510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

K080254

B. Purpose for Submission:

Marketing product in the U.S.

C. Manufacturer and Instrument Name:

Aperio Technologies, Inc.

ScanScope® XT System, IHC PR Breast Tissue Manual Read of Digital Slides

D. Type of Test or Tests Performed:

Manual interpretation of digital images for immunohistochemistry Progesterone Receptor (PR) stained slides

E. System Descriptions:

1. Device Description:

   The ScanScope® XT System is an automated digital slide creation, management, viewing and analysis system which consists of an automated digital microscope slide scanner, computer, color monitor, keyboard and digital pathology information management software and image analysis software. For this particular application slides are scanned and a digital image is generated that the pathologist may use for semi-quantitative assessment of PR immunohistochemistry stained histological specimens. This assessment may be performed without use of the image analysis software and the system software makes no independent interpretations of the data.

2. Principles of Operation:

   The ScanScope® XT System is intended to provide digital images to the pathologist to supplement the quantitative interpretation of PR immunohistochemistry stained breast cancer specimens. Formalin-fixed, paraffin embedded breast cancer specimens are stained with the Dako Monoclonal Mouse Anti-Human Progesterone Receptor (Clone PgP636) and Ventana CONFIRM™ anti-Progesterone Receptor (Clone 16) according to the package inserts. Slides are then scanned and digitized at high resolution using the ScanScope XT digital slide

scanner. The pathologist manually reads and interprets the digital image without use of image analysis software. The slide is then interpreted for progesterone receptor status using the percent positivity of tumor nuclei and/or staining intensity according to the laboratory's established interpretation criteria.

3. Modes of Operation:

    Computer-assisted interpretation

4. Specimen Identification:

    Specimens are identified by slide label (a digital image is taken of the slide label and stored with the digital slide) or by barcode, if provided by the user's laboratory information system.

5. Specimen Sampling and Handling:

    Immunohistochemical stained microslides can be loaded in the ScanScope XT manually (one at a time) or automatically. The ScanScope XT can automatically scan 120 slides contained in slide racks.

6. Calibration:

    Calibration of the ScanScope XT is an automated process which is re-verified as part of the scanning process for every scanned slide. If the calibration is not within predefined limits, then the user is prevented from scanning the slide and must take steps to assure that the scan is within acceptable limits.

    When the user scans a slide, the controller software automatically performs a "prescan". The prescan is a scan of a small region of the slide which contains clear glass or "white space". The brightness and color characteristics of the image are used to correct the resulting scanned image. The main functions of the prescan process are to automatically verify that no significant tissue is present, flatten the illumination field, correct the white balance, and measure bulb brightness.

7. Quality Control:

    The accuracy of the system depends on the laboratory following the quality control instructions recommended in the labeling of the IHC PR test kits.

8. Software:

    FDA has reviewed applicant's Hazard Analysis and Software Development processes for this line of product types:

Yes_____X___ or No_____

F. Regulatory Information:

1. Regulation section:

   21 CFR §864.1860 Immunohistochemistry reagents and kits

2. Classification:

   Class II

3 Product code:

   OEO (microscope, automated, digital image, manual interpretation)

4. Panel:

   Pathology 88

G. Intended Use:

1. Indication(s) 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 ScanScope® System is intended for use as an aid to the pathologist in the detection and quantitative measurement of PR (Progesterone Receptor) by manual examination of the digital slide of formalin-fixed, paraffin-embedded normal and neoplastic tissue immunohistochemically stained for PR on a computer monitor.

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

2. Special Conditions for Use Statement(s):

H. Substantial Equivalence Information:

1. Predicate Device Name(s) and 510(k) numbers:

2. Comparison with Predicate Device:

Similarities		
Item	Device	Predicate
Device type	… 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.	Same
Specimen Type	Formalin-fixed, paraffin-embedded stained by immunohistochemistry	Same
Method of interpretation	Manual interpretation of by pathologist (no image analysis)	same
Device Components	Automated digital slide scanner, computer, color monitor, keyboard, image analysis software and digital pathology information management software	same
Image acquisition	Slide scanner based on line scanning	same

Differences		
Item	Device	Predicate
Assay used	Dako Monoclonal Mouse Anti-Human Progesterone Receptor (Clone PgP636) and Ventana CONFIRM™ anti-Progesterone Receptor (Clone 16)	Dako Hercep™ Test

I. **Special Control/Guidance Document Referenced (if applicable):**

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Guidance for Industry and FDA Staff: Format for Traditional and Abbreviated 510(k)s

Guidance for Industry and FDA Staff: Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices

J. Performance Characteristics*:*

1. Analytical Performance:

 a. Accuracy:

The substantial equivalence study was based on comparison of manual reads of the digital slide to conventional manual microscopy. Specimen for the study were immunohistochemically stained at the clinical sites using Dako in vitro diagnostic (IVD) FDA cleared Monoclonal Mouse Anti-Human Progesterone Receptor (Clone PgR 636) (K020023). All manual scoring was performed in accordance with the reagent vendor's instructions for use.

