DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
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Silver Spring, MD 20993-0002

July 29, 2014

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

Re: k141109
Trade/Device Name: Aperio ePathology eIHC IVD System, AT Turbo and CS2 models
Regulation Number: 21 CFR 864.1860
Regulation Name: Immunohistochemistry reagents and kits
Regulatory Class: Class II
Product Code: NOT, NQN
Dated: April 29, 2014
Received: April 30, 2014

Dear Ms. 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 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. 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); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set

forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 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 the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Reena Philip -S

Reena Philip, Ph.D.
Director
Division of Molecular Genetics and Pathology
Office of *In Vitro* Diagnostics and
Radiological Health
Center for Devices and Radiological Health

Enclosure

Indication for Use

510(k) Number (if known):_K141109_____

Device Name: Aperio ePathology eIHC IVD System

Indication for Use:

The Aperio ePathology eIHC IVD System is an automated digital slide creation, management, viewing and analysis system. It is intended for in vitro diagnostic use as an aid to the pathologist in the display, detection, counting and classification of tissues and cells of clinical interest based on particular color, intensity, size, pattern and shape.

The IHC HER2 Image Analysis application is intended for use as an aid to the pathologist in the detection and semi-quantitative measurement of HER2/neu (c-erbB-2) in formalin-fixed, paraffin-embedded neoplastic tissue.

The IHC HER2 Image Analysis application is intended for use as an accessory to the Dako HercepTest™ to aid in the detection and semi-quantitative measurement of Her2/neu (c-erbB-2) in formalin-fixed, paraffin-embedded neoplastic tissue. When used with the Dako HercepTest™, it is indicated for use as an aid in the assessment of breast cancer patients for whom HERCEPTIN®(Trastuzumab) treatment is being considered.

Note: The IHC HER2 Image Analysis application is an adjunctive computer-assisted methodology to assist the reproducibility of a qualified pathologist in the acquisition and measurement of images from microscope slides of breast cancer specimens stained for the presence of HER-2 receptor protein. The IHC HER2 Image Analysis application is intended to be used on images viewed on a computer monitor. The accuracy of the test result depends upon the quality of the immunohistochemical staining. It is the responsibility of a qualified pathologist to employ appropriate morphological studies and controls as specified in the instructions for the Dako HercepTest™ to assure the validity of the IHC HER2 Image Analysis application assisted HER-2/neu score. The actual correlation of the Dako HercepTest™ to Herceptin® clinical outcome has not been established.

Prescription Use __X___ And/Or Over the Counter Use_____

(21 CFR Part 801 Subpart D) (21 CFR Part 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE; CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)

_____

Division Sign-Off

Office of In Vitro Diagnostic Device

Evaluation and Safety

510(k)_____

510(k) Number (if known):_K141109_____

Device Name: Aperio ePathology eIHC IVD System

Indication for Use:

The Aperio ePathology eIHC IVD System is an automated digital slide creation, management, viewing and analysis system. It is intended for in vitro diagnostic use as an aid to the pathologist in the display, detection, counting and classification of tissues and cells of clinical interest based on particular color, intensity, size, pattern and shape.

The IHC ER Image Analysis application is intended for use as an aid to the pathologist in the detection and quantitative measurement of ER (Estrogen Receptor) in formalin-fixed paraffin-embedded neoplastic tissue.

The IHC PR Image Analysis application is intended for use as an aid to the pathologist in the detection and quantitation measurement of PR (Progesterone Receptor) in formalin-fixed, paraffin-embedded neoplastic tissue.

It is indicated for use as an aid in the management, prognosis, and prediction of therapy outcomes of breast cancer.

Note: The IHC ER and PR Image Analysis applications are an adjunctive computer-assisted methodology to assist the reproducibility of a qualified pathologist in the acquisition and measurement of images from microscope slides of breast cancer specimens stained for the presence of estrogen and progesterone receptor proteins. The IHC ER and PR Image Analysis applications are intended to be used on images viewed on a computer monitor. The accuracy of the test result depends upon the quality of the immunohistochemical staining. It is the responsibility of a qualified pathologist to employ appropriate morphological studies and controls as specified in the instructions for the ER and PR reagent/kit used to assure the validity of the IHC ER and PR Image Analysis application assisted scores.

