510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
INSTRUMENT ONLY TEMPLATE

A. 510(k) Number:

K080910

B. Purpose for Submission:

To obtain clearance for a new device.

C. Manufacturer and Instrument Name:

BioImagene, Inc. PATHIAM System with iScan for HER2/neu

D. Type of Test or Tests Performed:

iScan instrument and image analysis software for detection of expression of HER2/neu

E. System Descriptions:

1. Device Description:
   The PATHIAM™ System is an instrument (iScan) and image analysis software system designed to assist the qualified pathologist in the consistent quantitative assessment of marker expression in immunohistochemically stained histological sections digital images. The sample tissue is breast tissue prepared using the DAKO HercepTest Reagent Kit. The PATHIAM system consists of the BioImagene iScan slide scanner, computer with the PATHIAM Software, monitor, keyboard and mouse.

   Hardware: The iScan slide scanning device captures digital images of formalin-fixed, paraffin-embedded tissues that are suitable for storage, viewing and visual analysis. The device includes a digital slide scanner, racks for loading glass slides, an Intel based PC, dual core, dual Xeon processor, PATHIAM Software, and a monitor.

   Software: The PATHIAM Software requires competent human intervention at all steps in the analysis process. The system is designed to complement the routine workflow of a qualified pathologist screening the immunohistochemically stained histological slides with additional quantitative data to assist the reproducibility of the slide interpretation. It allows the user to select the area of interest on the breast tissue image. The user marks the area of interest for the analysis. The system software makes no independent interpretations of the data. The software will act as a tool for the user, to improve consistency and data recording. The image

produced digitally may also be used independent of the software, by allowing the pathologist to count from the digital image, rather than from the microscope.

2. Principles of Operation:
The PATHIAM System digitizes formalin-fixed, paraffin embedded normal and neoplastic tissue and provides semi-quantitative analysis of extent and intensity of stained tissue, providing the pathologist with an aid to interpretation of the level of expression of HER2/neu in breast cancer tissue. The pathologist is presented with a digital image of the tissue section and a suggested staining score (0 to 3). The pathologist then makes an assessment of the digital image and reports his/her score. Alternately, the pathologist can simply use the digitized image to perform his interpretation of the level of expression, without employing the software.

3. Modes of Operation:

Semi-automated computer-assisted interpretation

4. Specimen Identification:

Instrument operator assigned using patient surgical pathology number (SPN).

5. Specimen Sampling and Handling:

Formalin-fixed paraffin embedded normal and neoplastic tissue

6. Calibration:

Not applicable

7. Quality Control:

The PATHIAM software assesses the quality of the image to ensure it passes minimum standards before it is analyzed.

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

2. Classification:

Class II

3 Product code:

NOT

4. Panel:

88 Pathology

G. Intended Use:

1. Indication(s) for Use:
PATHIAM-Assisted Scoring: Intended for clinical laboratory use as an accessory to the DAKO HercepTest to aid in the detection and semi-quantitative measurement of HER2/neu in formalin fixed, paraffin-embedded normal and neoplastic tissue. When used with the DAKO HercepTest, PATHIAM-Assisted scoring is indicated for use as aid in the assessment of breast cancer patients for whom HERCEPTIN® (Trastuzumab) treatment is being considered. The pathologist should verify agreement with the PATHIAM score.

HER2/neu results are indicated for use as an aid in the management, prognosis and predication of therapy outcomes of breast cancer. Note: The actual correlation of the DAKO HercepTest to HERCEPTIN® clinical outcome has not been established.

2. Special Conditions for Use Statement(s):

To be used only with DAKO HercepTest.

H. Substantial Equivalence Information:

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

K062756 PATHIAM IHC Module software for HER2/neu

2. Comparison with Predicate Device:

Similarities		
Item	Device (PATHIAM System)	Predicate (PATHIAM Software)
Indications for Use	Same	When used with the DAKO HercepTest, it is indicated for use as an aid in the assessment

Similarities		
Item	Device (PATHIAM System)	Predicate (PATHIAM Software)
		of breast cancer patients for whom HERCEPTIN.
Specimen type	Same	Formalin-fixed, paraffin embedded specimens stained by immunohistochemistry reagent for HER2/neu.
Method of Cell Detection	Same	Object identification of a digitized field of view of a pathology slide, using size, shape, color and intensity as observed by a software, and by visual observation of the digitized image by a health care professional.
Assay Used	Same	DAKO HercepTest™

Differences		
Item	Device (PATHIAM System)	Predicate (PATHIAM Software)
Intended Use	The PATHIAM System consists of the PATHIAM Software, the BioImagene iScan Slide Scanner, computer keyboard, monitor and mouse intended to detect and classify cells of clinical interest by analyzing digitized images of microscope slides based on object identification of cellular objects of particular intensity, shape, size and color.	The imaging software is intended to detect and classify cells of clinical interest by analyzing digitized images of microscope slides based on object identification of cellular objects of particular intensity, shape, size and color. The software can be used with a computer and image digitizer with features specified in the labeling.
Image Analysis System	Histologic observation by a pathologist through the BioImagene iScan slide scanner.	Histologic observation by a pathologist through a specified microscope/digital camera combination or slide scanner.
Hardware components	PATHIAM Software, BioImagene iScan slide scanner, computer and monitor.	Computer, either microscope with digitizing camera or slide scanner, keyboard, mouse, high resolution color monitor and hard drive for storage.
Software components	Version PATHIAM 1.1F accepts JPEG 2000 image files from iScan.	Version PATHIAM 1.0F

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

Not applicable

J. Performance Characteristics*:*

1. Analytical Performance:
    a. *Accuracy*:

    Comparison with Manual HercepTest Method:

    Values for staining intensity were obtained from a review of PATHIAM values by trained pathologists at three sites, who viewed both the digital images and the score provided by the software, and then selected an appropriate tissue score (0 to 3). Tissue samples for the study were all procured for a single site. The same pathologist read the same slides manually using the DAKO HercepTest package insert. The manual assessment took place seven days before the experiments with the PATHIAM System were completed at the sites.