Two Clinical Laboratory Improvement Amendments (CLIA) qualified clinical sites participated in the study. Prior to their participation in the study each clinical site obtained exemption status from an Institutional Review Board (IRB).

A total set of 180 formalin-fixed, paraffin-embedded breast tissue specimens from both clinical sites were used for the study; 80 slides from the first clinical site and 100 slides from the second clinical site.

The specimens at the first clinical site were selected based on their clinical scores on file to provide an equal distribution of PR slides in the percentage of positive nuclei ranges 0%, 1% to 4%, 5% to 9%, 10% to 49%, and 50% to 100%. The specimens at the second clinical site were routine specimens taken from their clinical operation, representing the true target population of cases in a typical clinical setting.

The study was performed primarily at the participating clinical sites and all parts except the scanning of glass slides were performed at their facilities using their typical workflow. The glass slides were prepared in the sites' clinical laboratories and read by board certified staff pathologists. For the scanning of glass slides ScanScope XT instruments were operated in a simulated clinical setting at Aperio (designed to be representative of a typical lab environment).

All ScanScope XT instruments used in the study were production units and were delivered, installed, and maintained in accordance with the approved procedures, per Aperio's QSPs (Quality Systems Procedures), and as described in product documentation and labeling.

At each site, three pathologists performed a blinded read of the glass slides using a microscope and reported the percentage of positive nuclei [0%, 1%, … 100%] and

overall average intensity score [0, 1+, 2+, or 3+] 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 performed a blinded read of the digital slides on a computer monitor and reported the percentage of positive nuclei and overall average intensity score for each of the slides.

Based on the manual microscopy average percentages of positive nuclei from the three pathologists, the glass slides used for the PR study provided the following percentages of positive nuclei distribution.

Percentage	Clinical Site 1	Clinical Site 2	Total
0%	29	33	62
[1%- 5%)	12	6	18
[5%-10%)	8	3	11
[10%-50%)	15	11	26
[50%-100%]	16	47	63
Total	80	100	180

PR Percentage of Positive Nuclei Distributions.

Based on the manual microscopy average intensity scores from the three pathologists, the glass slides used for the PR study provided the following average intensity score distribution.

Intensity Score	Clinical Site 1	Clinical Site 2	Total
0	26	31	57
1+	14	3	17
2+	20	12	32
3+	20	54	74
Total	80	100	180

PR Average Intensity Score Distributions.

As it can be seen from the ER and PR percentage of positive nuclei distributions, it was not possible to obtain an equal distribution of the percentage of positive nuclei in the range from 1% to 10%. This difficulty was founded in the limited representation of this percentage range in the true target population of cases.

All glass slides were scanned using a different ScanScope XT instrument for each clinical site.

The statistical analyses are presented across all slides for each of the methods: manual microscopy and reading digital slides on a computer monitor, and comparatively between methods for manual microscopy against reading digital slides on a computer monitor.

Percentage of Positive Nuclei - Progesterone Receptor (PR)
Statistical analyses are provided for each of the three commonly used clinical relevant cut-off thresholds ≥1%, 5%, and 10% that are applied to the percentage of positive nuclei. Percent Agreement (PA) along with an exact 95% Confidence Interval (CI) are shown for the dichotomous outcomes.

Cut-Off Threshold ≥ 1%

	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	87.5%	(78.2, 93.8)	85.0%	(75.3, 92.0)	87.5%	(78.2, 93.8)
Clinical Site 2	97.0%	(91.5, 99.4)	97.0%	(91.5, 99.4)	94.0%	(87.4, 97.8)

PR 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	92.5%	(84.4, 97.2)	77.5%	(66.8, 86.1)	82.5%	(72.4, 90.1)
Clinical Site 2	93.0%	(86.1, 97.1)	94.0%	(87.4, 97.8)	93.0%	(86.1, 97.1)

PR 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	83.8%	(73.8, 91.1)	91.3%	(82.8, 96.4)	83.8%	(73.8, 91.1)
Clinical Site 2	93.0%	(86.1, 97.1)	93.0%	(86.1, 97.1)	100%	(96.4, 100)

PR Manual Microscopy vs. Manual Digital Slide Reading – same Pathologist – Agreements.