Prescription Use __X___ And/Or Over the Counter Use_____
(21 CFR Part 801 Subpart D) (21 CFR Part 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE; CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)

_____
Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety
510(k)_____

Bundled 510(k) Summary

Leica Biosystems Imaging, Inc.

(Aperio ePathology eIHC IVD System)

21 CFR 807.92(a) (1):

Submitter's name and address:

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

Submitter's telephone and fax numbers:

Phone: (760) 539-1194
Fax: (760) 539-1116

Contact person:

Christine Kishi
Quality Assurance Specialist
1360 Park Center Dr.
Vista, CA 92081
christine.kishi@leicabiosystems.com

Date this 510(k) summary was prepared:

April 28, 2014

Bundled Submission Overview

21 CFR 807.92(a)(2): Device trade name and common name, and classification

Bundled Devices	
Trade Name	Aperio ePathology eIHC IVD System
Common Name	Digital pathology and image analysis system
Regulation Number	21 CFR 864.1860
Regulation Name	Immunohistochemistry reagents and kits
Regulatory Class	II
Product Codes	NOT, NQN
Bundled Indications	
Legally Marketed predicate device to which substantial equivalence is claimed	
Predicate Device	ScanScope XT
Manufacturer	Aperio Technologies
Predicate Device k#	K071128, K073677

21 CFR 807.92 requirements are specified individually below by cleared predicate device K #.

K071128 (HER2 Image Analysis):
21 CFR 807.92(a)(2):

Trade Name of Device: Aperio ePathology eIHC IVD System, AT Turbo and CS2 models.

Regulatory Section: 21 CFR 864.1860 Immunohistochemistry reagents and kits

Classification: Class II

Product Code: NOT (microscope, automated, image analysis, operator intervention)

21 CFR 807.92(a)(3): Legally marketed predicate device to which substantial equivalence is claimed:

Predicate Device: ScanScope® System XT

Manufacturer: Aperio Technologies, Inc.

Predicate Device k#: K071128

21 CFR 807.92(a)(4): Description of the device that is the subject of this premarket notification:

System: The Aperio ePathology eIHC IVD System ("System") is an automated digital slide creation, management, viewing and analysis system. The Aperio ePathology eIHC IVD System components consist of an automated digital microscope slide scanner, computer, color monitor, keyboard and digital pathology information management software. The system capabilities include digitizing microscope slides at high resolution, storing and managing the resulting digital slide images, retrieving and displaying digital slides, including support for remote access over wide-area networks, providing tools for annotating digital slides and entering and editing data associated with digital slides, and tools for image analysis of digital slides. Image analysis capabilities include the ability to quantify characteristics useful to Pathologists, such as measuring and scoring immunohistochemical stains applied to histology specimens, including the Dako HerceptTest™. The Dako HerceptTest™ reveals the presence of proteins such as Human Epidermal growth factor Receptor 2 (HER2). These results are indicated for use as an aid in the management, prognosis and prediction of therapy outcomes of breast cancer.

Hardware Operation: The ScanScope digital slide scanner creates high resolution, color digital slide images of entire glass slides in a matter of minutes. High numeric aperture 20x objectives, as found on conventional microscopes, are used to produce high-quality images. The ScanScope digital slide scanner employs a linear-array scanning technique that generates digital slide images that have no tiling artifacts and that are free from optical aberrations along the scanning axis.

Software Operation: The eSlideManager software (formally named Spectrum) is a full-featured digital pathology information management system. The software runs on a server computer called

a Digital Slide Repository (DSR), which stores digital slide images on disk storage such as a RAID array, and which hosts an SQL database that contains digital slide metadata. eSlideManager includes a web application and services which encapsulate database and digital slide image access for other computers. The eSlideManager server supports the capability of running a variety of digital slide image analysis algorithms on digital slides, and storing the results of the analysis into the database. ImageScope also includes support for locally or remotely connected image workstation computers, which run digital slide viewing and analysis software provided as part of eSlideManager.

