510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

I Background Information:

A 510(k) Number

K250414

B Applicant

Tribun Health

C Proprietary and Established Names

CaloPix

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:

For in Vitro Diagnostic (IVD) Use.

CaloPix is a software only device for viewing and management of digital images of scanned surgical pathology slides prepared from Formalin-Fixed Paraffin Embedded (FFPE) tissue. CaloPix is intended for in vitro diagnostic use as an aid to the pathologist to review, interpret and manage these digital slide images for the purpose of primary diagnosis. CaloPix 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 CaloPix.

CaloPix is intended to be used with the interoperable components specified in the below Table.

Scanner Hardware	Scanner Output file format	Interoperable Displays
Leica Aperio GT 450 DX scanner	SVS	Dell U3223QE
Hamamatsu NanoZoomer S360MD Slide scanner	NDPI	JVC Kenwood JD-C240BN01A

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

IV Device/System Characteristics:

A Device Description:

CaloPix, version 6.1.0 IVDUS, is a web-based software-only device that is intended to aid pathology professionals in viewing, interpreting and managing digital Whole Slide Images (WSI) of glass slides prepared from FFPE tissue specimens acquired from FDA cleared digital pathology scanners and viewed on FDA cleared displays as specified in the intended use Table above. The WSIs undergo intentional compression when visualized in CaloPix, as shown in Table below.

Scanner Hardware	Scanner Output file format	Compression Methods
Leica Aperio GT 450 DX scanner	SVS	Compressed to 94% of the source of SVS file, or JPEG Q = 94
Hamamatsu NanoZoomer S360MD Slide scanner	NDPI	Compressed to 100% of the source of NDPI file, or JPEG Q = 100.

CaloPix does not include any automated Image Analysis Applications that would constitute computer aided detection or diagnosis. CaloPix is for viewing digital images of scanned glass slides that would otherwise be appropriate for manual visualization by conventional light microscopy.

CaloPix is operated as follows:

1. After the WSI image is acquired using one of the intended scanners, in accordance with the WSI scanner Instructions for Use Manual and any additional standard laboratory procedures, the WSI becomes available in the scanner's file system. The WSI is then sent to end-user-provided image storage attached to the local network. (not part of the subject device).
2. The WSI is then ingested into the CaloPix database at which point the CaloPix workflow is initiated. Ingestion of the slides is performed through an integrated module that allows their automatic indexation based on patient data retrieved from the Laboratory Information Systems (LIS). After their ingestion, image files are stored in a CaloPix-specific file storage environment, that can be on premises or in the cloud. After ingestion, scanned WSIs can be organized in the CaloPix database consisting of folders (cases) containing patient identification data and other information from a LIS.
3. The reading pathologist selects a case from a worklist within CaloPix, whereby CaloPix fetches the associated images from the image storage.
4. The image quality and other image data must be manually evaluated in the viewer by the pathologist and deemed acceptable, prior to reviewing a WSI for diagnosis.
5. The reading pathologist uses CaloPix to view and interpret the images using the following functionalities:
    - Continuous zooming and panning
    - Measuring distances
    - Creating annotations during review using manual annotation tools and manual counting tools
    - Viewing and comparing multiple slide images simultaneously in multiple windows
    - Tracking of visited areas and annotations and digital bookmarks.
6. The above steps are repeated as required.
7. After viewing all images for a case, the pathologist will make a diagnosis. The diagnosis will be documented in another system, e.g., a LIS.
8. Upon conclusion of using the system, the pathologist clicks "Sign Out" in the user menu.

