510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
INSTRUMENT ONLY

I Background Information:

A 510(k) Number

K212361

B Applicant

PathAI, LLC

C Proprietary and Established Names

Novo

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:

Not applicable – software only device

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

Novo 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. Novo 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. Novo is intended for use with the Philips Ultra Fast Scanner and the Barco PP27QHD or Philips PS27QHDCR display.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

IV Device/System Characteristics:

A Device Description:

Novo is a web-based software-only device that is intended to aid pathology professionals in the viewing, interpretation, and management of digital whole slide images (WSIs) of scanned surgical pathology slides prepared from formalin-fixed paraffin embedded (FFPE) tissue using the Philips IntelliSite Pathology Solution (PIPS) Ultra Fast Scanner (UFS). Novo functionalities include image upload, image management, image conversion and viewing WSIs.

Novo is operated as follows:

1. The user prepares and scans slides and reviews the slide quality in accordance with the PIPS UFS indication for use (IFU) and any other laboratory specific procedures.
2. The user uploads WSIs to cloud storage using Novo and builds a patient accession using the patient's medical record number (MRN), date of birth (DOB) and accession ID to support linkage of one or more slides from a single procedure using patient identifiers in Novo.
3. Once slide image is acquired using PIPS UFS according to its IFU and becomes available in scanner database file systems, Novo will automatically initiate uploading the slide image (using Novo uploader) and corresponding metadata to persistent cloud storage. Integrity checks are performed at upload time when data is copied to storage. During review, the pathologist opens WSI images from storage [displayed as Deep Zoom Image (DZI) images] using Novo , performs further QC and reads WSI images of the slides to make a primary diagnosis. The workflow of a pathologist includes zooming and panning images.

After viewing all images belonging to a particular accession, the pathologist renders a diagnosis.

Novo operates with the following components:

Table 1: WSI Scanner and Displays

Manufacturer	Model
Philips Medical Systems Nederland B.V.	Ultra-Fast Scanner (UFS)
Barco N.V. Display	PP27QHD
Philips Display	PS27QHDCR

Table 2: Computer Environment/System Requirements

System	Details
Computer System	RAM: 4.0 GB Display Calibration tool: MediCal QAWeb Agent for Philips and Barco Displays
Display	Barco (PP27QHD) or Philips (PS27QHDCR) Pixel resolution: 2560w x 1440h Panel type: Color LCD Technology: IPS technology with a-Si Thin Film Transistor Physical size: 648.5 mm x 423 mm x 91.3 mm (with backlight disc)
Web Browser	Google Chrome 81.0 or later.
Network	Internet access Outbound traffic enabled to port 443 25 Mbps download and upload speed

C. Instrument Description Information:

1. Instrument Name:
   Not applicable – software only device

2. Specimen Identification:
   Novo uses digital pathology images obtained from the PIPS UFS of Hematoxylin and Eosin (H&E) stained glass slides. The reading pathologist selects a case (patient) from a worklist external to the subject 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 them obtained from these glass slides using the PIPS UFS.

4. Calibration:
   Not applicable

5. Quality Control:
   Before reading pathology images using the Novo device, the pathologist should ensure that all scanned slide images have been imported and for every case, view the thumbnails in the pathology image window to verify that each slide that should be in the case is present (manually verifying tissue block and staining information from LIS).

V Substantial Equivalence Information:

A Predicate Device Name(s):
Philips IntelliSite Pathology Solution (PIPS)

B Predicate 510(k) Number(s):
DEN160056

C Comparison with Predicate(s):

Device & Predicate Device(s):	K212361	DEN160056
Device Trade Name	Novo	Philips IntelliSite Pathology Solution (PIPS)
General Device Characteristic: Similarities		
Intended Use/ Indications For Use	Novo 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 pathology slides for primary diagnosis. Novo 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. Novo is intended for use with the Philips Ultra Fast Scanner	The Philips IntelliSite Pathology Solution (PIPS) is an automated digital slide creation, viewing, and management system. The PIPS 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 PIPS is not intended for use with frozen section, cytology, or non-FFPE hematopathology specimens. The PIPS comprises the Image Management System (IMS), the Ultra Fast Scanner (UFS) and Display. The PIPS 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