Overview of System Operation: The laboratory technician or operator loads glass microscope slides into either a specially designed slide carrier with a capacity of up to 400 slides for the ScanScope AT Turbo or a 5 slide slide-tray for the ScanScope CS2. The scanning process begins when the operator starts the ScanScope® scanner and finishes when the scanner has completed scanning of all loaded slides. As each glass slide is processed, the system automatically stores individual "striped" images of the tissue contained on the glass slide and integrates the striped images into a single digital slide image, which represents a histological reconstruction of the entire tissue section. After scanning is completed, the operator is able to view and perform certain analytical tests on the digital slides.

21 CFR 807.92(a)(5): Intended use and labeled indications for use:
The Aperio ePathology eIHC IVD System is an automated digital slide creation, management, viewing and analysis system. It is intended for in vitro diagnostic use as an aid to the pathologist in the display, detection, counting and classification of tissues and cells of clinical interest based on particular color, intensity, size, pattern and shape.

The IHC HER2 Image Analysis application is intended for use as an aid to the pathologist in the detection and semi-quantitative measurement of HER2/neu (c-erbB-2) in formalin-fixed, paraffin embedded neoplastic tissue.

The IHC HER2 Image Analysis application is intended for use as an accessory to the Dako HercepTest™ to aid in the detection and semi-quantitative measurement of HER2/neu (c-erbB-2) in formalin-fixed, paraffin-embedded neoplastic tissue. When used with the Dako HercepTest™, it is indicated for use as an aid in the assessment of breast cancer patients for whom HERCEPTIN® (Trastuzumab) treatment is being considered.

Note: The IHC HER2 Image Analysis application is an adjunctive computer-assisted methodology to assist the reproducibility of a qualified pathologist in the acquisition and measurement of images from microscope slides of breast cancer specimens stained for the presence of HER-2 receptor protein. The IHC HER2 Image Analysis application is intended to be used on images viewed on a computer monitor. The accuracy of the test result depends upon the quality of the immunohistochemical staining. It is the responsibility of a qualified pathologist to employ appropriate morphological studies and controls as specified in the instructions for the Dako HercepTest™ to assure the validity of the IHC HER2 Image Analysis application assisted HER-2/neu score. The actual correlation of the Dako HercepTest™ to Herceptin® clinical outcome has not been established.

21 CFR 807.92(a)(6): Technological characteristics:

The design, construction, energy source and other characteristics of the ScanScope System candidate device are considered to be substantially equivalent to the relevant features of the predicate device. A summary of the technological characteristics of the ScanScope System candidate device in comparison to the predicate device follows:

Method of cell detection. The method of cell detection is by colorimetric pattern recognition by microscopic examination of prepared cells by size, shape, hue and intensity as observed by a computer-automated, microscopic digital slide scanner system and/or by visual observation by a health care professional.

System Components. The system components comprising the Aperio ePathology eIHC IVD System candidate device are substantially equivalent to those in the predicate device; i.e., a computer-automated digital microscope slide scanner, computer, color monitor, and keyboard.

Energy Source. The electrical service is 100vAC – 240vAC, 50Hz/60 Hz, 2 amp, which is similar to the predicate device electrical service requirements.

21 CFR 807.92(b): 510(k) summaries for those premarket submissions in which determination of substantial equivalence is also based on an assessment of performance data shall contain the following information:

21 CFR 807.92(b)(1): Brief discussion of nonclinical tests submitted, referenced or relied on in this premarket notification:

The testing conducted to support this premarket notification includes - 1) System verification and validation testing and 2) System level performance testing using clinical samples. Each of these will be briefly summarized below:

1) *System Verification and Validation Testing*

Verification was conducted to ensure the specified Design Inputs met the Design Outputs as specified in the Marketing and/or Product Requirements and Requirement Specifications and Design Documents. Verification testing includes performance and physical testing, environmental testing, interface compatibility, user interface, worst case testing and negative testing as applicable.

Design validation was conducted following successful completion of Verification to ensure the design met user needs. Validation is conducted through running a Beta program and/or User Acceptance Testing (UAT) as applicable.

2) System Performance Testing

The system level performance testing for the Aperio ePathology eIHC IVD System was conducted through a series of internal studies. Each evaluated the accuracy of the HER2 image analysis algorithm on the updated ScanScope instruments.