Cut-Off Threshold ≥ 5%

	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)	85.0%	(75.3, 92.0)	83.8%	(73.8, 91.1)
Clinical Site 2	98.0%	(93.0, 99.8)	99.0%	(94.6, 99.98)	97.0%	(91.5, 99.4)

PR 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	85.0%	(75.3, 92.0)	76.3%	(65.4, 85.1)	88.8%	(79.7, 94.7)
Clinical Site 2	98.0%	(93.0, 99.8)	98.0%	(93.0, 99.8)	98.0%	(93.0, 99.8)

PR 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	78.8%	(68.2, 87.1)	90.0%	(81.2, 95.6)	85.0%	(75.3, 92.0)
Clinical Site 2	99.0%	(94.6, 99.98)	97.0%	(91.5, 99.4)	98.0%	(93.0, 99.8)

PR Manual Microscopy vs. Manual Digital Slide Reading – same Pathologist – Agreements.

Cut-Off Threshold ≥ 10%

	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)	92.5%	(84.4, 97.2)	88.8%	(79.7, 94.7)
Clinical Site 2	97.0%	(91.5, 99.4)	99.0%	(94.6, 99.98)	96.0%	(90.1, 98.9)

PR 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	82.5%	(72.4, 90.1)	80.0%	(69.6, 88.1)	87.5%	(78.2, 93.8)
Clinical Site 2	96.0%	(90.1, 98.9)	95.0%	(88.7, 98.4)	97.0%	(91.5, 99.4)

PR 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	82.5%	(72.4, 90.1)	81.3%	(71.0, 89.1)	90.0%	(81.2, 95.6)
Clinical Site 2	97.0%	(91.5, 99.4)	96.0%	(90.1, 98.9)	97.0%	(91.5, 99.4)

PR Manual Microscopy vs. Manual Digital Slide Reading – same Pathologist – Agreements.

The inter-pathologist agreements for reading digital slides were in the range of 76.3%-98.0% with confidence bounds from 65.4% to 99.8% and the inter-pathologist agreements for manual microscopy were in the range of 83.8%-99.0% with confidence bounds from 73.8% to 99.98%.

The agreements between the pathologists' manual microscopy and reading digital slides were in the range of 78.8%-100.0% with confidence bounds from 68.2% to 99.98%.

Intensity Score
Statistical analyses are provided for the intensity scores. Percent Agreement (PA) along with an exact 95% Confidence Interval (CI) are shown overall for all intensity score categories 0, 1+, 2+, and 3+ 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	61.3%	(49.7, 71.9)	58.8%	(47.2, 69.6)	61.3%	(49.7, 71.9)
Clinical Site 2	74.0%	(64.3, 82.3)	76.0%	(66.4, 84.0)	88.0%	(80.0, 93.6)

PR 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	66.3%	(54.8, 76.4)	66.3%	(54.8, 76.4)	58.8%	(47.2, 69.6)
Clinical Site 2	78.0%	(68.6, 85.7)	74.0%	(64.3, 82.3)	77.0%	(67.5, 84.8)

PR 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	70.0%	(58.7, 79.7)	62.5%	(51.0, 73.1)	70.0%	(58.7, 79.7)
Clinical Site 2	73.0%	(63.2, 81.4)	81.0%	(71.9, 88.2)	96.0%	(90.1, 98.9)

PR Manual Microscopy vs Manual Digital Slide Reading – same Pathologist – Agreements.

The inter-pathologist agreements for reading digital slides were in the range of 58.8%-78.0% with confidence bounds from 47.2% to 85.7% and the inter-pathologist agreements for manual microscopy were in the range of 58.8%-88.0% with confidence bounds from 47.2% to 93.6%.

The agreements between the pathologists' manual microscopy and reading digital slides were in the range of 62.5%-96.0% with confidence bounds from 51.0% to 98.9%.

The pair-wise observations of the intensity scores [0, 1+, 2+, and 3+] are summarized in 4x4 tables.

