510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:
k130775

B. Purpose for Submission:
Expansion of the Duet™ System applications to include the automated FISH detection and enumeration of gene rearrangements involving the ALK gene.
Modification of the Duet™ system from its previous configuration (Version 2.5) to contain an updated camera, display and slide loader in Version 3.5.

C. Manufacturer and Instrument Name:
Bioview, Ltd.

Duet™ System

D. Type of Test or Tests Performed:
As an adjunctive automated FISH enumeration tool, in conjunction with manual review of the digital image.

E. System Descriptions:

1. Device Description:
The Duet™ System is an automated scanning microscope and image analysis system. The Duet™ System workstation integrates a microscope, CCD camera, motorized stage, computer, keyboard, mouse, joystick, monitor and a dedicated software program. The Duet™ System scans cell samples in high resolution and in full color at high speed both in bright light and fluorescent illumination. The Duet™ System suggests classification of the cells according to their morphological features, their staining and fluorescent signals and allows the user to examine the results, correct them as needed and generate a report summarizing the sample's data.

This particular Duet™ system application is an accessory to h the Vysis® ALK Break Apart FISH Probe Kit.

2. Principles of Operation:
Samples are prepared according the instructions for the Vysis® ALK Break Apart FISH Probe kit. The user selects the appropriate areas for analysis in accordance with the ALK kit instructions. The Duet™ System automatically captures images for each of the selected areas. The user is instructed to select the cells for analysis, according the ALK kit instructions. An automatic algorithm detects fusion signals and non-fused orange and green signals in each cell and suggests a classification for the cell. The user is instructed to review the signal enumeration for all relevant cells. The total number of positive cells, negative cells and their percentage are automatically calculated and presented to the user. A pathologist confirms the calculated results by manual review of the digital image. In

the case of an equivocal sample (10 to 50% positive), additional cells are selected and analyzed. The mean of the two analyses will determine the final sample score.

3. Modes of Operation:

   Semi-automated computer assisted interpretation

4. Specimen Identification:

   Barcode reader

5. Specimen Sampling and Handling:

   Specimens are FFPE NSCLC tissue specimens on glass slides hybridized with the Vysis® ALK Break Apart FISH Probe kit.

6. Calibration:

   The system requires periodic calibration which should be performed only by BioView authorized personnel.

7. Quality Control:

   Control slides are prepared and run concurrently with patient slides according to the Vysis® ALK BREAK Apart Kit instructions. The control slides are tested on the Duet™ System according to the same procedure as patient slides. It is the responsibility of the pathologist to assure 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:

   Pathology (88)

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 aid 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 Hematopoietic cells stained by Giemsa stain, Immunohistochemistry or ISH (with brightfield and fluorescent) prepared from cell suspension.
   - Detect amniotic cells stained by FISH (using direct labeled DNA probes for chromosomes X, Y, 13, 18 and 21).
   - Detect aneuploidy for chromosomes 3, 7, 17 and loss of the 9p21 locus via FISH in urine specimens from subjects with transitional cell carcinoma of the bladder, probed by the Vysis Urovysion™ Bladder Cancer Kit.
   - Detect and quantify chromosome 17 and the HER-2/neu gene via fluorescence *in situ* hybridization (FISH) in interphase nuclei from formalin-fixed, paraffin embedded human breast cancer tissue specimens, probed by the Vysis® PathVysion™ HER-2 DNA Probe Kit. The Duet™ is to be used as an adjunctive automated enumeration tool, in conjunction with manual review of the digital image, to assist in determining HER-2/neu gene to chromosome 17 signal ratio.
   - Qualitatively detect rearrangements involving the ALK gene via fluorescence *in situ* hybridization (FISH) in formalin-fixed paraffin-embedded (FFPE) non-small cell lung cancer (NSCLC) tissue specimens, probed with the Vysis® ALK Break Apart FISH Probe Kit. The Duet™ is to be used as an adjunctive automated enumeration tool, in conjunction with manual review of the digital image.

   Note: The pathologist should verify the image analysis software application score.

2. Special Conditions for Use Statement(s):

   For prescription use only.

H. Substantial Equivalence Information:

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

   BioView Duet™ System, k061602

2. Comparison with Predicate Device:

Similarities		
Item	Device	Predicate
Specimen Type	Formalin-fixed paraffin-embedded non-small cell lung cancer (NSCLC) tissue specimens	Formalin-fixed paraffin-embedded (FFPE) breast cancer tissue specimens
Method of cell detection	Colorimetric pattern recognition by microscopic examination of prepared cells by size, shape, and intensity of counterstained nuclei as observed by an automated computer controlled microscopic and/or visual observation by a health care professional.	Same
Detection Method	Fluorescence *in situ* hybridization (FISH)	Same
Intended Use	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.	Same
Device components	• PC workstation • Camera • Monitor • Microscope • Motorized Stage • Software	Same

Differences		
Item	Device	Predicate
Probe Kit	Vysis® ALK Break Apart FISH Probe Kit	Vysis® PathVysion™ HER-2 DNA Probe Kit
Slide Capacity	Up to 200 slides	Up to 8 slides
Software Version	3.5	2.5
Camera	DAGE-MTI Excel	Sony DXC900 and JVC KY0F75U color 3CCD