Paraffin embedded breast tissue slides prepared with the appropriate Dako HER2 IHC test kit was used. The slides represented the range of HER2 scores (0, 1+, 2+ and 3+) that are observed clinically, and were scanned on the ScanScope instruments. The HER2 scores obtained from each of the updated ScanScope systems were evaluated for concordance with the scores obtained from the predicate device. These results were evaluated in a trichotomous (0 and1+, 2+, 3+) analysis.

The analysis acceptance criteria was percent agreement using an exact 95% lower confidence interval. Based on these tests and analyses, the updated ScanScope models passed the acceptance criteria for substantial equivalence to the original ScanScope XT.

21 CFR 807.92(b)(2): Brief discussion of clinical tests submitted, referenced or relied on in this premarket notification:

There are no clinical tests submitted, referenced or relied on in this submission.

K073677 (ER/PR Image Analysis):
21 CFR 807.92(a)(2):

Trade Name of Device:	Aperio ePathology eIHC IVD System, AT Turbo and CS2 models.
Regulatory Section:	21 CFR 864.1860 Immunohistochemistry reagents and kits
Classification:	Class II
Product Code:	NQN (Microscope, Automated, Image Analysis, immunohistochemistry, Operator Intervention, Nuclear Intensity and Percent Positivity)

21 CFR 807.92(a)(3): Legally marketed predicate device to which substantial equivalence is claimed:

Predicate Device:	ScanScope® System XT
Manufacturer:	Aperio Technologies, Inc.
Predicate Device k#:	K073677

21 CFR 807.92(a)(4): Description of the device that is the subject of this premarket notification:

System: The Aperio ePathology eIHC IVD System ("System") is an automated digital slide creation, management, viewing and analysis system. The Aperio ePathology eIHC IVD System components consist of an automated digital microscope slide scanner, computer, color monitor, keyboard and digital pathology information management software. The system capabilities include digitizing microscope slides at high resolution, storing and managing the resulting digital slide images, retrieving and displaying digital slides, including support for remote access over wide-area networks, providing tools for annotating digital slides and entering and editing data associated with digital slides, and tools for image analysis of digital slides. Image analysis capabilities include the ability to quantify characteristics useful to Pathologists, such as measuring and scoring immunohistochemical stains applied to histology specimens, including Dako ER/PR, which reveal the presence of ER (Estrogen Receptor) protein and PR (Progesterone Receptor) protein expression.These results are indicated for use as an aid in the management, prognosis and prediction of therapy outcomes of breast cancer.

Hardware Operation: The ScanScope digital slide scanner creates seamless true color digital slide images of entire glass slides in a matter of minutes. A high numeric aperture 20x, as found on conventional microscopes, is used to produce high-quality images. The ScanScope digital slide scanner employs a linear-array scanning technique that generates images free from optical aberrations along the scanning axis. The result is digital slide images that have no tiling artifacts and are seamless.

Software Operation: The eSlideManager software (formally named Spectrum) is a full-featured digital pathology management system. The software runs on a server computer called a Digital Slide Repository (DSR), which stores digital slide images on disk storage such as a RAID array, and which hosts an SQL database that contains digital slide metadata. eSlideManager includes a web application and services which encapsulate database and digital slide image access for other computers. The eSlideManager server supports the capability of running a variety of image analysis algorithms on digital slides, and storing the results of analysis into the database. ImageScope includes support for locally or remotely connected image workstation computers, which run digital slide viewing and analysis software provided as part of eSlideManager.

Overview of System Operation: The laboratory technician or operator loads glass microscope slides into either a specially designed slide carrier with a capacity of up to 400 slides for the ScanScope AT Turbo or a 5 slide slide-tray for the ScanScope CS2. The scanning process begins when the operator starts the ScanScope® scanner and finishes when the scanner has completed scanning of all loaded slides. As each glass slide is processed, the system automatically stores individual "striped" images of the tissue contained on the glass slide and integrates the striped images into a single digital slide image, which represents a histological reconstruction of the entire tissue section. After scanning is completed, the operator is able to view and perform certain analytical tests on the digital slides.

21 CFR 807.92(a)(5): Intended use and labeled indications for use:
The Aperio ePathology eIHC IVD System is an automated digital slide creation, management, viewing and analysis system.