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

Table 1: Interoperable Components for Use with CaloPix

Manufacturer	Model
Hamamatsu Photonics K.K.	Scanner: NanoZoomer S360MD Slide scanner Display: JVC Kenwood JD-C240BN01A
Leica Biosystems Imaging, Inc.	Scanner: Aperio GT 450 DX scanner Display: Dell U3223QE

Table 2: Computer environment / System requirements

Environment	Component	Minimum Requirements
Hardware	Computer	PC computer
	Processor	Minimum: Intel® Core™ i5 / AMD Ryzen 5 Recommended: Intel® Core™ i7 / AMD Ryzen 7
	Graphics card	Nvidia GeForce RTX 2060 / AMD Radeon RX 480
	Memory	Minimum: 4GB / Recommended: 8GB
	Network connectivity	10 Mbit/s between the client and the server
	Keyboard / Mouse / Trackpad	Standards keyboard and mouse supported by Windows 10 and higher versions Optional: 3D SpaceMouse Wireless, 3D SpaceMouse Pro from 3D connection
Software	Operating system	Windows 10 or higher
	Supported browsers	Google Chrome (version 91 and above) Microsoft Edge (version 106 and above)

B Instrument Description Information:

1. Instrument Name:
   CaloPix

2. Specimen Identification:
   CaloPix uses digital images of Hematoxylin and Eosin (H&E) stained glass slides obtained from the NanoZoomer S360MD Slide scanner (K213883) or the Aperio GT 450 DX Scanner (K232202). The reading pathologist selects a case (patient folder) 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 such as patient identifiers, barcodes, etc. CaloPix includes an automatic import module that automatically associates digitized glass slides with the correct case (patient folder), using the assigned specimen identifier.

3. Specimen Sampling and Handling:
   Specimen sampling and handling are performed upstream and independent of the use of CaloPix. Specimen sampling includes surgical pathology specimens such as biopsy or resection specimens which are processed using standard histology techniques. The Formalin-Fixed Paraffin Embedded (FFPE) tissue sections are H&E stained and scanned using the NanoZoomer S360MD slide scanner (K213883) or the Aperio GT 450 DX scanner (K232202).

4. Calibration:
   Not applicable

5. Quality Control:
   The scanning technician should perform quality control of all glass slides and WSIs following the scanner Instructions for Use and other laboratory procedures. Prior to using a WSI 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, Aperio GT 450 DX

B Predicate 510(k) Number(s):
K213883, K232202

C Comparison with Predicate(s):

<table>
<tr><th>Device & Predicate Device(s):</th><th>K250414</th><th>K213883</th><th>K232202</th></tr>
<tr><td>Device Trade Name</td><td>CaloPix</td><td>NanoZoomer S360MD Slide scanner system</td><td>Aperio GT 450 DX</td></tr>
<tr><th colspan="4">General Device Characteristic Similarities</th></tr>
<tr><td>Intended Use/Indications For Use</td><td>For in Vitro Diagnostic (IVD) Use.

CaloPix is a software only device for viewing and management of digital images of scanned surgical pathology slides prepared from Formalin-Fixed Paraffin Embedded (FFPE) tissue.
CaloPix is intended for in vitro diagnostic use as an aid to the pathologist to review, interpret and manage these digital slide images for the purpose of primary diagnosis.
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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 CaloPix.

CaloPix is intended to be used with the interoperable components specified in the below Table.
<table>
<tr><th>Scanner Hardware</th><th>Scanner Output file format</th><th>Interoperable Displays</th></tr>
<tr><td>Leica Aperio GT 450 DX scanner</td><td>SVS</td><td>Dell U3223QE</td></tr>
<tr><td>Hamamatsu NanoZoomer</td><td>NDPI</td><td>JVC Kenwood</td></tr>
</table></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 the JVC 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.</td><td>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.

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 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>
The Aperio GT 450 DX is not intended for use with frozen section, cytology, or non-FFPE hematopathology</td></tr>
</table>