	Pathologist 1				
	0	1+	2+	3+	Total
0	**30**	**0**	**0**	**2**	32
1+	**4**	**0**	**2**	**6**	12
Pathologist 2 2+	**4**	**0**	**3**	**12**	19
3+	**0**	**0**	**1**	**16**	17
Total	38	0	6	36	80

	Pathologist 1				
	0	1+	2+	3+	Total
0	**27**	**0**	**0**	**1**	28
1+	**4**	**0**	**2**	**5**	11
Pathologist 3 2+	**6**	**0**	**3**	**13**	22
3+	**1**	**0**	**1**	**17**	19
Total	38	0	6	36	80

	Pathologist 2				
	0	1+	2+	3+	Total
0	**25**	**1**	**2**	**0**	28
1+	**2**	**5**	**4**	**0**	11
Pathologist 3 2+	**5**	**5**	**7**	**5**	22
3+	**0**	**1**	**6**	**12**	19
Total	32	12	19	17	80

PR Manual Microscopy – Clinical Site 1 – Inter-Pathologists – Intensity Scores 4x4 Tables

		Pathologist 1				
		0	1+	2+	3+	Total
	0	**30**	0	0	0	30
	1+	1	1	0	1	3
Pathologist 2	2+	1	3	3	1	8
	3+	0	0	19	40	59
	Total	32	4	22	42	100

		Pathologist 1				
		0	1+	2+	3+	Total
	0	**32**	1	0	2	35
	1+	0	0	0	0	0
Pathologist 3	2+	0	2	5	1	8
	3+	0	1	17	39	57
	Total	32	4	22	42	100

		Pathologist 2				
		0	1+	2+	3+	Total
	0	**30**	3	1	1	35
	1+	0	0	0	0	0
Pathologist 3	2+	0	0	4	4	8
	3+	0	0	3	54	57
	Total	30	3	8	59	100

PR Manual Microscopy – Clinical Site 2 – Inter–Pathologists – Intensity Scores 4x4 Tables

Pathologist 1

Pathologist 2		0	1+	2+	3+	Total
	0	23	1	1	2	27
	1+	1	2	5	2	10
	2+	1	3	9	6	19
	3+	0	0	5	19	24
	Total	25	6	20	29	80

Pathologist 1

Pathologist 3		0	1+	2+	3+	Total
	0	23	5	7	5	40
	1+	0	0	1	1	2
	2+	2	1	7	5	15
	3+	0	0	5	18	23
	Total	25	6	20	29	80

Pathologist 2

Pathologist 3		0	1+	2+	3+	Total
	0	26	6	7	1	40
	1+	0	0	2	0	2
	2+	1	4	4	6	15
	3+	0	0	6	17	23
	Total	27	10	19	24	80

PR Manual Digital Slide Reading – Clinical Site 1 – Inter-Pathologists – Intensity Scores 4x4 Tables

	Pathologist 1				
	0	1+	2+	3+	Total
0	25	3	0	0	28
1+	0	2	0	0	2
Pathologist 2 2+	4	3	11	3	21
3+	0	0	9	40	49
Total	29	8	20	43	100

	Pathologist 1				
	0	1+	2+	3+	Total
0	29	6	0	0	35
1+	0	0	0	1	1
Pathologist 3 2+	0	2	6	3	11
3+	0	0	14	39	53
Total	29	8	20	43	100

	Pathologist 2				
	0	1+	2+	3+	Total
0	28	2	5	0	35
1+	0	0	0	1	1
Pathologist 3 2+	0	0	6	5	11
3+	0	0	10	43	53
Total	28	2	21	49	100

PR Manual Digital Slide Reading – Clinical Site 2 – Inter-Pathologists – Intensity Scores 4x4 Tables

Pathologist 1

Manual Microscopy	Manual Digital Slide Reading				
	0	1+	2+	3+	Total
0	25	5	5	3	38
1+	0	0	0	0	0
2+	0	1	5	0	6
3+	0	0	10	26	35
Total	25	6	20	29	80

Pathologist 2

Manual Microscopy	Manual Digital Slide Reading				
	0	1+	2+	3+	Total
0	26	4	1	1	32
1+	0	4	6	2	12
2+	0	2	8	9	19
3+	1	0	4	12	17
Total	27	10	19	24	80

Pathologist 3

Manual Microscopy	Manual Digital Slide Reading				
	0	1+	2+	3+	Total
0	28	0	0	0	28
1+	4	2	5	0	11
2+	7	0	9	6	22
3+	1	0	1	17	19
Total	40	2	15	23	80

