510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

I Background Information:

A 510(k) Number

K260964

B Applicant

Hamamatsu Photonics K.K.

C Proprietary and Established Names

NanoZoomer S540MD Slide scanner system

D Regulatory Information

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

II Submission/Device Overview:

A Purpose for Submission:

i. New device-NanoZoomer S540MD Slide scanner system

ii. Establish a Pre-Determined Change Control Plan (PCCP; version 01) for qualifying and adding additional FDA-cleared displays as interoperable components to the NanoZoomer S540MD.

B Type of Test:

Digital pathology whole slide imaging

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The NanoZoomer S540MD Slide scanner system ("NanoZoomer System") is an automated digital slide creation, viewing, and management system. 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. 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.

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.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

IV Device/System Characteristics:

A. Device Description:

The NanoZoomer S540MD Slide scanner system (C17400-01MD) is an automated system for creating diagnostic-quality digital images of glass slides containing FFPE tissue. Slide images may be viewed, stored, retrieved, duplicated, annotated, and/or shared, permitting the pathologist to make a primary diagnosis based on the review of the whole-slide images (WSIs).

The S540MD System includes the following subsystems:

1. The NanoZoomer S540MD Slide scanner creates digital WSIs of conventional histological glass slides containing surgical tissue samples. It can be loaded with 360 (20 slides/cassette) or 540 (30 slides/cassette) glass slides.
2. The S540MD Slide scanner includes hardware and firmware. There are no differences in firmware for the slide feeder compared to the S360MD as the S540MD except for the capacity of slides. Scanner control is the same for all other processes, including the imaging process and XYZ stage control. The S540MD Slide scanner has a touchscreen interface instead of the control panel in the S360MD.
3. Identical to the software used with the NanoZoomer S360MD Slide scanner system cleared in K213883, K233027 and K253606, it directs the scanner to create and store WSI images and allows the user to view, manipulate, and annotate them on the display monitor.
    - o NZAcquireMD allows the user to operate the scanner and to store and archive digital images. NZAcquireMD is software that scans pathology slides by controlling the hardware and firmware components required to acquire pathology images according to the specifications and procedures set by the user through the user interface.

o NZViewMD allows the user to view, manipulate, and annotate the image on the monitor.

4. The display monitors, a JVC Kenwood JD-C240 (K213883), Barco MDPC-8127 (K203364), or a 510(k)-cleared display that has been assessed in accordance with the PCCP for qualifying additional compatible displays. The display monitor allows the slide images to be viewed.

Principles of Operation

Glass slides are first transferred to a macro stage, where a whole-slide image is captured containing both the specimen and the barcode information present on each slide. The NZAcquireMD software uses the macro image to determine which areas of the slide need to be scanned in greater detail. Glass slides are then moved to a micro stage, where the S540MD slide scanner uses its motorized stage, 20x objective lens, CMOS camera, and LED light source to detect appropriate focusing points and scan the identified areas of interest in fine detail to create a high-resolution digital slide image. Images are automatically saved to the hard drive during scanning by using the included viewing software.

The S540MD System can be connected to a server and a display monitor over a customer-provided local area network ("LAN"). The data flow over the LAN connection is only meant for transferring, storing, or displaying images. The S540MD System does not use wireless communication in any form or any cloud communication.

B. Instrument Description Information:

a. Instrument Name:
NanoZoomer S540MD Slide scanner system

b. 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 formalin-fixed paraffin embedded (FFPE) tissue.

c. 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 Hematoxylin and Eosin (H&E) stained. Then digital images are obtained from these glass slides using the NanoZoomer S540MD Slide scanner.

d. Calibration:
When the system is launched (powered up), automatic system diagnosis is performed by the software using the provided calibration slides. This process evaluates the proper functioning of the light source, imaging sensor, and macro sensor and light source. When necessary, based on the automatic system diagnosis, adjustment of the shading correction and color

balance correction features are performed automatically by the system. Monthly cleaning such as dusting of the scan mechanism and optical components is also performed by the user. System administrators and field service personnel may also complete a system check following the NZAcquireMD Instructions for Use and the NZTuneMD service software and the calibration slides. This checks correction status and acquires correction data for whole slide and scanned images. Additional calibration and quality control procedures are performed during field service visits following procedures provided in the NanoZoomer S540MD Maintenance Manual. These include annual testing of several critical components in the system and annual calibration of the components and the display.