	S360MD Slide scanner | JD-C240BN01A		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.
Principle of Operation	After the WSIs are acquired by using the NanoZoomer S360MD Slide scanner or the Leica Aperio GT 450 DX scanner, the WSI are stored in customer provided image storage. During image review, the pathologist opens the WSI (in NDPI or SVS format, depending on the scanner used for digitization) from the image storage using CaloPix 6.1.0 IVDUS; performs further QC and then reads the WSI to make a diagnosis	The NanoZoomer System is a WSI system. The system's embedded image processing software is responsible for image acquisition and the processing of individual tiles prior to image composition or stitching. The NZAcquireMD software organizes all WSI tiles into a single NDPI file, which is a proprietary file format. WSI are automatically saved to the hard disk during scanning and may be viewed later by using the included viewing software. During the review, the pathologist opens WSI from the image storage attached to the 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 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.
Specimen Type	Digitized surgical pathology slides prepared from FFPE tissue	Same	Same
Image storage	Images are stored in the end-user- provided image storage attached to the local network or in the cloud.	Images are stored in the end-user-provided image storage attached to the local network	Images are stored in the end-user-provided image storage attached to the local network.
Type of Software Application	Internet browser-based application	PC-based installed application	Same
General Device Characteristic Differences			
Device Components	CaloPix image viewing software	WSI scanner (NanoZoomer S360MD Slide scanner), Image Management System (NZViewMD), Display	WSI scanner (Aperio GT450 DX scanner), Image Management System (Aperio WebViewer DX image viewing software), Display
Diagnostic Image File Formats	Hamamatsu NDPI. Leica SVS.	Hamamatsu NDPI.	Leica SVS and DICOM.
Image Manipulation Functions	Panning, zooming, image adjustments, annotations, distance/area measurements and manual counting.	Panning, zooming, image adjustments, annotations, distance/area measurements.	Panning, zooming, gamma functions, annotations, and measurements (distance).
End User's Interface	CaloPix	NZViewMD	Aperio WebViewer DX for Leica SVS, Sectra Digital Pathology Module (3.3) for Leica SVS and DICOM

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. ISO 14971 Third Edition 2019-12, 5-125, Medical devices – Applications of risk management to medical devices.
6. IEC 62304 Edition 1.1 2015-06 CONSOLIDATED VERSION, 13-79. Medical device software – Software life cycle processes.
7. IEC 62366-1 Edition 1.1 2020-06 CONSOLIDATED VERSION, 5-129, Application of usability engineering to medical devices.
8. IEC 82304-1 Edition 1.0 2016-10, 13-97, Health software - Part 1: General requirements for product safety.
9. ISO CIE 11664-6 Second edition 2022-08, 9-148, Colorimetry - Part 6: CIEDE2000 colour-difference formula
10. ISO 20417 First edition 2021-04 Corrected version 2021-12, 5-135, Medical devices - Information to be supplied by the manufacturer.
11. ISO 15223-1 Fourth edition 2021-07, 5-134, Medical devices - Symbols to be used with information to be supplied by the manufacturer - Part 1: General requirements.

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, CaloPix as specified below.

1. **Bench Testing - Pixelwise comparison test**
   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 3 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 and the comparator [predicate device IRMS]) and displays, as specified in the Table 3 below.

   For each of the configurations in Table 3 below, the device was tested with multiple slides across multiple regions of interest (ROI) at multiple magnification levels. A total of 30 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 (20x, 40x).

   Screenshots were captured for 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, two sets of images were collected: comparator (predicate device IRMS) and the subject device (CaloPix 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 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 3. Testing results demonstrated that WSIs reproduced by CaloPix are identical to images reproduced by the predicate devices.

Table 3: CaloPix Pixelwise Comparison Testing Results

Scanner	Image File Format	Subject Device /Browser	Comparator (Predicate device IRMS)	Display	Results
Hamamatsu NanoZoomer S360MD Slide scanner	NDPI	CaloPix /Chrome	NZViewMD	Display JVC Kenwood JD-C240BN01A	max (95th percentile ΔE_{00}) = 1.2452
					min (95th percentile ΔE_{00}) = 0.3661
					mean (95th percentile ΔE_{00}) = 0.6214
		CaloPix /Edge	NZViewMD		max (95th percentile ΔE_{00}) = 1.2452
					min (95th percentile ΔE_{00}) = 0.3661
					mean (95th percentile ΔE_{00}) = 0.6214
Leica Aperio GT450DX scanner	SVS	CaloPix /Chrome	Aperio WebViewer DX/Chrome	Display Dell U3223QE	max (95th percentile ΔE_{00}) = 2.0310
					min (95th percentile ΔE_{00}) = 0.4540
					mean (95th percentile ΔE_{00}) = 1.0303
		CaloPix /Edge	Aperio WebViewer DX/Edge		max (95th percentile ΔE_{00}) = 2.0310
					min (95th percentile ΔE_{00}) = 0.4540
					mean (95th percentile ΔE_{00}) = 1.0309

