May 20, 2019

Leica Biosystems Imaging, Inc.
Christine Kishi
Sr. RA Specialist
1360 Park Center Dr.
Vista, CA 92081

Re: K190332
Trade/Device Name: Aperio AT2 DX System
Regulation Number: 21 CFR 864.3700
Regulation Name: Whole slide imaging system
Regulatory Class: Class II
Product Code: PSY
Dated: February 13, 2019
Received: February 14, 2019

Dear Christine Kishi:

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 device 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/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm); 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 http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). 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 (http://www.fda.gov/DICE) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Yun-Fu Hu, Ph.D.
Deputy Director
Division of Molecular Genetics
and Pathology
OHT7: Office of In Vitro Diagnostics
and Radiological Health
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)*
K190332

Device Name
Aperio AT2 DX System

Indications for Use *(Describe)*
The Aperio AT2 DX System is an automated digital slide creation and viewing system. The Aperio AT2 DX 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 Aperio AT2 DX System is not intended for use with frozen section, cytology, or non-FFPE hematopathology specimens.

The Aperio AT2 DX System is composed of the Aperio AT2 DX scanner, the ImageScope DX review application and Display. The Aperio AT2 DX 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 the Aperio AT2 DX 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.

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510(k) Summary
Aperio AT2 DX System

I. Submitter

Leica Biosystems Imaging, Inc
1360 Park Center Dr.
Vista, CA 92081

II. Contact Person

Christine Kishi
Sr. Regulatory Affairs Specialist
1360 Park Center Dr.
Vista, CA 92081
christine.kishi@leicabiosystems.com
Phone: (760) 539-1194
Fax: (760) 539-1116

III. Device

Proprietary Name of the Device:	Aperio AT2 DX System
Classification Name:	Whole Slide Imaging System
Regulation Number:	21 CFR Part 864.3700
Regulatory Class:	Class II
Product code:	PSY

IV. Predicate Device

Philips IntelliSite Pathology Solution (PIPS)
DEN160056

V. Device Description

Clearance of this premarket application will enable the Aperio AT2 DX System comprised of a scanner and a viewing station for the primary diagnosis of formalin-fixed paraffin-embedded tissue.

System:

The Aperio AT2 DX System is an automated digital slide creation and viewing system. The system is comprised of an Aperio AT2 DX scanner instrument and a Viewing Workstation with a computer and a calibrated monitor executing ImageScope DX viewer software. The system capabilities include digitizing microscope slides at diagnostic resolution, retrieving and displaying digital slides, including support for remote intra-net access over computer networks, providing tools for annotating digital slides, entering data associated with digital slides and displaying the scanned slide images for primary diagnoses by Pathologists.

Image Acquisition:

The Aperio AT2 DX has a 400 glass slides capacity via an autoloader. High numeric aperture 20x objective, as found on conventional microscopes, is used to produce high-quality images. The Aperio AT2 DX digital slide scanner employs a linear-array scanning technique that generates images and accounts for merging scan stripes along the scanning axis. The result is seamless digital slide images.

The image acquisition software components include Console DX and Controller DX. The Console DX application is a user-interface for the operator. It allows users to initiate scanning and select appropriate slide areas to scan. The Controller DX application is a software subsystem that runs on the Aperio AT2 DX scanner Control PC.

Image Viewing:

The remote image viewing capabilities of the ImageScope DX software subsystem supports reading digital slides on a calibrated monitor, enabling Pathologists to make clinically relevant decisions analogous to those they make using a conventional microscope. ImageScope DX includes support for locally or intranet connected image Viewing Workstation computers, which run digital slide viewing. The software includes elements to support data confidentiality and integrity.

VI. Intended Use

The Aperio AT2 DX System is an automated digital slide creation and viewing system. The Aperio AT2 DX 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 Aperio AT2 DX System is not intended for use with frozen section, cytology, or non-FFPE hematopathology specimens.

The Aperio AT2 DX System is composed of the Aperio AT2 DX scanner, the ImageScope DX review application and Display. The Aperio AT2 DX 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 the Aperio AT2 DX System.

VII. Comparison of technological characteristics with the predicate device

Item	Predicate Device Philips IntelliSite Pathology Solution (PIPS) (DEN160056)	Candidate Device Aperio AT2 DX System
Intended Use/ Indications for Use	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	The Aperio AT2 DX System is an automated digital slide creation and viewing system. The Aperio AT2 DX 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 Aperio AT2 DX System is not intended for use with frozen section, cytology, or non-FFPE hematopathology specimens. The Aperio AT2 DX System is composed of the Aperio AT2 DX scanner, the ImageScope DX review application and Display. The Aperio AT2 DX System is for

Item	Predicate Device Philips IntelliSite Pathology Solution (PIPS) (DEN160056)	Candidate Device Aperio AT2 DX System
	pathologist to employ appropriate procedures and safeguards to assure the validity of the interpretation of images obtained using PIPS.	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 the Aperio AT2 DX System.
Specimen type	Surgical pathology slides prearped from formalin-fixed, paraffin-embedded tissue	Same
Principle of operation	The technician loads the slides into the WSI scanner. The scanner scans the slides and generates WSI image for each slide. The technician performs Quality Control (QC) on scanned WSI images and rescan the slide when QC is failed. The acquired WSI images are stored in an end user provided image storage attached to the local network. During 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.	Same
Device Components	WSI scanner (PIPS Ultra Fast Scanner), Image Management System and color monitor display	Same (Aperio AT2 DX scanner, ImageScope DX application, and color monitor display)

Differences		
Item	Device	Predicate
Whole Slide Imaging Scanner	Aperio AT2 DX scanner with loading capacity of 400 slides	Ultra Fast Scanner with loading capacity of 300 slides
Graphical User Interface	ImageScope DX	Image Management System
Monitor Display	Dell MR2416 monitor	PS27QHDCR

VIII. Performance Data

The performance testing was conducted via a series of studies that included Accuracy, Intra-System, Inter-System/Site, Within-Pathologist and Between-Pathologist precision.

