MAY 0 9 2014

Pre Market Notification Submission – 510(k)

510(K) SUMMARY
Duet™ System
510(k) Number k130775

5.1 Company Name

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5.3 Trade/Proprietary Name

Duet™ System

5.4 Classification Name

- Automated cell-location device and:
- Automated Fluorescence in situ Hybridization (FISH) Enumeration Systems.

5.5 Product Code/Regulation No.

- Automated cell-locating devices, product code: JOY, Regulation No. 864.5260.
- Automated Fluorescence in situ Hybridization (FISH) Enumeration Systems, product code: NTH, Regulation No. 866.4700.

5.6 Device Classification

Class II

5.7 Panel

Hematology and Immunology

5.8 Predicate Devices

- Duet™ System, manufactured by BioView Ltd., cleared under k030192, k040591, k050840, and k061602.
- Human manual visualization of formalin-fixed paraffin-embedded human lung cancer tissue specimens, probed by Vysis ALK Break Apart FISH Probe Kit (Hereinafter, ALK).

5.9 Intended 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:

1. Detect Hematopoietic cells stained by Giemsa stain, Immunohistochemistry or ISH (with brightfield and fluorescent) prepared from cell suspension.
2. Detect Amniotic cells stained by FISH (using direct labeled DNA probes for chromosomes X,Y,13, 18 and 21).
3. 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.
4. 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.
5. 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.

5.10 Device Description

The Duet™ System is a fully integrated imaging and scanning platform that automates time-consuming and difficult laboratory tasks of slide scanning.
The Duet™ System workstation integrates a microscope, CCD camera, motorized stage / slide-loader, computer, keyboard, mouse, joystick, monitor and a dedicated software program.
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 scans in high resolution cell samples at high speed both in bright light illumination and in fluorescent illumination.
The Duet™ System suggests classification of the cells according to their morphological features, their staining (Giemsa, IHC) and fluorescent signals, and allows the user to quickly examine the results, correct them as needed and generate a report summarizing the sample's data. The Duet™ system allows combined presentation of morphological and specific staining information of the same cell, for all the cells of the sample.

5.11 Performance Standards

No performance standards have been established for such device under Section 514 of the Federal Food, Drug, and Cosmetic Act. However, the Duet™ System complies with the following voluntary standards:

- IEC 60601-1-4
- ISO 14971:2012

5.12 Guidance

- Guidance for Industry and FDA Staff - Class II Special Controls Guidance Document: Automated Fluorescence in situ Hybridization (FISH) Enumeration Systems, issued March 23, 2005.
- Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices, issued May 11, 2005.

5.13 Substantial Equivalence

The Duet™ System with detection of the Vysis® ALK Break Apart FISH Probe Kit is as safe and effective as the previously cleared Duet™ System with detection of the Vysis® HER-2 DNA Probe Kit. The systems have similar intended use, technological characteristics, and principles of operation as its predicate device. The technological differences between the current Duet™ System and its predicate device which are listed in the table below raise no new issues of safety or effectiveness.
Performance data demonstrate that the current Duet™ System is as safe and effective as previously cleared Duet™ System. Thus, the Duet™ System is substantially equivalent.

A substantial equivalence table, which summarizes the differences between the current Duet™ system, and its predicate device, is provided below.

Characteristic	BioView Ltd. Duet™ System (Current)	BioView Ltd. Duet™ System (Predicate)
510k Number	**K130775**	**K061602**
Product Code	JOY 864.5260, NTH 866.4700	JOY 864.5260, NTH 866.4700
Intended 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: ▪ Hematopoietic cells stained by Giemsa stain, Immunohistochemistry or ISH (with bright field and fluorescent) prepared from cell suspension. ▪ Amniotic cells stained by FISH (using direct labeled DNA probes for chromosomes X, Y, 13, 18 and 21). ▪ Cells in urine specimens, stained by FISH (using the Vysis UroVysion™ Bladder Cancer Recurrence Kit for chromosomes 3, 7, 17 and 9p21 locus), from subjects with transitional cell carcinoma of the bladder. ▪ Amplification of the HER-2/neu gene via fluorescence in situ hybridization (FISH) in human breast cancer tissue specimens, probed by the Vysis® PathVysion™ HER-2 DNA Probe Kit. ▪ Detect qualitatively 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 visualization.	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: ▪ Hematopoietic cells stained by Giemsa stain, Immunohistochemistry or ISH (with bright field and fluorescent) prepared from cell suspension. ▪ Amniotic cells stained by FISH (using direct labeled DNA probes for chromosomes X, Y, 13, 18 and 21). ▪ Cells in urine specimens, stained by FISH (using the Vysis UroVysion™ Bladder Cancer Recurrence Kit for chromosomes 3, 7, 17 and 9p21 locus), from subjects with transitional cell carcinoma of the bladder. ▪ Amplification of the HER-2/neu gene via fluorescence in situ hybridization (FISH) in human breast cancer tissue specimens, probed by the Vysis® PathVysion™ HER-2 DNA Probe Kit.
Software Version	DUET SW 3.5	DUET SW 2.5
Specimen Type	formalin-fixed paraffin-embedded (FFPE) non-small cell Lung Cancer (NSCLC) tissue specimens	formalin-fixed paraffin-embedded (FFPE) Breast cancer tissue specimens