2. Turnaround Time

Turnaround times (TAT) for image loading, panning and zooming were tested with CaloPix when using all the supported browsers, as listed in table 4 below. A total of 20 biological glass slides, from a diverse set of human anatomic sites, were scanned using the intended scanners to generate 20 WSI in NDPI format and 20 WSI in SVS format. Below acceptance criteria was used:

- < 10 seconds to load and fully display an image in Field of View (FOV) across all images
- < 7 seconds to render the FOV while zooming and panning across all images

Test results for different scenarios met the test acceptance criteria and showed acceptable turnaround time for the intended use of the subject device, as shown in table 4 below.

Table 4: CaloPix Turnaround Time Testing Results

Scanner	Image File Format	Subject Device/Browser	Results (Seconds)		
			Loading and Display	Panning	Zooming
Leica Aperio GT 450 DX scanner	SVS	CaloPix/Chrome	Max = 2.0104 Min = 0.0323 Mean = 0.9439	Max = 0.6852 Min = 0.0042 Mean = 0.0029	Max = 6.0337 Min = 0.0029 Mean = 0.3437
		CaloPix/Edge	Max = 2.5425 Min = 0.4061 Mean = 1.0743	Max = 3.4777 Min = 0.0063 Mean = 0.0050	Max = 5.4922 Min = 0.0048 Mean = 0.1273
Hamamatsu NanoZoomer S360MD Slide scanner	NDPI	CaloPix/Chrome	Max = 0.2649 Min = 0.0444 Mean = 0.1106	Max = 0.4053 Min = 0.0025 Mean =0.0345	Max = 1.2409 Min = 0.0050 Mean = 0.1093
		CaloPix/Edge	Max = 0.2091 Min = 0.0234 Mean = 0.0820	Max = 3.4992 Min = 0.0054 Mean = 0.0529	Max = 3.3322 Min = 0.0068 Mean = 0.1675

3. **Measurement – length and area**
   Measurement accuracy testing was performed to demonstrate that CaloPix accurately represents length and area measurements across all the multiple magnification levels for each configuration as listed in below table 5. A total of 5 H&E-stained FFPE tissue glass slides from a diverse set of human anatomic sites were scanned using the intended scanners. All the supported browsers (Google Chrome, Microsoft Edge), 3 different magnifications, a minimum of 2 different orientations, and 2 types of measurements (length and area) were tested. Measurements accuracy was verified by comparing the measurements of markings made in CaloPix viewer to the measurements of markings made in NZViewMD viewer for the same Regions of Interest on slides. These measurement checks were also carried out between the CaloPix viewer and the Aperio WebViewer DX. Test results as listed in Table 5 show that the acceptance criteria which were pre-specified as the percentage error between measurements taken in CaloPix and in NZViewMD viewer or WebViewer DX viewer must be less than 1% were met. The subject device performed accurate measurements of length across multiple magnification settings with respect to its intended use.

Table 5: CaloPix Measurement Results

Scanner	Image File Format	Subject Device/Browser	Percentage Error (%)	
			Length Measurement	Area Measurement
Hamamatsu NanoZoomer S360MD Slide scanner	NDPI	CaloPix/Chrome	≤ 0.90	≤ 0.99
		CaloPix/Edge	≤ 0.94	≤ 0.91
Leica Aperio GT 450 DX scanner	SVS	CaloPix/Chrome	≤ 0.73	≤ 0.94
		CaloPix/Edge	≤ 0.73	≤ 0.81

4. **Human Factor (Usability) Testing**
   The usability test was conducted per FDA guidance "Applying Human Factors and Usability Engineering to Medical Devices (2016)". A summative human factors test, designed around critical user tasks and use scenarios using multiple representative users (pathologists), was conducted. 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. The CaloPix 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.