PR Manual Microscopy vs. Manual Digital Slide Reading – Clinical Site 1 – Same Pathologists Intensity Scores 4x4 Tables

Pathologist 1

		Manual Digital Slide Reading				
		0	1+	2+	3+	Total
	0	27	5	0	0	32
	1+	0	2	2	0	4
Manual Microscopy	2+	0	1	11	10	22
	3+	2	0	7	33	42
	Total	29	8	20	43	100

Pathologist 2

		Manual Digital Slide Reading				
		0	1+	2+	3+	Total
	0	26	2	2	0	30
	1+	1	0	2	0	3
Manual Microscopy	2+	0	0	7	1	8
	3+	1	0	10	48	59
	Total	28	2	21	49	100

Pathologist 3

		Manual Digital Slide Reading				
		0	1+	2+	3+	Total
	0	35	0	0	0	35
	1+	0	0	0	0	0
Manual Microscopy	2+	0	0	8	0	8
	3+	0	1	3	53	57
	Total	35	1	11	53	100

PR Manual Microscopy vs. Manual Digital Slide Reading – Clinical Site 2 – Same Pathologists Intensity Scores 4x4 Tables

b. Precision/Reproducibility:

This precision study was not done on the manual read of the digital slides, but using Aperio's IHC PR 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 PR slides and was used to quantify objectively the variability of the digital slides provided by the ScanScope systems. The intensity scores are derived by the algorithm from a range of threshold values per category as delineated in the table below. Intensity values are values from 0 to 255 where 0 indicates no intensity and 255 indicates the maximum intensity. The intensity values were used only for the precision studies and are not for clinical use.

Intensity Score	Algorithm Threshold Ranges
0	255 - 210
1+	209-186
2+	185 – 156
3+	155 - 0

10 PR slides with two slides in each of the percentage of positive nuclei ranges: 0%, 1% to 4%, 5% to 9%, 10% to 50%, and 51% to 100% were sampled from site 1 to be used in a suite of precision studies. The slides were sample in sequential order using the rounded average score of the manual microscopy scores provided by the three pathologists.

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.

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.

Aperio's image analysis algorithm is capable of calculating percentages of positive nuclei smaller than 1% in which case the algorithm also calculates the average intensity of those nuclei. As a percentage of positive nuclei smaller than 1% is considered to be completely negative, the intensity scores were corrected to be 0 and intensity values to be N/A for all cases where the percentage of positive nuclei was smaller than 1%.

If using the intensity score alone to determine PR status, the user should be aware that percentages of positive nuclei smaller than 1% may affect test results.

Intra-System: The slide scores provided by image analysis over 10 consecutive scans were analyzed for all 10 PR slides.

Percentage of Positive Nuclei
The image analysis results show an overall standard deviation of 0.54% (maximum 1.47%) and average range (maximum – minimum) of 1.06% (maximum 4.78%) for

the percentage of positive nuclei [0.0-100.0%] across all runs.

Intensity Scores
The image analysis results show an overall standard deviation of 0.9 (maximum 1.60) and average range (maximum – minimum) of 2.48 (maximum 4.27) for the intensity values [0-255] across all runs.

Inter-Day/Intra-System: The 10 PR slides were scanned on the same ScanScope system over 20 times on different days.

Percentage of Positive Nuclei
The image analysis results show an overall standard deviation of 0.54% (maximum 1.09%) and average range (maximum – minimum) of 1.52% (maximum 3.90%) for the percentage of positive nuclei [0.0-100.0%] across all runs.

Intensity Value
The image analysis results show an overall standard deviation of 1.44 (maximum 2.43) and average range (maximum – minimum) of 5.29 (maximum 11.39) for the intensity values [0-255] across all runs.

Inter-system: The slide scores provided by image analysis over 10 consecutive scans on three different ScanScope XT instruments were analyzed for all 10 PR slides.

Percentage of Positive Nuclei
The image analysis results on each of the three ScanScope systems show an overall average standard deviation of 0.54%, 0.53% and 0.75% (maximum 1.47%, 1.23%, 2.05%) and average range of 1.06%, 1.23%, and 1.50% (maximum 4.78%, 4.17%, 7.20%) for the percentage of positive nuclei [0.0-100.0%] across all runs.

The image analysis results of the three ScanScope systems combined show an overall average standard deviation of 0.87% (maximum 1.57%) and average range of 2.54% (maximum 8.13%) for the percentage of positive nuclei [0.0-100.0%] across all runs.