Characteristic	BioView Ltd. Duet™ System (Current)	BioView Ltd. Duet™ System (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
Device components	Automated microscope	Automated microscope
	Motorized stage with up to 200 slides using slide-loader	Motorized stage with up to 8-slides
	Color or monochrome CCD camera	Color CCD camera
	PC	PC
	Display: 22" high resolution monitor , optional 22" touch-screen with Pen pointing device	Display:17" high resolution LCD flat monitor

5.14 Performance Characteristics of the Duet™ System

A performance evaluation study was performed in order to evaluate the performance of the Duet™ System method to detect qualitatively rearrangements involving the ALK gene via fluorescence in situ hybridization in formalin-fixed paraffin-embedded non-small cell lung cancer tissue specimens, probed with the Vysis ALK Break Apart FISH Probe Kit, in terms of reproducibility and repeatability and its accuracy in comparison to the manual system.

A method comparison study was performed to provide evidence that all four previous indications cleared for the Duet™ system, can be used safely and effectively on the current system configuration that include different camera, optional slide loader and optional pen display.

Note: The performance of the Vysis ALK Break Apart Fish Probe Kit has been established with the Duet Version 3.5 configuration. Duet Version 2.5 was not validated for the ALK Break-apart test and it is not intended to perform this test.

The performance evaluation study report is comprised of the following studies, which are summarized below:

Study 1 – Precision/Reproducibility Performance - an evaluation of the performance of the Duet™ System in terms of reproducibility and repeatability, within a system and across systems.

Study 2 – Analytical Performance/Methods Comparison - a comparison of the Duet™ System method to manual scoring method.

Study 3 - Configurations method comparison – to verify that the four indications previously cleared for use with Duet version 2.5 can be used safely and effectively on the current system configuration (3.5) that contains a different camera, slide loader, and pen display.

5.14.1 Repeatability and Reproducibility Study

The purpose of this study was to evaluate the precision of the Duet™ System, for its performance with the ALK™ Kit, in terms of reproducibility and repeatability. For this purpose, the Duet™ System was evaluated in three parts, as described below:

I. Within-system and within-day
II. Within-system and between-day
III. Between-systems and sites.

Each of these studies were done using four (4) slides in each of the following categories of positive cells percentage : <10%, 10-25%, 25-50% and ≥ 50%. The study was conducted at three sites, and slides were prepared according to the probe manufacturer instructions.

Acceptance Criteria

The following acceptance criteria were defined:

- Positive samples: CV ≤ 25%
- Negative samples, with mean percentage below 4%: CV ≤180%
- Negative samples, with mean percentage above 4%: CV ≤70%

Repeatability and Reproducibility on Binary Outcome Data (Positive/Negative final result) demonstrated 100% repeatability and reproducibility in all R&R studies.

Repeatability and Reproducibility results on coefficient of variation (CV), for the three studies performed are summarized in the following table. It includes %CV Range for Individuals Slides and %CV Overall, derived from the Random Model. Note that very high CV% is expected in FISH samples with low counts. For example, if one reading finds one or two positive cells while other two readings find zero positive cells, the resulting CV% is higher than 170%.

A panel of 16 archived clinical specimen slides (4 samples in each of 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.

Category	Slide ID	Mean	Standard Deviation	Coefficient of Variation (%)
<10%	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
10-25%	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
25-50%	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
>50%	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 of on three different days. The shortest between-day interval was five days.

Category	Slide ID	Mean	Standard Deviation	Coefficient of Variation (%)
<10%	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

Category	Slide ID	Mean	Standard Deviation	Coefficient of Variation (%)
10-25%	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
25-50%	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
>50%	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.

