

510(k) Summary of Substantial Equivalence
Aperio Technologies, Inc.
(ScanScope® XT System)

OCT 10 2007

21 CFR 807.92(a):

21 CFR 807.92(a) (1):

Submitter's name and address:

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Date this 510(k) summary was prepared:

September 28, 2007

21 CFR 807.92(a)(2):

Trade Name of Device: ScanScope® XT System
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): Leally marketed predicate device to which substantial equivalence is claimed:

Predicate Device: Automated Cellular Imaging System (“ACIS”) and ACIS HER2 software application

Manufacturer: ChromaVision Medical Systems, Inc.

Predicate Device k#: k032113

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

System: The ScanScope® XT System is an automated digital slide creation, management, viewing and analysis system. The ScanScope® XT 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 facilities for annotating digital slides and entering and editing metadata associated with digital slides, and facilities 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, such as the Dako HerceptTest™, which reveal the presence of proteins such as Human Epidermal growth factor Receptor 2 (HER2), which may be used to determine patient treatment for breast cancer.

Hardware Operation: The ScanScope XT digital slide scanner creates high resolution, color digital slide images of entire glass slides in a matter of minutes. High numeric aperture 20x or 40x objectives, as found on conventional microscopes, are used to produce high-quality images. The ScanScope XT employs a linear-array scanning technique that generates digital slide images that have no tiling artifacts and that are essentially free from optical aberrations along the scanning axis.

Software Operation: The Spectrum™ software 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. Spectrum includes a web application and services which encapsulate database and digital slide image access for other computers. The Spectrum server supports the capability of running a variety of digital slide image analysis algorithms on digital slides, and storing the results of analysis into the database. Spectrum also includes support for locally or remotely connected image workstation computers, which run digital slide viewing and analysis software provided as part of Spectrum.

Overview of System Operation: The laboratory technician or operator loads glass microscope slides into a specially designed slide carrier with a capacity of up to 120 slides. 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 ScanScope 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 normal and 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 normal and 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 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 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 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:

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

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

Comparison studies:

a. Method comparison with predicate device:

The substantial equivalence study was based on comparison of image analysis to conventional manual microscopy.

A multi-site study was conducted at two clinical sites to compare the performance of Aperio's IHC HER2 Image Analysis to manual microscopy. 180 formalin-fixed, paraffin-embedded breast tissue specimens immunohistochemically stained using Dako's HerceptTest™ were used for this study; 80 specimens with approximately equal HER2 score distribution from site 1, and 100 routine specimens from site 2. At each site, three pathologists performed a blinded read of the glass slides using a microscope and reported the HER2 score for each of the slides. The glass slides were scanned at Aperio using a different ScanScope for each site, and after a wash-out period of over one week and randomization of the slides, the same three pathologists remotely viewed and outlined a representative set of tumor regions to be analyzed by the IHC HER2 image analysis. The pathologists received feedback on the way they outlined tumor regions for their first 3 to 7 slides before the slides were analyzed. The algorithm itself was run in batch mode

blinded from the pathologists to avoid any influence of the pathologists in their choice of the tumor regions. The algorithm was used “out of the box”. The algorithm reported the HER2 score for each of the three pathologists for each of the slides.

The statistical analyses are presented across all slides for each of the methods: manual microscopy and image analysis, and comparatively between methods for manual microscopy against image analysis.

Statistical analyses are provided for a trichotomous categorization of the HER2 scores combining 0 and 1+ and leaving 2+ and 3+ uncombined. Percentage Agreement (PA) along with an exact 95% Confidence Interval (CI) are presented overall for all trichotomous HER2 score categories combined and for each of the trichotomous HER2 score categories separately using a dichotomous outcome of that category vs. the two other categories.

	Pathologist 1 v 2		Pathologist 1 v 3		Pathologist 2 v 3	
	PA	PA 95% CI	PA	PA 95% CI	PA	PA 95% CI
Clinical Site 1	91.3%	(82.8, 96.4)	77.5%	(66.8, 86.1)	76.3%	(65.4, 85.1)
Clinical Site 2	84.0%	(75.3, 90.6)	82.0%	(73.1, 89.0)	90.0%	(82.4, 95.1)

Manual Microscopy - Inter-Pathologists - Agreements.

