K071671

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

21 CFR 807.92(a):

DEC 2 8 2007

21 CFR 807.92(a) (1):

Submitter's name and address:

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Date this 510(k) summary was prepared:

November 26, 2007

21 CFR 807.92(a)(2):

Trade Name of Device:	ScanScope® System
Regulatory Section:	21 CFR 864.1860 Immunhistochemistery 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:	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 ® System is an automated digital slide creation, management, viewing and analysis system. The ScanScope® 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 detect and quantify characteristics useful to Pathologists, such as detecting and quantifying certain proteins revealed by immunohistochemical stains applied to histology specimens. The remote digital slide viewing capabilities of the system support reading digital slides on a computer monitor, enabling Pathologists to make clinically relevant decisions analogous to those they make using a conventional microscope. Specifically, the system supports the pathologist in the detection and semi-quantitative measurement of HER-2/neu (c-erbB-2) by manual examination of the digital slide of formalin-fixed, paraffin-embedded normal and neoplastic tissue immunohistochemically stained for HER-2 receptors on a computer monitor.

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, interpret 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 Manual Read of Digital Slides application is intended for use as an aid to the pathologist in the detection and semi-quantitative measurement of HER-2/neu (c-erbB-2) by manual examination of the digital slide of formalin-fixed, paraffin-embedded normal and neoplastic tissue immunohistochemically stained for HER-2 receptors on a computer monitor. HER2 results are indicated for use as an aid in the management, prognosis and prediction of therapy outcomes of breast cancer.

The IHC HER2 Manual Read of Digital Slides application is intended for use as an accessory to the Dako HercepTest™ to aid the pathologist in the detection and semi-quantitative measurement of HER-2/neu (cerbB-2) by manual examination of the digital slide of formalin-fixed, paraffin-embedded normal and neoplastic tissue immunohistochemically stained for HER-2 receptors on a computer monitor. 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 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 method comparison study was performed to compare the manual examination or "reading" of digital slides on a computer monitor (hereinafter characterized as "reading" of digital slides) to conventional manual microscopic examination of glass slides with respect to the quantification of HER2 expression in breast tissue.

A total of one-hundred and eighty (180) formalin-fixed, paraffin-embedded breast tissue specimens from two (2) clinical sites were used for this study; eighty (80) specimens from the first clinical site with an approximately equal distribution of slides for the different HER2 scores (0, 1+, 2+, 3+) and one-hundred (100) specimens from the second clinical site taken from their clinical operation, representing the typical workflow distribution of cases encountered in a clinical setting. All specimens were immunohistochemically stained using Dako's FDA approved HerceptTest™ (P980018).

Three (3) different Pathologists at each clinical site performed a blinded manual examination of each glass slide using a conventional light microscope in accordance with the reagents' instructions for use. The Pathologists reported the HER2 scores of 0, 1+, 2+ or 3+ for each of the glass slides examined. The glass slides from each of the two clinical sites respectively were scanned using a different ScanScope® scanner instrument. After a wash-out period of over one (1) week and subsequent randomization of the slides, the same three (3) Pathologists at each clinical site performed a blinded manual read of each digital slide displayed on a computer monitor using the ScanScope XT System's remote viewing capability. The Pathologists reported a HER2 score of 0, 1+, 2+ or 3+ for each of the digital slides corresponding to their respective clinical site.

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.

	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	**70.0%**	(58.7, 79.7)	**71.3%**	(60.0, 80.8)	**71.3%**	(60.0, 80.8)
Clinical site 2	**86.0%**	(77.6, 92.1)	**79.0%**	(69.7, 86.5)	**77.0%**	(67.5, 84.8)

Manual Digital Slide Reading - Inter-Pathologists - Agreements.

	Pathologist 1		Pathologist 2		Pathologist 3	
	PA	PA 95% CI	PA	PA 95% CI	PA	PA 95% CI
Clinical site 1	**61.3%**	(49.7, 71.9)	**71.3%**	(60.0, 80.8)	**92.5%**	(84.4, 97.2)
Clinical site 2	**85.0%**	(76.5, 91.4)	**84.0%**	(75.3, 90.6)	**89.0%**	(81.2, 94.4)

Manual Microscopy vs. Digital Slide Reading - same Pathologist - Agreements.

