Hamamatsu Photonics K.K.
℅ Jeffrey Gibbs
Director
Hyman, Phelps & McNamara, P.C
700 Thirteenth Street NW, Suite 1200
Washington, D.C. 20005

September 27, 2022

Re: K213883
Trade/Device Name: NanoZoomer S360MD Slide scanner system
Regulation Number: 21 CFR 864.3700
Regulation Name: Whole slide imaging system
Regulatory Class: Class II
Product Code: PSY
Dated: December 9, 2021
Received: December 13, 2021

Dear Jeffrey Gibbs:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part

801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Shyam Kalavar
Branch Chief
Division of Molecular Genetics
and Pathology2
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K213883

Device Name
NanoZoomer S360MD Slide scanner system

Indications for Use *(Describe)*
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.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 79 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

510(k) Summary

In accordance with 21 C.F.R. § 807.92 the following summary of information is provided:

DATE: September 25, 2022

SUBMITTER:

Shinichi Fujisaka
812, Joko-cho, Higashi-ku
Hamamatsu City, Shizuoka Pref. Japan 431-3196
(81) 53-431-0155

PRIMARY CONTACT PERSON:

Jeffrey N. Gibbs, JD
Director
Hyman, Phelps, & McNamara, P.C.
T 202-737-4288

SECONDARY CONTACT PERSON:

Adrienne Lenz
Senior Medical Device Regulation Expert
Hyman, Phelps, & McNamara, P.C.
T 202-737-4292

DEVICE:

TRADE NAME: NanoZoomer S360MD Slide scanner system
COMMON/USUAL NAME: Whole Slide Imaging System
CLASSIFICATION NAME: Whole Slide Imaging System
REVIEW PANEL: 21 C.F.R. § 864.3700
PRODUCT CODE: PSY

PREDICATE DEVICE(S):

Philips IntelliSite Pathology Solution (PIPS) (DEN160056)

DEVICE DESCRIPTION:

The NanoZoomer S360MD Slide scanner system is an automated system for creating, viewing, and managing digital slides. The NanoZoomer S360MD Slide scanner system creates diagnostic-quality digital images of glass slides containing formalin-fixed paraffin-embedded ("FFPE") tissue. Each digital image covers an entire slide and typically contains billions of image pixels. Slide images may be viewed, stored, retrieved, duplicated, annotated, and/or shared, permitting the pathologist to make a primary diagnosis without needing to view the original glass slides through a light microscope.

The NanoZoomer S360MD Slide scanner system is comprised of the NanoZoomer S360MD Slide scanner, the NZViewMD Software and the JVC Kenwood JD-C240BN01A display.

INTENDED USE:

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.

TECHNOLOGY:

The proposed NanoZoomer System has similar indications for use to, and uses the same fundamental technology as, the legally marketed predicate device to which substantial equivalency is claimed, the Philips IntelliSite Pathology Solution ("PIPS") (DEN160056).

TABLE 1 COMPARISON OF SUBJECT AND PREDICATE DEVICES

Specification	NanoZoomer S360MD Slide scanner system	Philips IntelliSite Pathology Solution
Product Code	PSY	PSY
Regulation	21 C.F.R. § 864.3700	21 C.F.R. § 864.3700
Regulation Name	Whole Slide Imaging System	Whole Slide Imaging System
Classification	II	II
Intended Use	Intended for use in primary surgical pathology diagnosis in lieu of optical microscopy	Intended for use in primary surgical pathology diagnosis in lieu of optical microscopy
Indications for Use	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 he 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	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

Specification	NanoZoomer S360MD Slide scanner system	Philips IntelliSite Pathology Solution
	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.	safeguards to assure the validity of the interpretation of images obtained using PIPS.
Slide Feeder	360 slides	300 slides

DETERMINATION OF SUBSTANTIAL EQUIVALENCE:

SUMMARY OF NON-CLINICAL TESTS:

A number of verification and validation activities have been conducted for the NanoZoomer System. The product passed all verification and validation tests. Overall, the NanoZoomer System was found to be safe and effective for all intended users, uses, and use environments. Performance specifications of the NanoZoomer System are equivalent to the performance specifications of the PIPS. Any differences do not raise new or different questions of safety and effectiveness. These data demonstrate that the NanoZoomer System is at least as safe and effective as the predicate device.