It is intended for *in vitro* diagnostic use as an aid to the pathologist in the display, detection, counting and classification of tissues and cells of clinical interest based on particular color, intensity, size, pattern and shape.

The IHC ER Image Analysis application is intended for use as an aid to the pathologist in the detection and quantitative measurement of ER (Estrogen Receptor) in formalin-fixed paraffin-embedded neoplastic tissue.

The IHC PR Image Analysis application is intended for use as an aid to the pathologist in the detection and quantitation measurement of PR (Progesterone Receptor) in formalin-fixed, paraffin-embedded neoplastic tissue.

It is indicated for use as an aid in the management, prognosis, and prediction of therapy outcomes of breast cancer.

Note: The IHC ER and PR Image Analysis applications are an adjunctive computer-assisted methodology to assist the reproducibility of a qualified pathologist in the acquisition and measurement of images from microscope slides of breast cancer specimens stained for the presence of estrogen and progesterone receptor proteins. The IHC ER and PR Image Analysis applications are intended to be used on images viewed on a computer monitor. The accuracy of the test result depends upon the quality of the immunohistochemical staining. It is the responsibility of a qualified pathologist to employ appropriate morphological studies and controls

as specified in the instructions for the ER and PR reagent/kit used to assure the validity of the IHC ER and PR Image Analysis application assisted scores.

21 CFR 807.92(a)(6): Technological characteristics:

The design, construction, energy source and other characteristics of the Aperio ePathology eIHC IVD System candidate device are considered to be substantially equivalent to the relevant features of the predicate device. A summary of the technological characteristics of the ScanScope System candidate device in comparison to the predicate device follows:

Method of cell detection. The method of cell detection is by colorimetric and morphometric pattern recognition by microscopic examination of prepared cells by size, shape, color, and intensity as observed by a computer-automated, microscopic digital slide scanner system and/or by visual observation by a health care professional.

System Components. The system components comprising the ScanScope System candidate device are substantially equivalent to those in the predicate device; i.e., a computer-automated digital microscope slide scanner, computer, color monitor, and keyboard.

Energy Source. The electrical service is 100vAC – 240vAC, 50Hz/60 Hz, 2 amps which is similar to the predicate device electrical service requirements.

21 CFR 807.92(b): 510(k) summaries for those premarket submissions in which determination of substantial equivalence is also based on an assessment of performance data shall contain the following information:

21 CFR 807.92(b)(1): Brief discussion of non-clinical tests submitted, referenced or relied on in this premarket notification:

The nonclinical testing conducted to support this premarket notification includes - 1) System verification and validation testing and 2) System level performance testing using clinical samples. Each of these will be briefly summarized below:

1) *System Verification and Validation Testing*

Verification was conducted to ensure the specified Design Inputs met the Design Outputs as specified in the Marketing and/or Product Requirements and Requirement Specifications and Design Documents. Verification testing includes performance and physical testing, environmental testing, interface compatibility, user interface, worst case testing and negative testing as applicable.

Design validation was conducted following successful completion of Verification to ensure the design met user needs. Validation is conducted through running a Beta program and/or User Acceptance Testing (UAT) as applicable.

2) *System Performance Testing*

The system level performance testing for the ScanScope System was conducted through a series of internal studies. Each evaluated the accuracy of the ER and PR image analysis algorithms on the updated ScanScope instruments.

Paraffin embedded breast tissue slides prepared with the appropriate Dako ER and PR IHC test kits were used. The slides represented the range of ER and PR scores that are observed clinically, and were scanned on the ScanScope instruments. The ER and PR scores obtained from each of the updated ScanScope systems were evaluated for concordance with the scores obtained from the predicate device. These results were evaluated in a dichotomous (Positive vs Negative) analysis at two percent positive thresholds (1% and 10%).

The analysis acceptance criteria was percent agreement using an exact 95% lower confidence interval. Based on these tests and analyses, the updated ScanScope models passed the acceptance criteria for substantial equivalence to the original ScanScope XT.

21 CFR 807.92(b)(2): Brief discussion of clinical tests submitted, referenced or relied on in this premarket notification:

There are no clinical tests submitted, referenced or relied on in this submission.

….End of 510(k) Summary….