510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:
k110345

B. Purpose for Submission:
Modification of the intended use of ScanView system to include the detection and enumeration of the cells in urine specimens for chromosomes 3, 7, 17 and 9p21 locus stained by fluorescence *in situ* hybridization (FISH) with Vysis UroVysion™ Bladder Cancer Kit.

C. Manufacturer and Instrument Name:
Applied Spectral Imaging Ltd., ScanView System

D. Type of Test or Tests Performed:
Automated FISH detection and enumeration of the cells for chromosomes 3, 7, 17, and 9p21 locus in urine specimens from subjects with transitional cell carcinoma of the bladder.

E. System Descriptions:

1. Device Description:
   The ScanView System is an integrated digital imaging system constructed of an external microscope, motorized multi slide stage, camera, and a workstation. It is designed to acquire images of cells and enable identification and examination of cells of interest. Pathologists can view and scan cells and record the image, using both bright field and fluorescent illumination. The acquired images can be enhanced, archived, retrieved and printed. The automated microscope enables Z motion of the slide and the motorized stage enables its X-Y motions. The microscope also includes motorized filter turret containing fluorescence filters.
2. Principles of Operation:
   The ScanView System is a software controlled system that includes features such as: acquisition of images, views, editing, relocation, enhancement capabilities, automatic/manual counting, classification and printing. The ScanView System can also scan each field of view with several fluorescent filters, each in multiple focal planes, generating and displaying a combined image. The ScanView System works with fluorescence *in situ* hybridization (FISH) on urine samples stained by FISH using the Vysis UroVysion™ Bladder Cancer Kit. The system automatically captures cells from predefined regions and classifies the cells according to predefined cells categories. After the scanning, each cell is presented in a gallery and the pathologist can approve, modify or reject the call for each cell. The result is updated accordingly, saved in the database and optionally printed out in a report.
3. Modes of Operation:
   Semi-automated; manual capture of selected regions with computer-assisted interpretation
4. Specimen Identification:
   Manual keyboard entry into the Case Data Manager
5. Specimen Sampling and Handling:

Standardized cell preparations of urine specimens are applied to microscope slides and then hybridized with the Vysis UroVysion™ Bladder Cancer Kit.

6. Calibration:
   Calibration is prepared at the time of installation.
7. Quality Control:
   The accuracy of the system depends on the laboratory following the quality control instructions as recommended by the manufacture of the Vysis UroVysion™ Bladder Cancer Kit. The control slides are tested on the ScanView System according to the same procedure as patient slides. It is the responsibility of the pathologist to assure that the control slides meet quality acceptance criteria.
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 §866.4700 – Automated fluorescence *in situ* hybridization (FISH) enumeration systems
2. Classification:
   Class II
3 Product code:
   NTH – System, Automated scanning microscope and image analysis for fluorescence *in situ* hybridization (FISH) assays
4. Panel:
   Immunology (82)

G. Intended Use:

1. Indication(s) for Use:
   The ScanView System is an automated scanning microscope and image analysis system. It is intended for *in vitro* diagnostic use as an aiding tool to the pathologist or cytogeneticist in the detection, classification and enumeration of cells of interest based on color, intensity, size, pattern, and shape. The ScanView is indicated as an accessory to the following FDA cleared/approved devices to detect the following cell types:

   1. CEP® X Spectrum Orange™/CEP® Y Spectrum Green™ DNA Probe Kit and is limited to the analysis of CEP XY probes via high magnification capture and analysis of interphase nuclei. CEP XY is indicated for use to assess the effectiveness of bone marrow transplantation in opposite-sex transplants.
   2. Human breast cancer containing the HER-2/neu gene labeled in Red and the centromere of chromosome 17 labeled in Green via fluorescence *in situ* hybridization (FISH) in interphase nuclei from formalin-fixed, paraffin embedded human breast cancer tissue specimens with Vysis® PathVysion™ HER-2 DNA Probe kit. Results from the PathVysion™ Kit are intended for use as an adjunct to existing clinical and pathologic information used as prognostic factors in stage II, node-positive breast cancer patients. The

PathVysion™ kit is further indicated as an aid to predict disease-free and overall survival in patients with stage II, node positive breast cancer, treated with adjuvant cyclophosphamide, doxorubicin, and 5-fluorouracil (CAF) chemotherapy.

