

510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION DECISION SUMMARY

A. 510(k) Number:

k080909

B. Purpose for Submission:

New device

C. Manufacturer and Instrument Name:

Ikonisys, Inc., Ikoniscope® oncoFISH™ her2 Test System

D. Type of Test or Tests Performed:

An automated system for enumeration of fluorescence in situ hybridization (FISH) signals of HER-2/neu gene in human breast cancer specimens.

E. System Descriptions:

1. Device Description:

The Ikoniscope® oncoFISH her2 Test System is an automated scanning microscope system incorporating automated slide loading and handling, low and high magnification scanning to identify targets of interest and digital image acquisition, coupled with an image analysis workstation. Microscope slides, prepared according to the DNA probe manufacturers' specifications, are placed into a multiple slide cassette, and loaded into the Ikoniscope® oncoFISH her2 Test system. The system unloads each slide, scans each one, and returns it to the cassette automatically. During scanning, images of cells exhibiting the predetermined characteristics for FISH signals are digitally photographed and stored. After all the slides are scanned, the workstation provides an image gallery for each slide that displays the image of each cell meeting predetermined characteristics and quantity and places scanned nuclei into scorable categories, established according to the specifications in the DNA probes FDA cleared labeling. The operator/reader can then evaluate the cell nuclei, and make the diagnostic determination accordingly.

2. Principles of Operation:

The Ikoniscope® oncoFISH her2 Test System combines elements of existing technologies to perform its function. Fluorescence *In-Situ* Hybridization (FISH) uses commercially available, FDA cleared, DNA probes (not supplied with the test system). Samples are prepared according to the instructions for the Vysis® PathVysion™ HER-2 DNA Probe kit. The user selects the appropriate areas for analysis in accordance with the PathVysion™ kit instructions. The oncoFISH system scans and captures images for each of the selected areas and the automatic algorithm detects and enumerates the fluorescent signals. The user reviews the signal enumeration for all relevant cells and the results (total number of cells and overall signal ratio) are automatically calculated by the system.

There is no change in the system hardware from the previously cleared system. Software changes were implemented to support the new indication for use for HER-2/neu FISH automated enumeration. The device methodology is well

- established.
3. Modes of Operation:
Semi-automated
 4. Specimen Identification:
Barcode
 5. Specimen Sampling and Handling:
Samples should be obtained and handled according to the laboratory's standard operating procedures and following the protocol described in the package insert for the PathVysion probe kit.
 6. Calibration:
Calibration of the Ikoniscope is done at the time of installation by Ikonysis.
 7. Quality Control:
ProbeChek® quality control slides by Abbott should be used with the PathVysion probes as recommended by the probe manufacturer.
 8. Software:
FDA has reviewed applicant's Hazard Analysis and Software Development processes for this line of product types:
Yes X or No Comprehensive software documentation at a Moderate Level of Concern was provided

F. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
NTH	Class II	21 CFR 866.4700 Automated fluorescent in situ hybridization (FISH) enumeration system	Immunology 82

G. Intended Use:

1. Indication(s) for Use:
The Ikoniscope® oncoFISH® her2 Test System is an automated scanning microscope coupled with image analysis, acquisition and display functions. It is intended for in-vitro diagnosis as an aid to the technologist or pathologist in the detection, classification, and enumeration of cells of interest based on the ratio of HER-2 genes to CEP 17 genes. The Ikoniscope® oncoFISH® her2 Test System is intended to detect amplification of the HER-2/neu breast gene via fluorescence in situ hybridization (FISH) in formalin-fixed, paraffin-embedded human breast cancer tissue specimens.
2. Special Conditions for Use Statement(s):
For use only with PathVysion® HER-2 DNA Probe Kit (Abbott Molecular, Inc., Des Plaines, IL)

H. Substantial Equivalence Information:

1. Predicate Device Name(s) and 510(k) numbers:
BioView Duet™ System k050840, k061602
2. Comparison with Predicate Device:

Similarities		
Item	Device	Predicate
Intended Use	The Ikoniscope® oncoFISH® her2 Test System is an automated scanning microscope coupled with image analysis, acquisition and display functions. It is intended for in-vitro diagnosis as an aid to the technologist or pathologist in the detection, classification, and enumeration of cells of interest based on the ratio of HER-2 genes to CEP 17 genes. The Ikoniscope® oncoFISH® her2 Test System is intended to detect amplification of the HER-2/neu Breast gene via fluorescence in situ hybridization (FISH) in formalin-fixed, paraffin-embedded human breast cancer tissue specimens.	Same
Staining	Fluorescence In Situ Hybridization (FISH)	Same
Method of operation	Automated epi-fluorescent microscopy digital image capture of wave-length specific signals fluorescent signals	Same
Specimen Presentation	Automated	Same
Specimen Processing	Automated	Same
Clinical Decision Point	Amplified/Non-amplified	Same
Specimen Type	Tissue	Same
Enumeration	Ratio	Same

Differences		
Item	Device	Predicate
Magnification	Microscope: 4X, 20X, 100X	Microcopy: 10X, 40X