e. Quality Control:
Quality control (QC) activities are performed by the user. Prior to scanning slides using the NanoZoomer S540MD Slide scanner system, the user conducts QC of the slides per the laboratory's standards and professional guidelines (e.g., staining, cover-slipping, and barcode placement, etc.). After completing a scan, the user checks the image data and image quality using Quality Check mode in NZAcquireMD which includes the following steps:

- Display the Scan Result screen by selecting a slide for which scanning has been completed.
- Confirm scan area, focus quality, and barcode information. Confirm that the barcode information displayed above the slide image is consistent with the barcode label.
- Check the slide image to ensure all tissue on the slide are present within the scan area. Manually verifying tissue block with the scanned images is also performed as needed. Slides are rescanned if necessary.
  Before reading the scanned WSIs, 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:
NanoZoomer S360MD Slide scanner system

B. Predicate 510(k) Number:
K233027

C. Comparison with Predicate(s):
The subject device is similar to the predicate, having similar indications for use, intended use, technological characteristics as its predicate device, along with the implementation of a Predetermined Change Control Plan (PCCP) that specifies the protocols and acceptance criteria for validating and adding additional FDA-cleared displays as interoperable component to the NanoZoomer S540MD Slide scanner systems in a controlled manner, such that the device is as safe and as effective as the predicate.

The sponsor's PCCP for validating the use of additional FDA-cleared display is part of the Hamamatsu quality management system and comprises the following phases:

1. When a new FDA-cleared display is identified as the candidate, the candidate display, and its supplier will be evaluated based on various considerations. A design change request will be generated if the candidate display and its supplier pass the evaluation.
2. The candidate display will be tested with a set of FDA-approved test methods and acceptance criteria, including system-level tests for the complete WSI system specified in the PCCP. The tests will be conducted by a qualified tester according to the quality management system. If there is a failure detected during the test, the failure(s) will be recorded, and the design change will not be implemented.
3. If the candidate display meets the acceptance 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 NanoZoomer S540MD Slide scanner system without additional premarket review.
4. Any display-specific software will be verified by Hamamatsu to confirm it does not impact performance of the NanoZoomer S540MD Slide scanner systems.
5. The system labeling and company website will be revised to identify the new display according to the quality management system.

The similarities and differences between the subject and predicate devices are summarized in Table below.

Comparison with Predicate

Device & Predicate Device(s)	**S540MD System Subject Device**	**S360MD System Predicate Device (K233027)**
Device Trade Name	NanoZoomer S540MD Slide scanner system	NanoZoomer S360MD Slide scanner system
General Device Characteristic: Similarities		
Intended Use/ Indications for Use	The NanoZoomer S540MD Slide scanner system (“NanoZoomer System”) is an automated digital slide creation, viewing, and management system. 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. 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 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

	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.	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.
Intended Use	Intended for use in primary surgical pathology diagnosis in lieu of optical microscopy	Same
Viewer	NZViewMD	Same
Display	JVC Kenwood JD-C24BN01A BARCO MDPC-8127 Display, or FDA-cleared display validated per the PCCP to ensure performance requirements are met prior to modifications being implemented.	Same
Image File Formats	NDPi file format	Same
General Device Characteristic: Differences		
Slide Feeder	540 slides (18 cassettes; each holds up to 30 standard-sized slides) 360 slides (18 cassettes; each holds up to 20 standard-sized slides)	360 slides (12 cassettes; each holds up to 30 standard-sized slides)
User Interface	Keyboard and mouse allow the user to see the status of scanning and provide input to the scanning operation. In addition, the touch screen allows users to operate and monitor key scanning functions without accessing the operating software, including: • Start/Stop Scanning and Remove Racks • Set Scan Priority for Racks • Display Scan Status	Keyboard and mouse allow the user to see the status of scanning and provide input to the scanning operation.
Light Source	LED CCT:6500K CITIZEN CLU038-1210C4-653M2M2-F1	LED CCT:6500K CITIZEN CLU038-1210C4-653M2K1 This same LED is used in the modified S360MD System cleared in K253606.
Remote Service of Scanner	Remote maintenance may be performed using the customer's virtual private network (VPN) and Window's Remote Desktop Protocol (RDP) or using Teamviewer, Microsoft Teams, or WebEx software installed on the NanoZoomer S540MD Control PC.	Remote maintenance may only be performed using the customer's virtual private network ("VPN") and Window's Remote Desktop Protocol ("RDP"). No additional software should be installed on the computer targeted for remote maintenance.

