator (predicate device IRMS) image set was used as the reference to compare the subject device image set to determine whether all the 180 image-pairs were identical for each configuration and each intended display. Two images are considered identical if the 95th percentile of the pixelwise differences, computed using the International Commission on Illumination (CIE) color difference metric CIEDE2000 (ΔE_{00}), is less than 3 ΔE_{00} . Testing results showed that the pixelwise differences across all 180 image-pairs per configuration and per intended display were less than 3 ΔE_{00} . The maximum (max), minimum (min), and mean of the 95th percentile ΔE_{00} value were reported in Table 4. Testing results demonstrated that WSIs reproduced by HALO AP Dx are identical to images reproduced by the predicate devices.

Table 4. HALO AP Dx Pixelwise Comparison Testing Results

Scanner	Image File Format	Subject Device/ Browser	Comparator (Predicate device IRMS /Browser)	Display	Results
NanoZoomer S360MD Slide scanner	NDPI	HALO AP Dx/Chrome	NZViewMD	Barco MDPC-8127	max (95 th percentile ΔE_{00}) = 2.929 min (95 th percentile ΔE_{00}) = 0.703 mean (95 th percentile ΔE_{00}) = 1.466
		HALO AP Dx /Edge	NZViewMD		max (95 th percentile ΔE_{00}) = 2.939 min (95 th percentile ΔE_{00}) = 0.705 mean (95 th percentile ΔE_{00}) = 1.457
Aperio GT450DX scanner	SVS	HALO AP Dx /Chrome	Webviewer	Barco MDPC-8127	max (95 th percentile ΔE_{00}) = 2.69 min (95 th percentile ΔE_{00}) = 0.810 mean (95 th percentile ΔE_{00}) = 1.396
				DELL U3223QE	max (95 th percentile ΔE_{00}) = 2.417 min (95 th percentile ΔE_{00}) = 0.864 mean (95 th percentile ΔE_{00}) = 1.390
		HALO AP Dx /Edge	Webviewer	Barco MDPC-8127	max (95 th percentile ΔE_{00}) = 2.167 min (95 th percentile ΔE_{00}) = 0.807 mean (95 th percentile ΔE_{00}) = 1.385
				DELL U3223QE	max (95 th percentile ΔE_{00}) = 2.211 min (95 th percentile ΔE_{00}) = 0.869 mean (95 th percentile ΔE_{00}) = 1.384
	DICOM	HALO AP Dx /Chrome	Sectra UniView /Chrome	DELL U3223QE	max (95 th percentile ΔE_{00}) = 1.928 min (95 th percentile ΔE_{00}) = 0.689 mean (95 th percentile ΔE_{00}) = 1.411
		HALO AP Dx /Edge	Sectra UniView /Edge		max (95 th percentile ΔE_{00}) = 2.014 min (95 th percentile ΔE_{00}) = 0.880 mean (95 th percentile ΔE_{00}) = 1.406

2. Turnaround Time

The turnaround time for image opening, panning, and zooming were tested in the subject device when using all the supported browsers (Chrome, Edge) for each image format (NDPI, SVS, DICOM). The acceptance criteria were as follows:

- Average time to open cases shall not exceed 4 seconds.
- Average time to perform zoom operations and fully load all image tiles shall not exceed 3 seconds for the combined operations on any image in any browser.
- Average time to perform single Field of View (FOV) pan operations and fully load all image tiles shall not exceed 3 seconds.
- Average time to perform long-distance FOV pan operations and fully load all image tiles shall not exceed 3 seconds.
- Simulated use scaling up to 30 users viewing 200 images in a simulated pan/zoom routine should not produce median response times above 3 seconds over a time of 8 hours.

Test results for different scenarios met the test acceptance criteria and showed acceptable turnaround time for the intended use of the subject device.

3. Measurement – distance and area

The length and area measurement accuracy of the subject device was tested across multiple magnification levels. An image of a calibration scale slide with known object sizes was used to verify the measurement accuracy. A series of annotations were created to cover different orientations, different magnification levels and all the supported file formats (NDPI, SVS, DICOM) in all the intended browsers (Chrome, Edge). The differences between the actual and reported measurements were calculated for each annotation.

The acceptance criteria were as follows:

- The measurement comparisons shall match a distance within 0.005 mm or an area of 0.001mm².
- Resolution data is displayed correctly, and no distortion is presented in the image display.
- Annotation measurements will not be distorted at uneven magnification levels or when the user is zooming in and out on the slide image.

The average length measurement difference was less than 0.005mm, and the average area measurement difference was less than 0.001mm² when evaluated on scanned slides with objects of known sizes from the NanoZoomer S360MD scanning system and the Aperio GT 450 DX. The resolution data was displayed correctly with no distortion, and the annotation measurements were correct at uneven magnification levels and when zooming in and out. Test results showed that the subject device performed accurate measurements of length and area across multiple magnification settings with respect to its intended use.

4. Human Factor (Usability) Testing

Human factors study designed around critical user tasks and use scenarios performed by representative users were conducted for previously cleared HALO AP Dx, version 2.1, in K232833, per FDA's Guidance on Applying Human Factors and Usability Engineering to Medical Devices (2016). Human factors validation testing is not necessary as the user interface and workflow remain unchanged.

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.