Electrical safety testing was conducted in accordance with IEC61010-1 and IEC61010-2-101 with passing results. Electromagnetic compatibility testing was conducted in accordance with IEC 61326-2-6 for laboratory use of in vitro diagnostic equipment. The test results showed “pass” for emissions and immunity.

The evaluation of the level of concerns for the NanoZoomer software is a result of the risk analysis performed and the intended use of the NanoZoomer System. The level of concern was determined to be Moderate and the results of the risk management process do not show any unacceptable risk.

Human factors studies were designed around user tasks, and use scenarios performed by users were conducted. For all user groups, tasks were successfully completed.

Technical Studies:

Multiple studies were conducted to evaluate the performance of the NanoZoomer System as recommended in FDA's guidance, *Technical Performance Assessment of Digital Pathology Whole Slide Imaging Devices*.

a. *Slide Feeder*

   Information was provided on the configuration of the slide feed mechanism, including a physical description of the slide, the number of slides in queue (carrier), and the class of automation. Information was provided on the user interaction with the slide feeder, including hardware, software, feedback mechanisms, and Failure Mode and Effects Analysis (FMEA).

b. *Light Source*

   Descriptive information associated with the LED was provided. Testing information was provided to verify the intensity and spectral variation of the LED light incident on the slide over time.

c. *Imaging Optics*

   An Optical schematic with all optical elements identified from slide (object plane) to image sensor (micro camera) was provided. Descriptive information regarding the microscope objective and the magnification of imaging optics was provided. Testing information regarding the magnification, relative irradiance, optical distortions, and chromatics aberrations was provided.

d. *Mechanical Scanner Movement*

   Information and specifications on the configuration of the stage, method of movement, control of movement of the stage, and FMEA was provided. Test data to determine positioning accuracy and repeatability for the X-Y and Z stages was provided.

e. *Digital Imaging Sensor*

   Information and specifications on the sensor type, pixel information, responsivity specifications, noise specifications, readout rate, and digital output format were provided. Testing to measure and evaluate linearity, spatial uniformity, dark

current, noise, opto-electronic conversion function, and electron conversion factor of the sensor was provided.

f. Image Processing Software

Information and specifications on the exposure control, white balance, color correction, sub-sampling, pixel-offset correction, shading (flat-field) correction, and pixel-defect correction were provided. Testing confirmed that the pixel offset correction, shading and white balance, and color correction matrix functions work correctly.

g. Image Composition

Information and specifications on the scanning method and Z-stack depth, was provided. Test data to analyze the image composition performance was provided.

h. Image Files Format

Information and specifications on the compression method, compression ratio, file format, and file organization were provided. Testing demonstrated compression specifications were met.

i. Image Review Manipulation Software

Information and specifications for continuous panning, continuous zooming, discrete Z-axis displacement, comparison of slides in multiple windows, annotation tools, image enhancement, color manipulation (not for use in diagnostic procedures), tracking of visited areas and digital bookmarks was provided. Testing demonstrated the alignment precision of Z-stack images.

j. Computer Environment

Information and specifications on the computer hardware, operating system, memory, hard disk, graphics card, graphics card driver, color management settings, color profile, display interface and network were provided.

k. Display

Information and specifications on the technological characteristics of the display device, physical size of the viewable area and aspect ratio, backlight type and properties, frame rate and refresh rate, pixel array, pitch, pixel aperture ratio and subpixel matrix scheme, subpixel driving to improve grayscale resolution, supported color spaces, display interface, user controls of brightness, contrast, gamma, color space, power-saving options, etc., via the on-screen display menu,

color calibration tools, and frequency and nature of quality-control tests was provided. Test data to verify the performance of the display was provided.