	and the Barco PP27QHD or Philips PS27QHDCR display.	PIPS.
Image File Format	Philips UFS iSyntax File converted to device specific image format	Philips UFS iSyntax File
Internet Browser Based	Google Chrome	Same
General Device Characteristic: Differences		
Image Manipulation Functions	Panning, zooming, notes	Panning, zooming, color manipulation function, annotations, and measurements (distance & area)
Device Components	Image viewing software	Ultra Fast Scanner (UFS), Image Management System (IMS), Display
Principle of Operation	After WSI images are successfully acquired by using PIPS UFS, the WSI images and are stored in the cloud. During review, the pathologist opens WSI images from storage (displayed as DZI images), performs further QC and reads WSI images of the slides to make a diagnosis.	After WSI images are successfully acquired by using PIPS UFS, the WSI images are stored in IMS Application Server & Storage software that is not provided as part of the PIPS but may be located in a central server room separate from the workstation with the IMS viewing software and Display. During review, the pathologist opens WSI images from IMS Server & Storage, perform further QC and reads WSI images of the slides to make a diagnosis.
Image Storage	Images are stored in the cloud	Images are stored in an end user provided image storage (PIPS IMS Application Server & Storage) attached to the local network

VI Standards/Guidance Documents Referenced:

1. ANSI AAMI ISO 14971:2019, Medical devices – Applications of risk management to medical devices
2. IEC 62304:2006/AMD 1:2015, Medical Device Software – Software Life Cycle Processes
3. IEC 62366-1:2015, Medical devices – Part 1: Application of usability engineering to medical devices
4. IEC 82304-1:2016, Health software – Part 1: General requirements for product safety

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 for Novo device was performed. The new device was compared to the image management software component of the predicate device. The following testing was performed:

a. Bench Testing – Pixel-wise comparison test

A pixel-wise comparison test was performed to compare images reproduced by Novo and PIPS IMS for the same iSyntax file to demonstrate identical image reproduction. Thirty H&E-stained FFPE glass slides from various organs and tissue types were used in this test. The slides were scanned with the PIPS UFS, and each slide image was read by a qualified pathologist to choose three regions of interest (ROIs) that included relevant, biologically representative anatomical features. Each ROI was selected with the relevant features placed at the center at magnification levels 20x and 40x. A total of 180 ROIs were made available for both PIPS IMS and Novo to display on the screen using the default settings.

Cypress, a JavaScript-based end-to-end testing framework, was used to capture the screenshots. The Cypress built-in screenshot functionality captured the image sized 1458 pixels by 897 pixels by specifying the HTML canvas element that was displayed. The captured screenshots were then aligned and converted to RGB pixel data using the python imaging library Pillow.

The RGB pixel data was bound to the sRGB color space and converted to the CIELAB color space. The color difference of each corresponding pixel-pair was calculated using the CIEDE2000 (ΔE_{00}) formula for further analysis.
For each ROI, the ΔE_{00} histogram was calculated as well as its cumulative distribution function, which allows for observation of many statistical results such as maximum ΔE_{00}, minimum ΔE_{00}, 99-percentile, 4-ΔE_{00}, area-over-the-curve, etc.

Test results show that the color differences (ΔE00) between Novo and PIPS/IMS are not zero. Test results are shown in Table 3 below.

Table 3: Pixel-Wise Comparison Test Results

Statistical Results	ΔE00 Value (n=180)
Minimum Mean	0.50
Maximum Mean	1.97
Average Mean	1.10
Minimum Median	0.46
Maximum Median	1.61
Average Median	0.93

Further, testing was conducted to compare Novo-generated images with JPEG-compressed PIPS/IMS-generated images. Test results show that the Novo-generated images are similar to PIPS/IMS-generated images that had been JPEG-compressed at quality 95.

Based on the findings from bench testing, an additional clinical study was performed to establish the safety and effectiveness of the device.

b. Clinical Study

A clinical study was conducted to demonstrate that viewing, reviewing, and diagnosing WSIs of H&E stained FFPE tissue slides using Novo [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.

This study included 264 cases which were representative of the breadth and range of organs, sample types and diagnosis including challenging diagnoses in histopathology. Study cases included one representative H&E slide per case. Slides were scanned using the FDA cleared Philips UFS at 40x magnification at one site and reviewed by the study pathologists at their individual sites using the Novo device and a Barco PP27QHD monitor, as specified by Phillips UFS and Novo IFU. Images were checked for image quality according to scanner instructions before upload to the platform.

Three (3) pathologists read all cases which were deidentified, using MD and MO with a washout of two (2) weeks in between the MD and MO. All 3 reading pathologists read the slides for all cases at their individual sites using both MD and MO. The reading pathologists were provided with 3 batches of slides. A case report form (CRF) was completed to document the reading pathologist's diagnosis for each batch, and each read (MD and MO). Reads from both modalities (MD or MO) were adjudicated by one independent pathologist who was not part of the study to determine agreement with the GT and to each other, using standardized pre-defined definitions of harm as follows: 1) concordant, 2) major discordant or 3) minor discordant.

The primary endpoint was to demonstrate that the proportion of major discordances between diagnosis based on MD and GT diagnosis is no worse than 0.04 above the proportion of major discordances between diagnosis based on MO and GT. The secondary endpoint was to show the observed proportion of concordances between diagnosis based on glass slides and WSI is at least 95%.

Of the 264 cases, one slide was not available for scanning due to breakage and was excluded from both primary and secondary analysis; a second slide was marked as "adjudication not available" and was excluded from primary analysis; a third slide was excluded from both analysis since the slide ID was not confirmed by one of the pathologists. Therefore, the primary analysis included 261 cases and the secondary analysis included 262 cases.

The differences in major discordance rates between MD and GT compared to MO and GT were -0.1% (95% CI, -2.05, 1.78) for all organs as shown in Table 4 below. The upper limit of the CI for the major discordance rate was 1.78%, which is less than the prespecified noninferiority threshold of 4%, therefore meeting the primary objective of the study.

Table 4: Clinical Study Results Based on Major Discordance Rates, all organs

Modality	(n/N)	Discordance Rate (%)	95% CI (%)
MO vs GT	(132/783)	16.9	(13.05, 20.79)
MD vs GT	(131/783)	16.7	(12.86, 20.64)
Difference		-0.1	(-2.05, 1.78)

Secondary analysis (Table 5 below) showed the observed proportion of concordances between diagnosis based on MO and MD was 95.7%, which surpasses the secondary objective of concordance between MO and MD of at least 95%.

Table 5: Concordance Rate Between MO and MD

Modality	(n/N)	Concordance Rate (%)	Bootstrap 95% CI
MO vs MD	(752/786)	95.7	(93.74, 97.35)

The major discordance rate between MO and MD by organ is shown in Table 6 below.

Table 6: Major Discordance Rates by Organ and Modality

Organ Type	Major discordance rate		
	Manual digital (MD) % (n/N)	Manual optical (MO) % (n/N)	Difference% (MD – MO)
Adrenal	0 (0/3)	0 (0/3)	0
Anus	6.06 (2/33)	9.09 (3/33)	-3.03
Bladder	45.83 (11/24)	45.83 (11/24)	0
Brain/Neuro	16.67 (1/6)	0 (0/6)	16.67
Breast	28.33 (34/120)	25.83 (34/120)	2.5
Colon	13.58 (11/81)	11.11 (9/81)	2.47
Esophagus/GE Junction	21.21 (7/33)	12.12 (4/33)	9.09
Gynecological/Ovary	20 (3/15)	20 (3/15)	0
Kidney/Neoplastic	0 (0/21)	0 (0/21)	0

Organ Type	Major discordance rate		
	Manual digital (MD) % (n/N)	Manual optical (MO) % (n/N)	Difference% (MD – MO)
Liver/BD	0 (0/6)	0 (0/6)	0
Lymph Node	0 (0/24)	4.17 (1/24)	-4.17
Oral Cavity	3.03 (1/33)	3.03 (1/33)	0
Pancreas	16.67 (2/12)	16.67 (2/12)	0
Prostate	19.81 (41/207)	22.22 (46/207)	-2.42
Respiratory	0 (0/36)	0 (0/36)	0
Salivary Gland	0 (0/6)	0 (0/6)	0
Skin	9.72 (7/72)	13.89 (10/72)	-4.17
Soft Tissue (Tumors)	20 (3/15)	20 (3/15)	0
Stomach	6.67 (1/15)	6.67 (1/15)	0
Thyroid	33.33 (7/21)	33.33 (7/21)	0

Overall, these results demonstrate that the PathAI Novo image viewer is safe and effective when used by pathologists for primary diagnoses purposes.

c. Turnaround Time for the image to be fully loaded while opening a slide for panning/zooming

Turnaround time (TAT) testing was performed for WSI file processing and DZI loading, panning, and zooming in the subject device. The subject device demonstrated acceptable turnaround time with respect to its intended use for opening the first image and panning and zooming within the image.

d. Human Factors testing

Human factors study designed around critical user tasks and use scenarios performed by representative users were conducted. A systematic evaluation of task-based usability including critical tasks required for operation of the device were evaluated at multiple sites using multiple users. All tasks associated with reviewing and reporting results for cases including confirmation that all slides belonging to specific cases are reviewed before reporting results, were included in the study. Overall, the results of the human factors testing are acceptable.

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.