Tables 1-3: Concordance Between the PATHIAM System and Manual Scores of HercepTest® stained Breast Tissue

Table 1. Site 1. Manual vs. PATHIAM

Site 1	Manual 0-1+	Manual 2+	Manual 3+
PATHIAM 0-1+	71	17	4
PATHIAM 2+	0	25	19
PATHIAM 3+	0	1	39

Percent Agreement =135/176 X 100 = 77%
Overall % agreement (95% EXACT CI): 77% (70% - 83%)

Table 2. Site 2. Manual vs. PATHIAM

Site 2	Manual 0-1+	Manual 2+	Manual 3+
PATHIAM 0-1+	80	4	0
PATHIAM 2+	13	37	0
PATHIAM 3+	0	16	26

Percent Agreement =143/176 X 100 = 81%
Overall % agreement (95% EXACT CI): 81% (75% - 87%)

Table 3. Site 3. Manual vs. PATHIAM

Site 3	Manual 0-1+	Manual 2+	Manual 3+
PATHIAM 0-1+	86	7	0
PATHIAM 2+	3	28	9
PATHIAM 3+	0	2	41

Percent Agreement =155/176 X 100 = 88%
Overall % agreement (95% EXACT CI): 88% (82% - 92%)

Tables 4-6 – Comparison Manual Scoring between Sites

Table 4. Site 1 vs. 2. Manual vs. Manual

Site 1	Manual 0-1+	Manual 2+	Manual 3+
Manual 0-1+	70	1	0
Manual 2+	21	22	0
Manual 3+	2	34	26

Percent Agreement = 118/176 X 100 = 67%
Overall % agreement (95% EXACT CI): 67% (60% - 74%)

Table 5. Site 2 vs. 3. Manual vs. Manual

Site 2	Manual 0-1+	Manual 2+	Manual 3+
Manual 0-1+	86	7	0
Manual 2+	3	30	24
Manual 3+	0	0	26

Percent Agreement = 142/176 X 100 = 81%
Overall % agreement (95% EXACT CI): 81% (74% - 86%)

Table 6. Site 3 vs. 1. Manual vs. Manual

Site 3	Manual 0-1+	Manual 2+	Manual 3+
Manual 0-1+	69	20	0
Manual 2+	2	22	13
Manual 3+	0	1	49

Percent Agreement =140 /176 X 100 = 80%
Overall % agreement (95% EXACT CI): 80% (73% - 85%)

Tables 7-9 – Comparison PATHIAM Scoring between Sites

Table 7. Site 1 vs. 2. PATHIAM vs. PATHIAM

Site 1 vs. 2	PATHIAM 0-1+	PATHIAM 2+	PATHIAM 3+
PATHIAM 0-1+	83	9	0
PATHIAM 2+	1	40	3
PATHIAM 3+	0	1	39

Percent Agreement =162/176 X 100 = 92%
Overall % agreement (95% EXACT CI): 92% (87% - 96%)

Table 8. Site 2 vs. 3. PATHIAM vs. PATHIAM

Site 2 vs. 3	PATHIAM 0-1+	PATHIAM 2+	PATHIAM 3+
PATHIAM 0-1+	82	2	0
PATHIAM 2+	11	35	4
PATHIAM 3+	0	3	39

Percent Agreement =156/176 X 100 = 89%
Overall % agreement (95% EXACT CI): 89% (83% - 93%)

Table 9. Site 3 vs. 1. PATHIAM vs. PATHIAM

Site 3 vs. 1	PATHIAM 0-1+	PATHIAM 2+	PATHIAM 3+
PATHIAM 0-1+	88	5	0
PATHIAM 2+	4	34	2
PATHIAM 3+	0	5	38

Percent Agreement =160/176 X 100 = 91%
Overall % agreement (95% EXACT CI): 91% (86% - 95%)

b. *Precision/Reproducibility*:

In the reproducibility study between pathologists and the PATHIAM System the PATHIAM System was tested by analyzing images of the same set of 176 stained tissue specimens by three pathologists at three sites. Pathologists recorded their estimation of the score from the score provided by the PATHIAM System plus their review of the digital images provided by the software. Concordance for the PATHIAM System values between labs ranged from 89% to 92%.

BioImagene iScan Slide Scanner Reproducibility
1. iScan Slide Scanner Precision
   Eight samples with manual scores of 0, 1+, 2+ and 3+ were scanned 5 times on the iScan slide scanner. The percent agreement was calculated to be 97% (39/40).

2. Inter-run/Inter System Reproducibility
   Eight samples with manual scores of 0, 1+, 2+ and 3+ were scanned 5 times on 3 different iScan slide scanners. The agreement between the PATHIAM System scores for different scans is 100% and for different iScan slide scanners is 100%.

   c. *Linearity*:

      Not applicable

   d. *Carryover*:

      Not applicable

   e. *Interfering Substances*:

      Not applicable

2. Other Supportive Instrument Performance Data Not Covered Above:

   None

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.