	Pathologist 1 v 2		Pathologist 1 v 3		Pathologist 2 v 3	
	PA	PA 95% CI	PA	PA 95% CI	PA	PA 95% CI
Clinical Site 1	88.8%	(79.7, 94.7)	93.8%	(86.0, 97.9)	86.3%	(76.7, 92.9)
Clinical Site 2	87.0%	(78.8, 92.9)	92.0%	(84.8, 96.5)	89.0%	(81.2, 94.4)

Image Analysis - Inter-Pathologists - Agreements.

	Pathologist 1		Pathologist 2		Pathologist 3	
	PA	PA 95% CI	PA	PA 95% CI	PA	PA 95% CI
Clinical Site 1	92.5%	(84.4, 97.2)	90.0%	(81.2, 95.6)	77.5%	(66.8, 86.1)
Clinical Site 2	90.0%	(82.4, 95.1)	79.0%	(69.7, 86.5)	90.0%	(82.4, 95.1)

Manual Microscopy vs Image Analysis – same Pathologist - Agreements.

The inter-pathologists agreements for the performed (blinded) image analysis (PA: 86.3-93.8%) were comparable to the inter-pathologists agreements for manual microscopy (PA: 76.3-91.3%). The agreements between the pathologists’ manual microscopy and performed (blinded) image analysis (PA: 77.5-92.5%) were comparable to the inter-pathologists agreements for manual microscopy (PA: 76.3-91.3%).

Analytical Performance:

a. Precision:

The precision of the ScanScope XT System was determined in a suite of intra-run/intra-system, inter-run/intra-system and inter-systems studies. Eight HER2 slides from the

comparison study were selected to provide two slides in each of the HER2 score classes 0, 1+, 2+ and 3+.

Intra-run/intra-system: The slide scores provided by Image Analysis over ten consecutive scans were analyzed for all eight HER2 slides. The data show perfect agreement (100%) for the calculated HER2 scores across all runs.

Inter-run/intra-system: The slide scores provided by Image Analysis over twenty scans on different days were analyzed for all eight HER2 slides. The data show perfect agreement (100%) for the calculated HER2 scores across all runs.

Inter-systems: The slide scores provided by Image Analysis over ten consecutive scans on three different ScanScope scanner instruments were analyzed for all eight HER2 slides. The data show perfect agreement (100%) for the calculated HER2 scores across all systems and across all runs.

21 CFR 807.92(b)(3): Conclusions drawn from the nonclinical and clinical tests:

Based on the results of the clinical studies described in this 510(k) submission, it is concluded that the ScanScope System device is as safe and effective (therefore substantially equivalent) as the predicate device as an aid in the assessment of specimens from breast cancer patients for whom Herceptin® (Trastuzumab) treatment is being considered.

....End of 510(k) Summary....



Food and Drug Administration
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Rockville MD 20850

Perry Johnston
Aperio Technologies
1430 Vantage Court
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Vista, California 92081

OCT 10 2007

Re: k071128

Trade/Device Name: Scanscope XT System
Regulation Number: 21 CFR 864.1860
Regulation Name: Immunohistochemistry reagents and kits
Regulatory Class: Class II
Product Code: NOT
Dated: April 20, 2007
Received: April 23, 2007

Dear Mr. Johnston:

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.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. 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 Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820). This letter

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will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at 240-276-0450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding postmarket surveillance, please contact CDRH's Office of Surveillance and Biometric's (OSB's) Division of Postmarket Surveillance at 240-276-3474. For questions regarding the reporting of device adverse events (Medical Device Reporting (MDR)), please contact the Division of Surveillance Systems at 240-276-3464. You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (240) 276-3150 or at its Internet address <http://www.fda.gov/cdrh/industry/support/index.html>.

Sincerely yours,



Robert L. Becker, Jr., M.D., Ph.D.

Director

Division of Immunology and Hematology

Office of *In Vitro* Diagnostic Device Evaluation
and Safety

Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): K071128

Device Name: ScanScope® XT System

Indications for Use:

The ScanScope 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.

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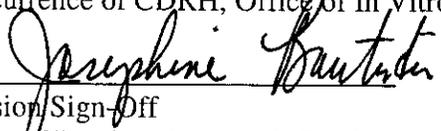
Prescription Use X
(Part 21CFR 801 Subpart D)

AND/OR

Over-The-Counter Use _____
(Part 21 CFR 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) K071128