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

A. 510(k) Number:

K050840

B. Purpose for Submission:

BioView, LTD is modifying the indications for use of the Duet™ system to include the detection and enumeration of urine specimen cells from subjects with transitional cell carcinoma of the bladder, probed by the Vysis UroVysion™ Bladder Cancer Recurrence Kit.

C. Manufacturer and Instrument Name:

BioView LTD., Duet™ System

D. Type of Test or Tests Performed:

Detection and enumeration of urine specimen cells from subjects with transitional cell carcinoma of the bladder, probed by the Vysis Uro Vysion™ Bladder Cancer Recurrence Kit which has been cleared by the FDA.

E. System Descriptions:

1. Device Description:

   The Duet System is a fully integrated imaging and scanning platform designed to enable identification and examination of cells of interest using a special dual-scan process. Cytological analysis experts can scan any slide, using both bright field and fluorescent illumination. While each type of scanning can be run by the Duet system independently, Duet has the ability to run both types of scans on the same slide, without losing the important data from either of the scans. Captured images from the first scan are saved as a "historical record" and can then be used for comparison during the second scanning stage. The images can be displayed side-by-side in a gallery of captured snapshots, referred to as targets.

2. Principles of Operation:

   The Duet System is software controlled and includes features such as: acquisition of images, views, editing, relocation, enhancement capabilities, automatic/manual counting and classification, printing, export of images and backups. The Duet System can also scan each field of view with several fluorescent filters instead of only one, generating and displaying a combined image for each field of view.

3. Modes of Operation:

   a. Automatic scanning provides a gallery of targets that the system captures for all identified fields.

   b. Manual scanning provides interactive control over the microscope. This enables a user-controlled scan of any slide under either bright field or fluorescent illumination.

4. Specimen Identification:

   Individual specimen slide case details are entered in a Slide Configuration dialog box where case details and a name are assigned to a slide. The scan process (fluorescent or brightfield), mode of scanning (automatic or interactive), scan task, and scan program (coordinates) details are entered.

5. Specimen Sampling and Handling:

   Standardized cell preparations on peripheral blood, bone marrow, amniotic fluid, and urine specimens, are applied to microscope slides.

6. Calibration:

   Calibration is recommended at least once every 6 months by Bio View service personnel.

7. Quality Control:

   N/A

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 864.5260 Automated cell locating device

2. Classification:

   Class II

3 Product code:

   JOY

4. Panel:

   81 (Hematology)

G. Intended Use:

1. Indication(s) for Use:

   The Duet 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 in the detection, classification and counting of cells of interest based on color, intensity, size, pattern, and shape. The Duet System is intended to detect the following cell types: 1. Hematopoietic cells stained by Giemsa stain, Immunohistochemistry or ISH (with bright field and fluorescent) prepared from cell suspension; 2. Amniotic cells stained by FISH (using direct labeled DNA probes for chromosomes X, Y, 13, 18, and 21); 3. Cells in urine specimens, stained by FISH (using the Vysis Uro Vysion™ Bladder Cancer Recurrence Kit for chromosomes 3, 7,17, and loss of the 9p21 locus) from subjects with transitional cell carcinoma of the bladder.

2. Special Conditions for Use Statement(s):

   N/A

H. Substantial Equivalence Information:

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

   a. Duet System (K040591)

   b. UroVysion Bladder Cancer Recurrence Kit (K011031)

c. Auto Vysion System (K041875)

2. Comparison with Predicate Device:

Similarities		
Item	Device	Predicate
Intended Use	Automated scanning microscope and image analysis system	Same
Environment Used	Cytogenetic Laboratory	Same
Software Controlled	Yes, including off-line mode	Same
Equipment and Accessories	PC workstation, camera, monitor, computer, microscope, motorized stage, software, frame grabber, connection to printers, cables	Same
Light Source	Halogen Lamp Mercury Lamp	Same

Differences		
Item	Device	Predicate
Indications for Use	1.Detects hematopoietic cells stained by Geimsa stain, IHC, or ISH; 2. Detects amniotic cells stained by FISH (using direct labeled DNA probes for chromosomes X,Y, 13, 18, and 21); 3. Detects aneuploidy for chromosomes 3, 7, 17, and loss of 9p21 locus via FISH in urine specimens from subjects with transitional cell carcinoma of the bladder, probed by the Vysis Uro Vysion Bladder Cancer Recurrence Kit.	1.Detects hematopoietic cells stained by Geimsa stain, IHC, or ISH; 2. Detects amniotic cells stained by FISH (using direct labeled DNA probes for chromosomes X,Y, 13, 18, and 21).