3. Cells in urine specimens, stained by fluorescence *in situ* hybridization (FISH) using Vysis UroVysion™ Bladder Cancer Kit to detect aneuploidy for chromosomes 3, 7, 17, and loss of the 9p21 locus, from persons with hematuria suspected of having bladder cancer. The results are intended for use, in conjunction with and not in lieu of current standard diagnostic procedures, as an aid for initial diagnosis of bladder carcinoma in patients with hematuria and subsequent monitoring for tumor recurrence in patients previously diagnosed with bladder cancer.

The ScanView System is to be used as an adjunctive automated enumeration tool in conjunction with manual visualization.

2. Special Conditions for Use Statement(s):
   For Prescription Use Only.

H. Substantial Equivalence Information:

1. Predicate Device Name(s) and 510(k) numbers:
   Duet™ System, k050840
   ScanView System, k101291
2. Comparison with Predicate Device:

Similarities and Differences			
Item	Device ScanView System	Predicate	
		Duet™ System k050840	ScanView System k101291
Indications for Use	To detect interphase nuclei CEP XY for use to assess the effectiveness of bone marrow transplantation in opposite-sex transplants using CEP® X Spectrum Orange™/CEP® Y Spectrum Green™ DNA Probe kit.	Not applicable	Same
Indications for Use	To detect human breast cancer containing the HER-2/neu gene labeled in Red and the centromere of chromosome 17 labeled in Green via fluorescence *in situ* hybridization (FISH) in interphase nuclei from formalin-fixed, paraffin embedded human breast	Not applicable	Same

Similarities and Differences			
Item	Device ScanView System	Predicate	
		Duet™ System k050840	ScanView System k101291
	cancer tissue specimens with Vysis® PathVysion™ HER-2 DNA Probe kit		
Indications for Use	To detect aneuploidy for chromosomes 3, 7, 17, and loss of the 9p21 locus via fluorescence *in situ* hybridization (FISH) using Vysis UroVysion™ Bladder Cancer Kit in urine specimens from persons with hematuria suspected of having bladder cancer or from patients previously diagnosed with bladder cancer.	Same	Not applicable
Probe Kit	Vysis® PathVysion™ HER-2 DNA Probe kit	Not applicable	Same
Probe Kit	CEP® X Spectrum Orange™/CEP® Y Spectrum Green™ DNA Probe kit	Not applicable	Same
Probe Kit	Vysis UroVysion™ Bladder Cancer Kit	Same	Not applicable
Device Components	Automated microscope, PC, keyboard and control panel, color monitor, CCD Camera, and motorized stage	Same	Same
Spatial resolution	1280 x 1024	Not known	Same
Detection Method	FISH	Same	Same

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

Class II Special Controls Guidance Document: Automated Fluorescence *in situ* Hybridization (FISH) Enumeration Systems, 23 May 2005.
Guidance for Industry and FDA Staff: "Statistical Guidance on Reporting Results from Studies Evaluating Diagnostic Tests"; March 2007.
Guidance for the Content of Premarket Submission for Software Contained in Medical Device, CDRH, May 2005.

J. Performance Characteristics*:*

1. Analytical Performance:
   a. Accuracy:

A method comparison study was conducted at four clinical sites: 35 slides from site 1, 129 slides from site 2, 11 slides from site 3 and 20 slides from site 4 for a total of 195 slides. Measurements of the 195 slides using results obtained from the ScanView System were compared to the manual method.

The manual evaluation through the microscope eyepieces was performed in accordance with the instructions stated in the Vysis UroVysion™ Bladder Cancer Kit protocol. For each slide, the first 25 morphologically abnormal cells were analyzed. If ≥4 of the 25 cells were observed with gains for 2 or more chromosomes (3, 7 or 17) in the same cell, or >12 of the 25 cells were detected with zero 9p21 signals, the analysis was stopped and the case was considered positive. If no positive cell in the first 25 cells was detected, the analysis continued until 4 cells with multiple chromosomes were detected, or 12 cells with zero 9p21 signals, or until the whole slide had been analyzed.

For ScanView System, each slide was scanned using automatic scan method on hybridization region. The system scanned slide, detected the cells, reported the counts of the red (CEP 3), green (CEP 7), aqua (CEP 17) and gold (9p21) signals for each cell and classified the cells to normal and abnormal classes. After scanning, an image gallery of the analyzed cells along with their signal count and the relevant statistic was presented to the pathologist who would review the resultant cells and make decision on reject or modify the classification of each cell. The results interpretation criteria used for manual method according to instruction of UroVysion™ Bladder Cancer Kit protocol was followed for the ScanView Bladder FISH System to determine the positive/negative result for each sample.