		Remote maintenance is performed in the modified S360MD System cleared in K253606

VI Standards/Guidance Documents Referenced:

- FDA Guidance: Technical Performance Assessment of Digital Pathology Whole Slide Imaging Devices. Guidance for Industry and Food and Drug Administration Staff. April 20, 2016
- FDA Guidance: Cybersecurity in Medical Devices: Quality System Considerations and Content of Premarket Submissions Guidance for Industry and Food and Drug Administration Staff. February 2026
- FDA Guidance: Content of Premarket Submissions for Device Software Functions. Guidance for Industry and Food and Drug Administration Staff Document. June 14, 2023
- IEC 61010-1:2010 + AMD1:2016 Safety requirements for electrical equipment for measurement, control, and laboratory use – Part 1: General requirements
- IEC 61010-2-101:2018 Safety requirements for electrical equipment for measurement, control and laboratory use – Part 2-101: Particular requirements for in vitro diagnostic (IVD) medical equipment
- IEC 61326-2-6:2020 – Electrical equipment for measurement, control and laboratory use – EMC requirements – Part 2-6: Particular requirements – In vitro diagnostic (IVD) medical equipment
- IEC 61326-1:2020 – Electrical equipment for measurement, control and laboratory use – EMC requirements – Part 1: General requirements

VII Performance Characteristics:

A. Analytical Performance:

1. Precision/Reproducibility: Not applicable
   The precision study was previously conducted for the predicate device (K213883) per the Special Control in 21 CFR 864.3700(b)(1)(iv)(A) and 864.3700(b)(1)(iv) (B). A new precision study was not conducted for the current device because a pixel-wise comparison study demonstrated equivalent image quality between the S540MD and S360MD Slide scanner systems.

2. Linearity:
   Not applicable

3. Analytical Specificity/Interference:
   Not applicable

4. Assay Reportable Range:
   Not applicable

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):
   Not applicable

6. Detection Limit:
   Not applicable

7. Assay Cut Off:
   Not applicable

8. Accuracy (Instrument):
   Not applicable

9. Carry-Over:
   Not applicable

B. Technical Performance Assessment:

The following component-level technical performance assessment tests were provided:

1. **Light Source:** Specifications and performance characterization of the LED light source were provided, including bulb type, spectral power distribution, output adjustment control, intensity and spectral variation over a single slide, a single workday, and the expected device lifetime.

2. **Imaging Optics:** Specifications and performance characterization of the imaging optics were provided, including the optical schematic, magnification, relative irradiance uniformity, optical distortion, and chromatic aberrations (lateral and longitudinal).

3. **Mechanical Scanner Movement:** Specifications and performance characterization of the X-Y stage and Z stage were provided, including stage configuration, materials, method of movement, resolution, speed, travel distance, control method, and positional accuracy and repeatability.

4. **Digital Image Sensor:** Specifications and performance characterization of the digital image sensor were provided, including sensor type, pixel information, linearity, spatial uniformity, noise, dark current, electron conversion factor, and digital readout rate and output format.

5. **Image Processing Software:** Design of the embedded image processing software was provided, including pixel offset correction, white balance and shading correction, color correction, distortion correction, tile cutout and image blending, and exposure control.

6. **Image file format:** Specifications of the NDPi proprietary file format were provided, including header, tags, file organization, compression method, compression type, and compression ratio.

7. **Image Composition:** Specifications of the image composition process were provided, including the scanning pattern, tile merging algorithm, automatic background correction, scanning speed, Z-stack depth, and focus quality metric.