Category	Slide ID	Mean	Standard Deviation	Coefficient of Variation (%)
<10%	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
10-25%	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
25-50%	BV Val 07	44.0%	1.7	3.9

Category	Slide ID	Mean	Standard Deviation	Coefficient of Variation (%)
	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
>50%	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

Conclusions:

- Overall %CV's derived from the Mixed Model were all well below the performance goals specified
- Of the 48 slides, each measured three (3) times, a single slide displayed a %CV above the 25% performance goal specified; %CV for the positive slide in the "Day" study was 27%, where the next highest %CV was 17.1%
- For binary outcomes:
  a. Repeatability was 100%
  b. Reproducibility was 100%

We thus conclude that the acceptance criteria were met and the Duet™ system is repeatable and reproducible.

5.14.2 Analytical Performance (Method Comparison) Study

The purpose of this study was to demonstrate the accuracy of the Duet™ System method for detection of 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, in comparison to the manual scoring method.

The study consisted of a total of 113 specimen slides. Out of these 113 slides, 32 slides were positive and 11 were equivocal.
The slides were prepared and probed using the ALK Kit, according to the manufacturer, while each slide was screened both manually and using the Duet™ system.

Acceptance Criteria
The objective of this study is to demonstrate that the Duet™ System is concordant with manual counting.

The statistical analysis performed for the pooled results included levels of agreement with the manual. The statistical analysis presented in the following tables below demonstrates the accuracy of the Duet™ system as indicated by its high level of agreement in comparison to the manual method.

		Manual scoring		
	Final Result	-	+	Total
With Duet Method	-	81	1	82
	+	0	31	31
	Total	81	32	113

Method comparison - Summary of Pooled Results

Accuracy Parameter	Value	Lower 95% CI	Upper 95% CI
Percent Agreement with Manual Negative	100%	95.5%	100%
Percent Agreement with Manual Positive	96.9%	84.3%	99.5%
Percent Overall Agreement	99.1%	95.2%	99.8%

Conclusion:
The test demonstrated that the acceptance criteria were met.
High correlation was found between the manual method and the results of the Duet™ System method, showing excellent accuracy in detecting positive and negative samples, as defined by the ALK Kit and the manual method. The overall agreement between both methods (the Duet™ and the manual) was 99.1% (95%, CI 95.2%-99.8%). No significant differences between the studies in the three sites were found, rendering the pooled analysis is valid.

5.14.3 Configurations Method Comparison Study

This study was intended to provide evidence that the changes in hardware configuration that includes different camera, optional slide loader and an optional pen display have not impacted performance with the indications cleared in previous 510(k) submissions.

The study was performed with the following guidelines:

- The study included comparison of patient slides from each of the four previously cleared indications: Hematopoietic cells, Amniotic cells, Bladder-cancer cells probed by Urovysion and Breast-cancer cells probed by Her-2 PathVysion probe.
- Same slides were evaluated on the cleared Duet™ configuration (version 2.5) and by the current submission configuration (version 3.5).
- Each of the previously cleared indications was tested using patient slides samples. Samples were selected to cover the intended use of both Normal, Abnormal and near the medical decision/cut-off (as applicable). Clinical specimen were selected from each relevant sample type and from each scoring category.

Results summary:

- The test sets included all required slides.
- Final interpretation of results was identical in all slides between new configuration and cleared configuration.
- The differences in numerical results between new configuration and cleared configuration met the pre-defined acceptance criteria for each test, in all slides.

5.15 Final Conclusion

BioView Ltd. believes that the Duet™ System is substantially equivalent to the combination of its predicate devices in terms of Intended Use, Indications for Use, technological characteristics and mode of operation. Any differences between the Duet™ System and its predicate devices do not raise new safety or effectiveness issues, based on the performance results and the analysis of similarities and differences presented above.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center - WO66-G609
Silver Spring, MD 20993-0002

May 9, 2014

BIOVIEW LTD.
ORLY MAOR
25A SIRKIN ST.
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ISRAEL

Re: K130775
Trade/Device Name: Duet™ System
Regulation Number: 21 CFR 866.4700
Regulation Name: Automated fluorescence in situ hybridization (FISH) enumeration systems
Regulatory Class: II
Product Code: NTH
Dated: May 3, 2014
Received: May 6, 2014

Dear Ms. Maor:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Reena Philip -S

Reena Philip, PhD
Director
Division of Molecular Genetics and Pathology
Office of *In Vitro* Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
k130775

Device Name
Duet™ System

Indications for Use *(Describe)*
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:
1. Detect Hematopoietic cells stained by Giemsa stain, Immunohistochemistry or ISH (with brightfield and fluorescent) prepared from cell suspension.
2. Detect Amniotic cells stained by FISH (using direct labeled DNA probes for chromosomes X,Y,13, 18 and 21).
3. 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.
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5. Qualitatively detect rearrangements involving the ALK gene via fluorescence in situ hybridization (FISH) in formalin-fixed paraffin-embedded (FFPE) non-
5-5
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.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

Yun-fu Hu -S

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