The results of comparison study by evaluating 195 slides with the ScanView Bladder FISH System and with the manual method are summarized below:

		Manual Method		
		Positive	Negative	Total
ScanView Method	Positive	41	0	41
	Negative	1	153	154
	Total	42	153	195

Positive Agreement: 97.6% (95% CI: 87.7% – 99.6%)
Negative Agreement: 100.0% (95% CI: 97.6% – 100.0%)
Overall Agreement: 99.5% (95% CI: 97.2% – 99.9%)

b. *Precision/Reproducibility*:
A total of six (6) patient slides stained with UroVysion™ Bladder Cancer Kit were tested to examine the precision and reproducibility of the performance of the automatic system. The slides were scanned and reviewed according to ScanView operating instructions. The slides were selected to cover the range

of the intended use and include three positive slides (two positives near the cutoffs), and three negative slides. Each slide was scanned and examined for three runs per day for three different days at three different locations with different systems and different operators. The results of repeatability and reproducibility of within run/within instrument, between days and between instruments (systems) based on cell classification are presented below:

Slide	Cells (manual)		Within Run/Day			Between Days			Between Systems		
			Mean	Std	%CV	Mean	Std	%CV	Mean	Std	%CV
1	Normal	66	58.3	8.6	14.8	68.0	10.2	14.9	77.0	4.4	6.7
	Abnormal	7	7.7	1.2	15.1	8.3	2.1	25.0	7.7	1.5	19.9
2	Normal	45	52.7	3.5	6.7	52.0	3.6	6.9	51.3	7.2	14.1
	Abnormal	15	15.7	1.5	9.8	16.0	1.0	6.3	17.0	1.0	5.9
3	Normal	116	127.0	15.9	12.5	132.0	10.2	7.7	127.7	5.9	4.6
	Abnormal	18	19.0	2.6	13.9	17.7	3.1	17.3	16.3	0.6	3.5
4	Normal	113	141.3	10.1	7.0	133.0	7.0	5.3	142.0	22.1	15.5
	Abnormal	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
5	Normal	62	78.0	11.5	14.8	76.0	7.0	9.2	75.7	3.5	4.6
	Abnormal	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
6	Normal	201	187.3	11.0	5.9	189.0	7.0	4.8	203.7	15.3	7.5
	Abnormal	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

The reproducibility was also analyzed based on signal distributions of CEP 3, CEP 7, CEP 17, and LSI 9p21 for each slide. All negative slides showed a signal distribution of below the recording criteria, e.g. record the chromosomal pattern only if there is a gain (i.e., 3 or more signals) of two or more of CEP 3, 7, 17 or there is a loss of LSI 9p21. The results of signal distribution of four probes in 3 positive slides are summarized in the table below.

Slide	Probe	Within Run/Day			Between Days			Between Systems		
		Mean	Std	%CV	Mean	Std	%CV	Mean	Std	%CV
1	CEP 3	5.5	1.3	24.5	5.3	1.2	22.5	5.2	1.2	22.7
	CEP 7	4.4	0.8	17.8	4.3	0.8	17.7	4.2	0.7	17.6
	CEP 17	3.8	1.0	25.7	4.0	0.9	21.7	3.8	0.9	23.9
	LSI9p21	4.7	1.1	23.0	4.6	1.0	21.6	4.4	1.1	24.7
2	CEP 3	4.7	1.2	26.0	4.7	1.1	23.7	4.6	1.1	22.9
	CEP 7	4.4	0.8	17.8	4.5	1.1	23.4	4.4	1.0	22.2
	CEP 17	4.3	1.2	27.4	4.4	1.1	25.3	4.4	1.1	25.6
	LSI9p21	2.2	0.8	37.6	2.2	0.8	37.5	2.2	0.8	35.6
3	CEP 3	2.0	0.4	22.7	1.9	0.4	22.7	1.9	0.4	22.0
	CEP 7	2.0	0.4	18.9	2.0	0.4	19.0	2.0	0.4	19.9
	CEP 17	2.0	0.4	21.4	2.0	0.4	20.6	1.9	0.4	19.4
	LSI9p21	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

To assess the variation in observed signal values, the data were further analyzed with additional statistical models. Results indicated that the large variation (%CV) observed in the signal distribution is due to the heterogeneity of differences within each slide and not from measurement error of the device.

c. *Linearity*:
Not applicable.

d. *Carryover*:
Not applicable.

e. *Interfering Substances*:
Not applicable.

2. Other Supportive Instrument Performance Data Not Covered Above:
Not applicable

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.