8. **Image Review Manipulation Software:** Specifications of the NZViewMD viewer software were provided, including continuous panning and zooming, discrete Z-axis navigation (Z-stack), simultaneous display and synchronization of multiple images, annotation tools and digital bookmarks, image enhancement and color manipulation, and tracking of visited areas and annotations.

9. **Computer environment:** Specifications of the Control PC and Viewer PC were provided, including the operating system, CPU, memory, storage, graphics card, display interface, and network connectivity.

The following system-level technical performance assessment tests were performed with the S540MD System**:**

1. **Color Reproducibility:** Test data to quantify the accuracy and precision of the end-to-end color transformation from the slide to display monitors, Barco MDPC-8127 and JVC JD-C240BN01A, were provided. The mean CIEDE2000 values for each of the three enrolled S540MDs were below the pre-defined maximum acceptable value and all three passed the test.

2. **Spatial Resolution:** Test data based on ISO 12233:2014 to evaluate the spatial resolution, including the composite optical performance of all components during the image acquisition phase, was provided using a Hamamatsu model Z7034-01F01 chrome-on-glass slide. All three enrolled S540MDs passed the pre-defined acceptance criterion.

The similarities in the design were evaluated based on FDA's guidance Technical Performance Assessment of Digital Pathology Whole Slide Imaging Devices ("TPA Guidance") and 21 C.F.R. § 864.3700(b)(1)(iii). The following system-level technical performance assessments submitted for the S360MD System in K213883 are utilized for the S540MD System:

- Display (K213883 and K233027)
- Focusing Test
- Whole Slide Tissue Coverage
- Stitching Error Test
- Turnaround Time

<u>NanoZoomer S540MD Slide Scanner System Pixel-Wise Comparison Study:</u>

A pixel-wise comparison (PWC) study was conducted to evaluate the difference in image quality between NanoZoomer S540MD and S360MD Slide scanner systems. Most of the components in the imaging pipelines of the predicate and subject devices are identical. Therefore, a PWC study was conducted in lieu of a clinical study to assess the image quality equivalency between the devices. The test data was to demonstrate that the difference between subject and predicate device instances, i.e., systems with the same model numbers but different serial numbers, is equal to or less than that among FDA-cleared predicate device instances. For each comparison, two scanned images of the same glass slide—generated by two different device instances—were compared at the pixel level using the standard CIEDE2000 color difference metric (ΔE). Each

comparison yielded a distribution of ΔE values, and the Wasserstein-1 metric was used to quantify the distance between two dE distributions, where a smaller distance indicates greater agreement between the distributions. The acceptance criterion, i.e., image quality equivalence between the subject scanner units and predicate scanner units, was met if the minimum Wasserstein-1 distance to a predicate unit was lower than the maximum Wasserstein-1 distance observed among predicate-unit (S360MD) comparisons.
The study was conducted with three S540MD units and three S360MD units using 13 clinical glass slides. Study results showed that all S540MD units met the predefined acceptance criterion.

C. Clinical Studies
No clinical studies were required to demonstrate substantial equivalence of the NanoZoomer S540MD Slide scanner system since PWC studies demonstrated image quality equivalency between the devices.

VIII Pre-determined Change Control Plan (PCCP)
Hamamatsu provided PCCP (version 01) is similar to PCCP cleared in K233027 and will be followed to validate compatibility of additional FDA-cleared displays with the NanoZoomer S540MD Slide scanner system, including specific performance requirements that must be met prior to updating the device labeling to reference the newly added displays. The PCCP also includes verification that any display-specific software will not impact performance of the NanoZoomer S540MD software. With inclusion of the PCCP, future changes to add additional FDA-cleared displays to the labeling can be made in accordance with the PCCP without a premarket submission. The Hamamatsu website will provide information on additional displays that are compatible with the NanoZoomer S540MD Slide scanner systems and allow users to request updated versions of the system labeling.

IX Proposed Labeling:
The labeling supports the finding of substantial equivalence for NanoZoomer S540MD Slide scanner system.

X Conclusion:
The submitted information on the NanoZoomer S540MD Slide scanner system and S360MD Slide scanner system in this premarket notification is complete and supports a substantial equivalence decision to the predicate device cleared in K233027.