Differences		
Item	Device	Predicate
Constraints	1. Full reliance on the expertise and judgment of the pathologist for examination and correction. All final diagnoses must be made by qualified medical using all information available from the clinical evaluation and other diagnostic procedures. 2. The system does not suggest an interpretation, diagnosis, or treatment. 3. For use with the Uro Vysion Kit, the user should be familiar with the kit instructions. All quality controls, limitations, precautions, and warnings of the kit are valid for Duet scanning and analysis methods.	1. Full reliance on the expertise and judgment of the pathologist for examination and correction. All final diagnoses must be made by qualified medical using all information available from the clinical evaluation and other diagnostic procedures. 2. The system does not suggest an interpretation, diagnosis, or treatment.
Cell Source	Peripheral blood Amniotic fluid Bone marrow Voided urine from subjects with transitional cell carcinoma of the bladder.	Peripheral blood Amniotic fluid Bone marrow
Preparation Techniques	General-The system has been designed to work with standard cytogenetic preparation techniques used in cytogenetic labs. Staining- The cells are centrifuged and dropped on high quality slides, stained with selected cytogenetic stains.	General-The system has been designed to work with standard cytogenetic preparation techniques used in cytogenetic labs. Staining- The cells are centrifuged and dropped on high quality slides, stained with selected cytogenetic stains.

Differences		
Item	Device	Predicate
…continued…	For voided urine from subjects with transitional cell carcinoma, all preparation steps should be done according to instructions of the Vysis Uro Vysion Bladder Cancer Kit.	
Stop Criteria defined for use with the Uro Vysion Kit for FISH	FISH Positive (Multiple gain): 4 cells with gains for two or more chromosomes (3, 7, 17) in the same cell.	N/A

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

N/A

J. Performance Characteristics*:*

1. Analytical Performance:

a. Accuracy:

Comparison studies were conducted to compare the equivalency of the Duet method to the manual scoring method for detection and enumeration of slides probed by the Vysis UroVysion Bladder Cancer Recurrence Kit. Studies were conducted at BioView's laboratory in cooperation with Meir Hospital in Kfar-Saba, Israel and at the DIANON System's Laboratory in Stratford, Connecticut.

Table 1. Analysis of Agreement between Methods and Predictive Values, BioView lab

Agreement of Duet method with Manual method-Positive	95.5%
Agreement of Duet method with Manual method-Negative	91.2%
Overall Percentage of Agreement	92.9%
Positive Predictive Value	93.3%
Negative Predictive Value	93.9%

Table 2. Analysis of Kappa Value, BioView Lab

Measure of Agreement Kappa.	Value	Asymp. Std. Error	Approx. T	Approx. Sig.
Valid Cases, N=78	0.869	0.057	7.679	<0.0001

Table 3. Analysis of Agreement Measurement and Predictive Values, DIANON lab

Agreement of Duet method with Manual method-Positive	97.1%
Agreement of Duet method with Manual method-Negative	98.3%
Overall Percentage of Agreement	97.8%
Positive Predictive Value	97.1%
Negative Predictive Value	98.3%

Table 4. Analysis of Kappa Value, DIANON Lab

Measure of Agreement Kappa	Value	Asymp. Std. Error	Approx. T	Approx. Sig.
Valid Cases, N=94	0.954	0.032	9.254	<0.0001

Table 5. Pooled Results, Analysis of Agreement Measurement and Predictive Values

Agreement of Duet method with Manual method-Positive	96.2%
Agreement of Duet method with Manual method-Negative	95.7%
Overall Percentage of Agreement	95.0%
Positive Predictive Value	95.0%
Negative Predictive Value	96.7%

Table 6. Analysis of Kappa, Pooled Results

Measure of Agreement Kappa	Value	Asymp. Std. Error	Approx. T	Approx. Sig.
Valid Cases, N=172	0.918	0.030	12.042	<0.0001

b. Precision/Reproducibility:

Reproducibility was determined using four slides, with each slide analyzed on three different systems and three times on one of these systems. The slides were selected to cover the range of the intended use, to include two negative slides, one positive slide, and one near the medical decision cutoff. Two operators performed the study at BioView Lab, in cooperation with Meir Hospital, Kafar Saba, Israel.

System reproducibility, measured by its consistency, was demonstrated by calculating the percentage of agreement between measurements. A high, value indicates a small variance between different runs on the same machine, relative to the differences between machines. The calculated results of the variance within the measurements using the same Duet System showed 100% agreement (12 out of 12), with 97.1% (11 out of 12) agreement between systems. The overall agreement level was 95.0%.

c. Linearity:

N/A

d. Carryover:

N/A

e. Interfering Substances:

N/A

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.