The percent agreements between the pathologists' manual microscopy and manual read of digital slides ranged from 61.3% to 92.5% with confidence bounds from 49.7% to 97.2%; the inter-pathologists agreements for manual microscopy ranged from 76.3% to 91.3% with confidence bounds from 65.4% to 96.4%.

The inter-pathologists agreements for the manual read of digital slides ranged from 70.0% to 86.0% with confidence bounds from 58.7% to 92.1%; the inter-pathologists agreements for manual microscopy ranged from 76.3% to 91.3% with confidence bounds from 65.4% to 96.4%.

Analytical Performance:

a. Precision/Reproducibility:

This precision study was not done on the manual read of the digital slides but using Aperio's IHC HER2 image analysis algorithm. The image analysis algorithm detects and quantifies the same cell features and uses the same scoring scheme as the pathologists reading IHC HER2 slides and was used to quantify objectively the variability of the digital slides provided by the ScanScope systems.

Eight HER2 slides with two slides per HER2 score 0, 1+, 2+ and 3+were sampled from one of the clinical sites to be used in a suite of precision studies. The slides were sampled in sequential order using the rounded average score of the manual microscopy scores provided by the three pathologists.

	Slide 1	Slide 2	Slide 3	Slide 4	Slide 5	Slide 6	Slide 7	Slide 8
Pathologist 1	0	0	0	1	2	2	3	3
Pathologist 2	0	0	1	1	2	2	3	3
Pathologist 3	1	0	1	0	2	2	3	3
Average	0	0	1	1	2	2	3	3

HER2 scores provided by 3 Pathologists for the sampled slides.

Separate studies were conducted to analyze the system introduced variability separately from the variability introduced by the pathologists. Pathologist precision studies were only performed to be able to put the system variability into perspective to the variability introduced by the pathologists.

System precision studies used the same tumor regions for analysis over all runs to eliminate the influence by the pathologists. Pathologist precision studies used the same digital slides to eliminate the influence of the system.

The precision studies analyzed the changes in the system response by extending the analysis of the HER2 score to the underlying cumulative percentages of 3+, 2+ and 1+ cells on which the HER2 score calculations are based. Cumulative percentages of 3+, 2+ and 1+ cells are defined as the percentages of 3+ cells, 3+ and 2+ cells and 3+, 2+ and 1+ cells.

Note that only the accuracy of the HER2 scores was evaluated in the Clinical Comparison to Manual Microscopy.

Intra-System

The eight HER2 slides were scanned 10 times on the same ScanScope system. The image analysis results show perfect agreement (100%) for the calculated HER2 scores and an overall average standard deviation of 0.69% (maximum 2.46%) and average range (maximum – minimum) of 1.22% (maximum 7.14%) for the cumulative percentages of 3+, 2+ and 1+ cells (range from 0.0 to 100.0%) across all runs.

Inter-Day/Intra-System

The eight HER2 slides were scanned on the same ScanScope system over 20 times on different days. The image analysis results show perfect agreement (100%) for the calculated HER2 scores and an overall average standard deviation of 0.67% (maximum 2.43%) and average range of 1.68% (maximum 12.07%) for the cumulative percentages of 3+, 2+ and 1+ cells across all runs.

Inter-System

The same eight HER2 slides were scanned 10 times on three different ScanScope systems. The image analysis results show perfect agreement (100%) for the calculated HER2 scores across all systems and all runs. The image analysis results on each of the three ScanScope systems show an overall average standard deviation of 0.69%, 0.59% and 0.57% (maximum 2.46%, 1.65%, 1.34%) and average range of 1.22%, 1,14% and 1.20% (maximum 7.14%, 5.09%, 4.70%) for the cumulative percentages of 3+, 2+ and 1+ cells respectively over all runs. The image analysis results of the three ScanScope systems combined show an overall average standard deviation of 0.78% (maximum 2.41%) and average range of 1.93% (maximum 8.95%) respectively for the cumulative percentages of 3+, 2+ and 1+ cells over all runs.

The following table shows the cumulative percentages of 3+, 2+ and 1+ cells (%) for image analysis of the eight HER2 slides (#S) for the three ScanScope systems.