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

Determination of Intended Use for 510(k) Devices; Guidance for CDRH Staff
Guidance for Content of Premarket Submissions of Software Contained in Medical
Devices FDA - General Principles of Software Validation
Medical Device Requirements - Human Factors and the FDA
FDA Guidance Document for In Vitro Diagnostics Devices that utilizes In Situ
Hybridization technology for detection of Somatic Mutations – 1996
FDA Good Automated Manufacturing Practices – Guide for Validation of Automated
Systems (ISPE/GAMP Forum, 2001)
FDA Guidance Document for Off-The Shelf Software Use in Medical Devices - 1999

J. Performance Characteristics:

1. Analytical Performance:

a. *Accuracy:*

Four clinical laboratories provided previously manually enumerated PathVysion slides for the method comparison study. The PathVysion slides from the four collection sites were tested at two (2) clinical laboratories with two (2) Ikoniscope® oncoFISH her2 systems. Each collection site provided 25 consecutive amplified (positive) and 25 non-amplified (negative) PathVysion slides for oncoFISH her2 testing. The H&E slides with the scribed area of interest for each corresponding PathVysion slide were used for the oncoFISH her2 testing. A total of 182 slides were enumerated by the PathVysion manual and oncoFISH her2 methods. The slides consisted of 100 non-amplified slides with a HER2/CEP17 ratio of 0.8 – 1.91 and 82 amplified slides with a HER2/CEP17 ratio of 2.02 – 11.3 by manual PathVysion. Reasons for the discordant results were poor slide quality, high background or few cells (n=3); operator not properly selecting amplified images from scan (n=3) or region of interest (ROI) identified on the H&E and PathVysion slides differ (n=1).

Overall Agreement was 94.5% (172/182), Positive Percent Agreement 91.5% (75/82) and Negative Percent Agreement 97% (97/100).

Table 1. Ikoniscope oncoFISH her2 vs. PathVysion Manual Read

		Manual PathVysion		
		Amplified	Non-amplified	Total
Ikoniscope oncoFISH her2	Amplified	75	3	78
	Non-amplified	7	97	104
	Total	82	100	182

b. *Precision/Reproducibility:*

A panel of six (6) breast cancer specimens, consisting of 2 each with HER2/CEP17 ratios of 0.8 – 1.7; 1.8 – 2.2; and > 2.2 by previously performed manual PathVysion were evaluated at 3 clinical sites over 3 non-consecutive

days. Manual PathVysion results were determined after which the samples were evaluated with the oncoFISH her2 system. Six slides could not be evaluated due to poor quality. Results of the reproducibility study are shown below in Table 2.

Table 2. Reproducibility Results.

Specimen	Statistic	Manual PathVysion HER2/CEP17 ratio			Ikoniscope oncoFISH HER2/CEP17 ratio		
		Site 1	Site 2	Site 3	Site 1	Site 2	Site 3
1	Mean	1.83	1.51	1.83	1.9	1.48	1.92
1	SD	0.15	0.12	0.01	0.05	1.013	0.34
1	C.V. (%)	8.33	8.03	0.31	2.41	8.63	17.68
1	N	3	3	3	3	3	3
2	Mean	1.77	1.14	1.69	1.98	1.23	1.5
2	SD	0.06	0.1	0.06	0.15	0.13	0.06
2	C.V. (%)	3.27	8.68	3.29	7.52	10.35	3.92
2	N	3	3	3	2	2	3
3	Mean	1.17	0.99	1.12	1.16	1	1.54
3	SD	0.06	0.01	0.1	0.06	0.05	0.26
3	C.V. (%)	4.95	1.17	9.32	4.8	4.49	16.92
3	N	3	3	3	3	3	3
4	Mean	1.2	0.9	1.13	1.36	0.83	1.36
4	SD	0.1	0.02	0.07	0.03	0.1	0.03
4	C.V. (%)	8.33	2.37	6.26	2.55	11.93	1.85
4	N	3	2	2	3	2	3
5	Mean	10.47	6.01	7.75	11.92	6.67	10.47
5	SD	1.84	0.31	1.83	0.85	0.69	0.77
5	C.V. (%)	17.63	5.08	23.68	7.1	10.38	7.31
5	N	3	3	3	3	3	3
6	Mean	2.1	1.33	2.13	1.75	1.07	1.56
6	SD	0.1	0.26	0.43	0.25	0.01	0.31
6	C.V. (%)	4.76	19.27	20.15	14.26	0.66	19.64
6	N	3	3	3	3	2	3

Sites 1 and 3 each had discordant results between manual PathVysion and oncoFISH her2 for slide #6, while Site 2 reported this slide as non-amplified for both manual PathVysion and oncoFISH. Slides 1 and 2 were indeterminate ($HER2/CEP17 = 1.8 - 2.2$) based on their original PathVysion results but in this reproducibility study, these two slides were found non-amplified by both manual PathVysion (mean ratios 1.14 – 1.83) and oncoFISH (mean ratios = 1.23 – 1.98) by all three sites. Two (2) manual PathVysion slides were not readable due to no cells to score or failed hybridization. Four (4) Ikoniscope oncoFISH slides could not be analyzed with one had no cells to score, one with insufficient cells and two

unacceptable scan. