510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

I Background Information:

A 510(k) Number

K230839

B Applicant

Proscia, Inc.

C Proprietary and Established Names

Concentriq 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:

Not applicable – software only device

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for the Use below.

B Indication(s) for Use:

For In Vitro Diagnostic Use

Concentriq® 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 these digital slide images for the purpose of primary diagnosis. Concentriq® 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 the validity of the interpretation of images using Concentriq Dx. Concentriq Dx is intended for use with the Hamamatsu NanoZoomer S360MD Slide scanner and JVC JD-C240BN01A monitor.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

IV Device/System Characteristics:

A Device Description:

Concentriq Dx 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 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.

Concentriq Dx is operated as follows:

1. After the WSI image is acquired using the Hamamatsu NanoZoomer S360MD Slide scanner accordance to the WSI scanner Instructional Manual and any additional standard laboratory procedures, the WSI from the local file system is ingested into Concentriq Dx at which point the Concentriq Dx workflow is initiated.
2. The reading pathologist selects a case from a worklist external to the subject device or from within the subject device, whereby the subject device fetches the associated images from the image storage.
3. The image quality and other image data is evaluated and deemed acceptable, prior to using a whole slide image for diagnosis.
4. The reading pathologist uses the subject device to view and interpret the images using the following actions:
    - Zoom and pan the image
    - Measure distances in the image
    - Annotate the image
    - View multiple images side by side
5. The above steps are repeated as required.

6. After viewing all images for a case, the pathologist will make a diagnosis. The diagnosis will be documented in another system, e.g., a Laboratory Information System (LIS).
7. Upon conclusion of using the system, the pathologist clicks "Sign Out" in the user menu.

Concentriq Dx is designed to be deployed to a customer-managed infrastructure and may be accessed on the user's workstation browser. Concentriq Dx operates with and is validated for use with the components specified the tables below:

Table 1: WSI Scanner and Display

Manufacturer	Model
Hamamatsu	NanoZoomer S360MD Slide scanner
JVC Display	JD-C240BN01A

Table 2: Computer Environment/System Requirements:

Workstation Component	Specifications
Processor	2 GHz processor or higher with at least 4 cores
Memory	8 GB or higher
Monitor	JVC JD-C240BN01A for use with Hamamatsu NanoZoomer S360MD Slide scanner
Network connectivity	100 Mbps. (1 Gbps LAN recommended) connection
Keyboard / Mouse / Trackpad	Windows 10 compatible Optional: 3Dconnexion SpaceMouse Pro, 3Dconnexion SpaceMouse Compact
Operating system	Windows 10
Supported browsers	Google Chrome 96 and above, Microsoft Edge 95 and above
Antivirus software	McAfee, Norton, or equivalent

B Instrument Description Information:

1. Instrument Name:

   Not applicable – software only device

2. Specimen Identification:

   Concentriq Dx uses digital images of Hematoxylin and Eosin (H&E) stained glass slides obtained from the NanoZoomer S360MD Slide scanner. The reading pathologist selects a case (patient) from a worklist whereby the subject device fetches the associated images from

the 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 NanoZoomer S360MD Slide scanner.

4. Calibration:

   Not applicable

5. Quality Control:

   Prior to using a whole slide image for diagnosis, the pathologist should ensure that all scanned slide images have been imported for every case and the images are of acceptable quality for diagnostic purposes. The pathologist reviews scanned images from all the slides associated with a case before rendering a diagnosis.

V Substantial Equivalence Information:

A Predicate Device Name(s):

NanoZoomer S360MD Slide scanner system

B Predicate 510(k) Number(s):

K213883

C Comparison with Predicate(s):

The following table summarizes the similarities and differences between the Concentriq Dx and the predicate device, NanoZoomer S360MD Slide scanner System.

Device & Predicate Device(s):	K230839	K213883
Device Trade Name	Proscia Concentriq® Dx	NanoZoomer System (NZViewMD)
General Device Characteristic: Similarities		
Intended Use/ Indications For Use	For In Vitro Diagnostic Use Concentriq® Dx is a software only device intended for viewing and management of digital images of scanned surgical pathology slides	NanoZoomer S360MD Slide scanner system ('NanoZoomer System") is an automated digital slide creation, viewing, and management system. The NanoZoomer System is intended for

Device & Predicate Device(s):	K230839	K213883
	prepared from formalin-fixed paraffin embedded (FFPE) tissue. It is an aid to the pathologist to review, interpret and manage these digital slide images for the purpose of primary diagnosis. Concentriq® 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 the validity of the interpretation of images using Concentriq Dx. Concentriq Dx is intended for use Hamamatsu NanoZoomer S360MD Slide scanner and JVC JD-C240BN01A monitor.	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 the NC Kenwood JD-C240BN01A display. 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.
Image File Format	Hamamatsu's NZAcquireMD software organizes all WSI tiles into a single .ndpi file, which is a proprietary file format.	Same (.ndpi)
Type of Software Application	Internet Browser based	Windows based
Image Manipulation Functions	Panning, zooming, image adjustments, annotations, and distance/area measurements	Same
User Interface	Concentriq Dx	NZViewMD
General Device Characteristic: Differences		
Device Components	Image Management Software	Scanner, Image Management Software, Display
Principle of Operation	After the WSI are acquired by using NanoZoomer S360MD Slide scanner, the WSI are stored	After WSI are acquired by using NanoZoomer S360MD Slide scanner, the WSI are automatically saved to the

Device & Predicate Device(s):	K230839	K213883
	in customer provided image storage. During image review, the pathologist opens the WSI (displayed as .ndpi images) from the image storage using Concentriq Dx; performs further QC and then reads the WSI to make a diagnosis.	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.

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. ANSI AAMI ISO 14971:2019, Medical devices – Applications of risk management to medical devices
4. IEC 62304:2006/AMD 1:2015, Medical Device Software – Software Life Cycle Processes
5. IEC 62366-1:2015, Medical devices – Part 1: Application of usability engineering to medical devices
6. IEC 82304-1:2016, Health software – Part 1: General requirements for product safety
7. CIE ISO 11664-6 First edition 2014-02-01 - Colorimetry - Part 6: CIEDE2000 colour-difference formula

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 Concentriq Dx. The subject device was compared to the image management software component of the predicate devices image review manipulation software (IRMS, as defined in FDA guidance document, "Guidance for Industry – 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.

a. Bench Testing – Pixel-wise comparison test

The objective of the study was to validate the performance of Concentriq® Dx in processing and rendering images produced by the Hamamatsu NanoZoomer S360MD Slide scanner system (NZ) in the native and proprietary NDPI format (Predicate Device). In addition, the Concentriq® Dx image fidelity and performance between the Concentriq Dx image viewer software (Test Device) and the Hamamatsu NZViewMD software image viewer were evaluated.

A total of 30 whole slide images of formalin-fixed paraffin-embedded (FFPE) tissue glass slides from a diverse set of human anatomic sites, including but not limited to Breast, Colon, Esophagus, Skin and Prostate were used in the analysis. These slides were scanned using the NanoZoomer 360MD scanner. For each of the 30 tissue slides, 6 ROIs were captured, including 3 at 20x and 3 at 40x magnification, for a total of 180 ROIs. Each ROI was captured under 3 viewer environments: the Predicate Device, the Test Device under Google Chrome, and the Test Device under Microsoft Edge. The image data of all the ROIs were provided for verification.

Test results were provided by computing the ΔE value between each pair of corresponding pixels using the CIEDE2000 color difference equation. Test results showed that the 95th percentile of the pixel-wise color difference in any image pair between the subject and predicate device was not less than 3 CIEDE2000 (i.e., < 3 ΔE00 was not achieved). Therefore, a clinical validation study was conducted to supplement the non-clinical performance test data to support the performance of the device.

b. Clinical Validation Study

A clinical study was conducted to demonstrate that viewing, reviewing and diagnosing WSIs of H&E stained FFPE tissue slides using the Concentriq Dx [manual digital read (MD)] is non-inferior to glass slide reads using optical (light) microscopy [manual optical read (MO)]. The primary endpoint of the study was the difference in major discordance rates between MD and MO when compared to the original sign-out pathologic diagnosis, defined as the ground truth (GT) diagnosis.

The study included 275 samples that represented the breadth and range of organs in routine

clinical practice which also including challenging sample types and diagnoses in histopathology. Study samples included one representative H&E slide per case. Of the 275 samples, the diagnosis for one slide was not available due to a missing data point and was excluded from all statistical analyses. Therefore, all analyses included 274 individual samples.

The glass slides were scanned using the FDA-cleared Hamamatsu NanoZoomer S360 MD Slide Scanner at 40x magnification at one site and reviewed by 3 study pathologists at their individual sites using the Concentriq Dx device and a JVC JD-C240BN01A monitor, as specified by the NanoZoomer instructions for use (IFU) and the Concentriq Dx IFU. Images were reviewed for image quality according to the NanoZoomer IFU prior to uploading to the Concentriq Dx platform.

Three pathologists read all deidentified glass slide samples using the MD and MO modalities with a washout of 2 weeks between each separate modality read. All 3 reading pathologists read the slides for all cases using both MD and MO. The reading pathologists were provided with 3 batches of slides and the batches were randomized for each modality read. 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 an independent pathologist who did not participate in any of the MD or MO reads to determine agreement with the GT and to each other to determine concordance, minor discordance or major discordance between the study diagnosis (by WSI and glass methods) and the GT. A major discordance was defined as a difference in diagnosis that would be associated with a clinically important difference in patient management. A minor discordance was defined as a difference in diagnosis that would not be associated with a clinically important difference in patient management.

The primary endpoint was the difference in major discordance rates between MD and MO diagnoses relative to GT diagnoses. The primary analysis evaluated the null hypothesis that the difference in major discordances rates between MD and MO is not less than 0.04 (4% of slides) using a one-sided noninferiority assessment. A secondary analysis was to evaluate the major discordance rate between the MO and MD diagnoses.

The difference in the major discordance rate between MD and GT compared to MO and GT were -0.1% (95% CI, -1.0, 0.4) for all cases across the 3 reading pathologists (N: 274*3=822) as shown in Table 4 below. The upper limit of the confidence interval (CI) for the difference in the major discordance rate was 0.4%, which is less than the prespecified noninferiority threshold of 4%; therefore, the clinical study met the primary study endpoint.

Table 3. Clinical Study Results Based on Major Discordance Rates

Modality	(n/N)	Discordance Rate (%)	95% CI (%)
MO vs GT	21/822	2.6	(0.2, 6.2)
MD vs GT	20/822	2.4	(0.2, 5.8)
Difference		-0.1	(-1.0, 0.4)

The major discordance rate between each modality (MO and MD) and the GT by organ is shown in Table 4 below.

Table 4. Major Discordance Rates Relative to GT by Organ Type

Organ Type	MO v GT Discordance Rate% (n/N)	MD v GT Discordance Rate% (n/N)	Difference (%)
Adrenal	0.0% (0/3)	0.0% (0/3)	0.0
Anus/Perianal	0.0% (0/33)	0.0% (0/33)	0.0
Bladder	0.0% (0/24)	0.0% (0/24)	0.0
Brain/Neuro	0.0% (0/6)	0.0% (0/6)	0.0
Breast	2.6% (3/117)	2.6% (3/117)	0.0
Colorectal	4.4% (4/90)	4.4% (4/90)	0.0
GE Junction	17.8% (8/45)	17.8% (8/45)	0.0
Gynecological	0.0% (0/15)	0.0% (0/15)	0.0
Kidney	4.8% (1/21)	4.8% (1/21)	0.0
Liver/Bile Duct	0.0% (0/6)	0.0% (0/6)	0.0
Lymph Node	0.0% (0/24)	0.0% (0/24)	0.0
Oral Cavity	0.0% (0/33)	0.0% (0/33)	0.0
Pancreas	0.0% (0/12)	0.0% (0/12)	0.0
Prostate	1.0% (2/210)	1.0% (2/210)	0.0
Respiratory	2.8% (1/36)	0.0% (0/36)	-2.8
Salivary Gland	0.0% (0/6)	0.0% (0/6)	0.0
Skin	1.1% (1/90)	1.1% (1/90)	0.0
Soft Tissue Tumors	0.0% (0/15)	0.0% (0/15)	0.0
Stomach	0.0% (0/15)	0.0% (0/15)	0.0
Thyroid	4.8% (1/21)	4.8% (1/21)	0.0

Table 5 below shows the observed proportion of major discordance between the diagnosis based on MO and MD was 0.9%.

Table 5. Major Discordance Rate Between MO and MD

Modality	(n/N)	Discordance Rate (%)	95% CI (%)
MO vs MD	7/822	0.9	(0.1, 1.8)

The cumulative data of the clinical study support the conclusion that Concentriq Dx is safe and effective when used by pathologists in rendering a primary diagnosis as compared to a glass slide assessment when used according to the device intended use.

c. Turnaround Time

Turnaround time was measured and recorded for the time to initially load an image and the time to load an image when panning and zooming while using Concentriq Dx to view WSI images acquired on the predicate devices. The results of each test scenario met the success criteria. The test execution demonstrated acceptable image load time during different scenarios anticipated during regular use of Concentriq Dx.

d. Measurements – area and distance

Measurement accuracy was demonstrated through a study comparing the measurements of markings made in the Concentriq viewer to those on a calibration slide with a grid of known dimensions. Study data showed that the distance and area measurements made in the Concentriq Dx viewer were consistent with the ground truth. These results demonstrated acceptable measurements accuracy with respect to its intended use.

e. Human Factors (Usability) Testing

A human factors summative study was conducted to assess the use-related safety and effectiveness of Concentriq Dx with representative users in a representative use environment to provide adequate evidence that the user interface design (including the device and labeling) supports safe and effective use.

The evaluation method was based on applicable content of the human factors process, human factors validation testing and risk management guidance as described in the 2016 Food and Drug Administration Guidance titled "Applying Human Factors and Usability Engineering to Medical Devices" and the Consensus Standard titled "AAMI HE75:2009 and IEC 62366-1:2015 Medical devices – Part 1: Application of Usability Engineering to Medical Devices".

The Concentriq Dx device has been found to be safe and effective for the intended users, uses and use environments.

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.