	S#1			S#2			S#3			S#4		
	3+ %	3+, 2+ %	3+, 2+, 1+ %	3+ %	3+, 2+ %	3+, 2+, 1+ %	3+ %	3+, 2+ %	3+, 2+, 1+ %	3+ %	3+, 2+ %	3+, 2+, 1+ %
ScanScope #1	**0.0**	**0.0**	**1.6**	**0.0**	**0.0**	**0.0**	**0.0**	**0.9**	**25.9**	**0.1**	**1.1**	**11.7**
ScanScope #2	**0.0**	**0.0**	**1.7**	**0.0**	**0.0**	**0.0**	**0.0**	**0.9**	**25.9**	**0.0**	**1.2**	**11.7**
ScanScope #3	**0.0**	**0.0**	**1.6**	**0.0**	**0.0**	**0.0**	**0.0**	**0.7**	**25.0**	**0.1**	**1.0**	**11.4**

	S#5			S#6			S#7			S#8		
	3+ %	3+, 2+ %	3+, 2+, 1+ %	3+ %	3+, 2+ %	3+, 2+, 1+ %	3+ %	3+, 2+ %	3+, 2+, 1+ %	3+ %	3+, 2+ %	3+, 2+, 1+ %
ScanScope #1	**13.7**	**58.1**	**99.7**	**1.7**	**50.7**	**97.5**	**39.5**	**73.9**	**99.8**	**50.5**	**51.5**	**95.5**
ScanScope #2	**14.0**	**60.1**	**99.7**	**1.6**	**51.6**	**97.3**	**41.5**	**74.1**	**99.8**	**51.3**	**51.9**	**95.5**
ScanScope #3	**13.2**	**58.5**	**99.5**	**1.7**	**48.9**	**97.2**	**37.2**	**73.5**	**99.7**	**50.4**	**51.4**	**95.3**

Intra-Pathologist

One pathologist read the same eight HER2 slides 5 times using manual microscopy and 5 times using a manual read of digital slides on a computer monitor. Between reads, the pathologist respected a wash-out period of over four days.
The manual microscopy results show 2 outliers out of 40 scores (5%) and the manual read of digital slides results show 3 outliers out of 40 scores (7.5%). Outliers are defined as scores that are different from the median values of the scores provided by the pathologist over 5 runs of the method.

Inter-Pathologists

Three pathologists read the same eight HER2 slides using manual microscopy and using a manual read of digital slides on a computer monitor (used the data from the clinical comparison to manual microscopy study).
The following table shows the HER2 Scores [0, 1, 2, 3] given by the three Pathologists (P1, P2, P3) in the comparison study using manual microscopy for the eight HER2 Slides (S1, S2, … S8).

R#	S1	S2	S3	S4	S5	S6	S7	S8
P1	0	0	0	1	2	2	3	3
P2	0	0	1	1	2	2	3	3
P3	1	0	1	0	2	2	3	3
Average	0	0	1	1	2	2	3	3

The following table shows the HER2 Scores [0, 1, 2, 3] given by the three Pathologists (P1, P2, P3) in the comparison study using the manual read of the digital slides for the eight HER2 Slides (S1, S2, … S8).

R#	S1	S2	S3	S4	S5	S6	S7	S8
P1	1	0	1	1	3	3	3	3
P2	1	0	1	2	3	3	3	3
P3	1	0	1	0	2	2	3	2
Average	1	0	1	1	3	3	3	3

The manual microscopy results show 3 outliers out of 24 scores (12.5%) and the manual read of digital slides results show 5 outliers out of 24 scores (21%). Outliers are defined as scores that are different from the median values of the scores provided by the three pathologists in this study.

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….

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

DEC 2 8 2007

Aperio Technologies
C/O Perry Johnston
1430 Vantage Court
Suite 106
Vista, California 92081

Re: k071671
Trade/Device Name: Scanscope XT System
Regulation Number: 21 CFR 864.1860
Regulation Name: Immunohistochemistry Reagents and Kits
Regulatory Class: Class II
Product Code: OEO
Dated: June 18, 2007
Received: June 19, 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

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 Biometrics' (OSBs') 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): K071671

Device Name: ScanScope® 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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The IHC HER2 Manual Read of Digital Slides application is intended for use as an accessory to the Dako HercepTest™ to aid the pathologist in the detection and semi-quantitative measurement of HER-2/neu (c-erbB-2) by manual examination of the digital slide of formalin-fixed, paraffin-embedded normal and neoplastic tissue immunohistochemically stained for HER-2 receptors on a computer monitor. 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 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) K071671