l. Color Reproducibility

Test data to quantify the accuracy and precision of the color transformation from the slide to the display monitor was provided.

m. Spatial Resolution

Test data to evaluate the spatial resolution, including the composite optical performance of all components in the image acquisition phase was provided.

n. Focusing Test

Test data to demonstrate that the focus quality is clinically acceptable for a variety of histologic preparations, including different tissue types, stain intensities, specimen thicknesses, and stain types was provided.

o. Whole Slide Tissue Coverage

Test data to demonstrate that the entire tissue specimen on the clinical slide is detected by device was provided.

p. Stitching Error

Test data to assess the quality of WSI stitching boundaries for clinical slides exhibiting a variety of histologic preparations, including different tissue types, stain intensities, specimen thicknesses, and stain types was provided.

q. Turnaround Time

Test data to evaluate the average time required to execute zooming and panning operations, and to refresh the display in response to user input was provided.

SUMMARY OF CLINICAL TESTS:

Two clinical studies were conducted with the NanoZoomer System: 1) feature detection and 2) primary diagnosis.

The feature detection study evaluated the repeatability and reproducibility of histological feature detection when using the WSI method. The study was divided into the following sub-studies:

- Scans from the same scanner (intra-scanner precision)

- Scans from different scanners at the same site (inter-scanner precision)
- Scans from different scanners at different sites (inter-site precision)

TABLE 2: INTRA-SCANNER STUDY RESULTS

System	Number of Pairwise Agreements	Number of Comparison Pairs	Agreement Rate and 95% CI	
			%	95% CI
Scanner 1	924	1134	94.3	(92.8, 95.7)
Scanner 2	934	1134	95.0	(93.5, 96.3)
Scanner 3	941	1134	94.3	(92.8, 95.7)
Total	2799	3402	94.5	(93.7, 95.3)

TABLE 3: INTER-SCANNER STUDY RESULTS

Systems Compared	Number of Pairwise Agreements	Number of Comparison Pairs	Agreement Rate and 95% CI	
			%	95% CI
Scanner 1 v Scanner 2	874	1134	92.5	(90.4, 94.2)
Scanner 1 v Scanner 3	880	1134	93.1	(91.2, 94.9)
Scanner 2 v Scanner 3	861	1134	91.4	(89.3, 93.4)
Total	2615	3402	92.4	(90.7, 93.8)

TABLE 4: INTER-SITE STUDY RESULTS

Sites Compared	Number of Pairwise Agreements	Number of Comparison Pairs	Agreement Rate and 95% CI	
			%	95% CI
Site 1 vs. Site 2	309	378	93.1	(90.9, 94.9)
Site 1 vs. Site 3	308	378	93.6	(91.5, 95.4)
Site 2 vs. Site 3	310	378	93.7	(91.6, 95.5)
Total	927	1134	93.4	(91.8, 94.9)

The data show that the studies met the acceptance criterion of the lower limit of the 95% confidence interval (CI) of the Average Positive Agreement exceeding 85%.

The Primary Diagnosis Study successfully met the primary endpoint of the study by demonstrating non-inferiority to light microscopy of glass slides in the viewing of surgical

pathology slides during the process of determining a primary diagnosis. The results of the Hamamatsu Photonics Primary Diagnosis Study are very similar to prior studies of digital pathology devices (0.4% difference for the NanoZoomer System compared to glass vs. 0.4% differential for PIPS, and a 3.5% major discordance rate for the NanoZoomer System vs. 4.7% for PIPS).

The acceptance criteria as follows:

- The upper bound of the two-sided 95% CI of the difference between the overall major discordance rates of WSI diagnoses and Glass diagnoses was required to be ≤4%.
- The major discordance rate of the WSI diagnoses was required to be ≤7%.