Differences		
Item	Device	Predicate
Display	• 22" High Resolution LED Display • Touch-screen high resolution LED display with a pen pointing-device	17" High resolution LCD Display
Slide Loader	• "Accord Plus" (single slide stage configuration). • "Allegro Plus" (8-slide stage configuration); • "Duet-3" (50 slide loader configuration; • "Encore" (200 slide loader configuration)	• "Accord Plus" (single slide stage configuration). • "Allegro Plus" (8-slide stage configuration);

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

Guidance for Industry and FDA Staff – Class II Special Controls Guidance Document: Automated Fluorescence *in situ* Hybridization (FISH) Enumeration Systems

Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices

J. Performance Characteristics:

1. Analytical Performance:

a. Accuracy:

Slides containing formalin-fixed paraffin-embedded (FFPE) tissue specimens from patients with non-small cell lung cancer (NSCLC) were hybridized with the FDA approved Vysis® ALK Break Apart FISH Probe Kit according to the manufacturer's instructions.

Each site was asked to prepare at least 30 slides from which at least 8 slides should be either equivocal or positive. The slides were taken from archived slides that were previously counted and analyzed manually. The staff was guided that the slides were selected in consecutive order.

At three clinical sites, a total of 113 slides including 12 cases in the equivocal zone were analyzed. Method comparison results for all three sites combined are presented below in Table 1:

Table 1: Method Comparison of Duet™ System vs. Manual Method- All sites combined

		Manual Method		
		Negative	Positive	Total
Duet Method	Negative	81	1	82
	Positive	0	31	31
	Total	81	32	113

Overall agreement: 99.1% (95% CI: 95.2% - 99.8%)
Negative percent agreement: 100% (95% CI: 95.5% - 100%)
Positive percent agreement: 96.9% (95% CI: 84.3% - 99.5%)

b. Precision/Reproducibility:

A panel of 16 archived clinical specimen slides (spanning 4 value ranges : <10%, 10-25%, >25-50% and >50%) were chosen to establish device within-run, between day and between site variability.

Within-run: Three runs for each of the panel members were performed on the same day.

Slide ID	Mean	Standard Deviation	Coefficient of Variation (%)
CYNK-40	2.0 %	0.0	0.0
CYNK-63	3.3%	1.2	34.6
CYNK-64	1.3 %	1.2	86.6
CYNK-65	4.0 %	2.0	50.0
CYNK-49	7.3%	1.2	15.7
CYNK-53	12.3%	1.5	12.4
CYNK-55	6.7%	1.2	17.3
CYNK-67	16.0%	1.0	6.3
BV Val 13	48.7%	9.2	19.0
BV Val 07	50.7%	8.1	16.1
BV Val 11	34.0%	3.0	8.8
CYNK-41	30.3%	4.0	13.3
BV Val 09	74.7%	4.2	5.6
BV Val 10	57.3%	4.2	7.3
CYNK-36	69.3%	5.8	8.3
CYNK-50	53.0%	8.5	16.1

Between-day: Variability was assessed by assessing panel member performance on three different days. The shortest between-day interval was five days.

Slide ID	Mean	Standard Deviation	Coefficient of Variation (%)
CYNK-57	3.0 %	5.2	173.2
CYNK-63	2.0%	2.0	100.0
CYNK-64	0.7 %	1.2	173.2
CYNK-65	2.7 %	1.2	43.3
CYNK-53	14.0%	0.0	0.0
CYNK-67	15.7%	1.2	7.4
CYNK-69	10.3%	3.5	34.0
CYNK-70	10.7%	2.1	19.5
BV Val 13	56.7%	3.1	5.4
BV Val 07	51.0%	5.6	10.9
BV Val 11	40.0%	10.8	27.0
CYNK-47	29.3%	3.1	10.4
BV Val 03	64.7%	3.1	4.7
BV Val 06	55.3%	3.1	5.5
BV Val 09	70.0%	12.0	17.1
CYNK-50	52.3%	7.5	14.3

Site-to-Site: Reproducibility was validated by testing each slide three times, each at a different site and Duet system.

Slide ID	Mean	Standard Deviation	Coefficient of Variation (%)
CYNK-57	4.0 %	4.0	100.0
CYNK-63	4.0%	0.0	0.0
CYNK-64	3.7 %	3.2	87.7
CYNK-65	3.3 %	1.2	34.6
CYNK-53	12.0%	2.0	16.7
CYNK-55	10.3%	2.1	20.1
CYNK-67	20.3%	4.2	20.5
CYNK-69	9.7%	0.6	6.0
BV Val 07	44.0%	1.7	3.9
BV Val 11	36.7%	2.5	6.9
CYNK-41	35.0%	4.6	13.1
CYNK-47	35.0%	5.0	14.3
BV Val 06	58.7%	3.1	5.2
BV Val 09	76.7%	8.3	10.9
BV Val 10	55.3%	2.3	4.2
BV Val 02	79.3%	12.9	16.2

c. Linearity:

Not applicable.

d. Carryover:

Not applicable.

e. Interfering Substances:

Not applicable.

2. Other Supportive Instrument Performance Data Not Covered Above:

A number of probes (intended use points 1-4) were previously cleared for use with device version 2.5. In order to determine whether the performance of these probes on device version 3.5 has been impacted, additional technical descriptions and performance data were reviewed comparing performance of the two instrument versions. The additional technical descriptions and performance data were sufficient to demonstrate that device performance has not been impacted by the instrument version change.

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.