The accuracy was evaluated by analyzing the concordance of the diagnoses made using the Aperio AT2 DX System (also known as WSIR diagnosis) with the gold standard reference diagnoses (the original sign-out pathologic diagnosis), and the concordance of traditional light microscope slide review (MSR) diagnoses with the gold standard reference diagnoses. Accuracy was assessed by analyzing major discrepancy rates for each study modality versus the gold standard reference diagnosis and calculating the difference between the major discrepancy rates for WSIR diagnosis and MSR diagnosis. Major discrepancy was defined as a difference in diagnoses that resulted in a clinically important difference in patient management.

The acceptance criteria were as follows:

- The upper bound of the two-sided 95% CI of the difference between the overall major discrepancy rates of WSIR diagnoses and MSR diagnoses is ≤4%.
- The upper bound of the two-sided 95% CI of the overall major discrepancy rate of the WSIR diagnoses is ≤7%.

The precision of the Aperio AT2 DX System was evaluated in 3 studies.

- For the Intra-System Precision study, the objective was to assess precision within each of three independent systems, and overall within system precision.
- For the Inter-System/Site Precision study, the objective was to assess precision between systems/sites (three independent systems at three different sites) and overall between system/site precision.
- For the Within- and Between-Pathologist Precision study, the objective was to assess precision within and between pathologists (using images generated from a single system), overall within pathologist precision, and overall between pathologist precision.

The Precision was considered acceptable if the lower bounds of the 2-sided 95% confidence intervals (CIs) of the overall agreements for each precision component (e.g. intra-system, inter-system/site) were ≥ 85%.

Table 1. Intra-System Study: Agreement Within Systems

System	Number of Pairwise Agreements	Number of Comparison Pairs	Agreement Rate and 95% CI*		
			% Agreement	Lower	Upper
System 1	193	201	96.0%	91.0%	100%
System 2	201	201	100%	98.2%	100%
System 3	199	204	97.5%	93.6%	100%
Overall	**593**	**606**	**97.9%**	**95.9%**	**99.5%**

*A bootstrap approach was used to calculate 95% CIs with the following exception. When the agreement estimate was 100%, the Arcsine (variance stabilizing transformation) approach that corrected for the continuity was used to calculate CIs (Pires and Amado, 2008).

Table 2. Inter-System/Site Study: Agreement Between Systems

System	Number of Pairwise Agreements	Number of Comparison Pairs	Agreement Rate and 95% CI*		
			% Agreement	Lower	Upper
System 1 vs System 2	195	202	96.5%	94.1%	99.0%
System 1 vs System 3	194	202	96.0%	93.1%	98.5%
System 2 vs System 3	193	202	95.5%	92.6%	98.0%
Overall	**582**	**606**	**96.0%**	**93.6%**	**98.2%**

*A bootstrap approach was used to calculate 95% CIs.

Table 3. Within/Between -Pathologist Study: Agreement Within Pathologists

Pathologist	Number of Pairwise Agreements	Number of Comparison Pairs	Agreement Rate and 95% CI*		
			% Agreement	Lower	Upper
Pathologist 1	561	606	92.6%	89.6%	95.7%
Pathologist 2	595	606	98.2%	96.3%	99.7%
Pathologist 3	571	606	94.2%	91.4%	96.9%
Overall	**1727**	**1818**	**95.0%**	**92.9%**	**96.8%**

*A bootstrap approach was used to calculate 95% CIs.

Table 4. Within- and Between-Pathologist Study: Agreement Between Pathologists

Pathologist Comparison	Number of Pairwise Agreements	Number of Comparison Pairs	Agreement Rate and 95% CI*		
			% Agreement	Lower	Upper
Pathologist 1 vs Pathologist 2	572	606	94.4%	91.6%	96.9%

Pathologist 1 vs Pathologist 3	562	606	92.7%	89.9%	95.4%
Pathologist 2 vs Pathologist 3	579	606	95.5%	93.1%	97.7%
Overall	**1713**	**1818**	**94.2%**	**91.7%**	**96.4%**

*A bootstrap approach was used to calculate 95% CIs.

Table 5. Overall Major Discrepancy Rates for the WSIR and MSR Modalities and the Difference Between the Overall Major Discrepancy Rates

	WSIRD Major Discrepancy*			**MSRD Major Discrepancy***			**Difference in Major Discrepancy Rates (WSIRD minus MSRD)**	
	Total Reads	**Rate (%)**	**Model 95% CI**	**Total Reads**	**Rate (%)**	**Model 95% CI**	**%**	**Model 95% CI**
Observed	7509	3.73	-	7522	3.28	-	0.45	-
Model		3.64	(3.21, 4.12)		3.20	(2.80, 3.65)	0.44	(-0.15%, 1.03%)

MSRD = MSR diagnosis, WSIRD = WSIR diagnosis

IX. Conclusions

The clinical study results demonstrate that AT2 DX System is substantially equivalent to the predicate device.