In addition, there were no significant differences observed in outcomes by organ.

TABLE 5: MAJOR DISCORDANCE RATES BY ORGAN

		WSI Major Discordance		***Glass Major Discordance***		***WSI-Glass Difference***
Organ		***N***	***%***	***N***	***%***	***% Difference***
Breast	Observed	1198	5.3%	1200	4.8%	0.6%
	Modeled	1198	5.2%	1200	4.6%	0.6%
Prostate	Observed	1200	1.2%	1200	1.8%	-0.7%
	Modeled	1200	1.2%	1200	1.8%	-0.7%
Respiratory*	Observed	400	10.3%	400	9.8%	0.5%
	Modeled	400	10.4%	400	9.9%	0.5%
Colorectal	Observed	600	0.7%	600	0.5%	0.2%
	Modeled	600	0.7%	600	0.5%	0.2%
GE Junction	Observed	400	6.0%	400	3.5%	2.5%
	Modeled	400	6.1%	400	3.5%	2.5%
Stomach	Observed	400	1.5%	400	0.8%	0.8%
	Modeled	400	1.5%	400	0.7%	0.7%
Skin	Observed	700	5.7%	700	4.6%	1.1%
	Modeled	700	5.7%	700	4.6%	1.1%
Lymph Node	Observed	400	1.8%	400	1.8%	0.0%
	Modeled	400	1.8%	400	1.8%	0.0%
Bladder	Observed	400	6.3%	400	4.3%	2.0%
	Modeled	400	6.2%	400	4.2%	2.0%
Gynecological	Observed	600	3.5%	600	3.5%	0.0%
	Modeled	600	3.6%	600	3.6%	-0.0%
Liver/	Observed	200	2.0%	200	1.5%	0.5%

		WSI Major Discordance		*Glass Major Discordance*		*WSI-Glass Difference*
Organ		***N***	***%***	***N***	***%***	***% Difference***
Bile Duct	Modeled	200	2.0%	200	1.5%	0.5%
Endocrine	Observed	400	4.5%	400	3.3%	1.3%
	Modeled	400	4.5%	400	3.3%	1.2%
Brain/Neuro	Observed	240	0.8%	240	0.4%	0.4%
	Modeled	240	0.8%	240	0.4%	0.4%
Kidney	Observed	200	0.5%	200	1.5%	-1.0%
	Modeled	200	0.5%	200	1.5%	-1.0%
Salivary Gland	Observed	200	1.0%	199	1.5%	-0.5%
	Modeled	200	1.0%	199	1.5%	-0.5%
Hernial/Peritoneal[+]	Observed	40	0.0%	40	0.0%	0.0%
Gallbladder[+]	Observed	40	0.0%	40	0.0%	0.0%
Appendix[#]	Observed	40	5.0%	40	0.0%	5.0%
Soft Tissue Tumors[#]	Observed	79	1.3%	79	0.0%	1.3%
Anus/Perianal	Observed	200	2.0%	200	3.5%	-1.5%
	Modeled	200	2.0%	200	3.5%	-1.5%
Other Miscellaneous[+]	Observed	60	0.0%	60	0.0%	0.0%

** - includes: Lung, Bronchus, Larynx, Oral Cavity, & Nasopharynx*

+ - MMRM could not be fit for organs for which no major discordances were observed: Hernial/Peritoneal, Gallbladder, and Other miscellaneous.

 # - MMRM failed to converge for Appendix and Soft Tissue Tumors

While not an endpoint or prospective analysis for this study, the Hamamatsu Photonics NanoZoomer Primary Diagnosis study results demonstrated a strong similarity to the results of the studies conducted by Philips Medical Systems comparing light microscopy to whole slide imaging.

CONCLUSION:

Hamamatsu Photonics K.K. considers the NanoZoomer S360MD Slide scanner system to be substantially equivalent to the predicate device.