The image analysis results show minimal variation from one ScanScope system to another as shown in the following table that shows the mean over all runs of the reported percentage of positive nuclei [0.0-100.0%] and the corresponding standard deviation (in parentheses) for the 10 PR slides (S#) for the three ScanScope systems.

	S#1	S#2	S#3	S#4	S#5	S#6	S#7	S#8	S#9	S#10
ScanScope #1	0.00 (0.00)	0.11 (0.03)	0.20 (0.08)	1.54 (0.04)	3.72 (0.31)	12.77 (0.26)	18.14 (1.47)	35.01 (0.43)	46.90 (0.60)	73.09 (0.24)
ScanScope #2	0.00 (0.00)	0.12 (0.02)	0.14 (0.05)	1.59 (0.05)	4.44 (0.60)	12.64 (0.27)	17.75 (1.23)	35.21 (0.32)	47.28 (0.55)	72.15 (0.69)

ScanScope #3	0.00 (0.00)	0.13 (0.02)	0.10 (0.00)	1.52 (0.04)	2.52 (0.17)	10.34 (0.18)	18.00 (2.05)	33.13 (0.83)	45.72 (0.55)	71.06 (0.61)

Intensity Scores

The image analysis results on each of the three ScanScope systems show an overall average standard deviation of 0.9%, 1.01%, and 0.93% (maximum 1.60%, 1.64%, 1.48%) and average range of 2.48%, 2.62%, and 2.60% (maximum 4.27%, 5.09%, 4.85%) for the intensity values [0-255] across all runs.

The image analysis results of the three ScanScope systems combined show an overall average standard deviation of 1.35% (maximum 2.03%) and average range of 4.55% (maximum 6.86%) for the intensity values [0-255] across all runs.

The image analysis results show minimal variation from one ScanScope system to another as shown in the following table that shows the mean over all runs of the reported percentage of positive nuclei [0.0-100.0%] and the corresponding standard deviation (in parentheses) for the 10 PR slides (S#) for the three ScanScope systems.

	S#1	S#2	S#3	S#4	S#5	S#6	S#7	S#8	S#9	S#10
ScanScope #1	N/A	N/A	N/A	160.1 (0.97)	203.7 (0.45)	191.8 (0.50)	186.1 (1.60)	176.2 (0.65)	148.6 (0.99)	139.9 (0.53)
ScanScope #2	N/A	N/A	N/A	160.0 (1.49)	204.1 (0.67)	191.6 (0.20)	184.1 (1.64)	175.6 (0.40)	149.3 (0.95)	141.2 (0.81)
ScanScope #3	N/A	N/A	N/A	160.5 (1.46)	202.6 (0.45)	191.7 (0.26)	185.5 (1.49)	175.9 (0.38)	152.7 (0.89)	143.5 (0.77)

Intra-Pathologist: One pathologist read the same 10 PR slides 5 times using manual microscopy and 5 times using a manual read of digital slides on a computer monitor. A wash-out period of over four days was used between the pathologist's reads.

Percentage of Positive Nuclei

The manual microscopy results show an overall average standard deviation of 6.73% (maximum 16.73%) and average range of 9.8% (maximum 40%) and the manual read of digital slides results show an overall average standard deviation of 11.81% (maximum 28.72%) and average range of 16.2% (maximum 75%).

Intensity Scores

The manual microscopy results show 8 outliers out of 50 scores (16%) and the manual read of digital slides results show 9 outliers out of 50 scores (18%). 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 10 PR slides using manual microscopy and using a manual read of digital slides on a computer monitor (this data was taken from the clinical comparison to manual microscopy study).

Percentage of Positive Nuclei

The manual microscopy results show an overall average standard deviation of 13.30% (maximum 32.15%) and average range of 17.2% (maximum 60%) and the manual read of digital slides results show an overall average standard deviation of 11.3% (maximum 20.82%) and average range of 16.0% (maximum 40%).

Intensity Scores

The manual microscopy results show 7 outliers out of 30 scores (23%) and the manual read of digital slides results show 7 outliers out of 30 scores (23%). Outliers are defined as scores that are different from the median values of the scores provided by the three pathologists.

   c. *Linearity*:

   d. *Carryover*:

   e. *Interfering Substances*:

2. Other Supportive Instrument Performance Data Not Covered Above:

K. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

L. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.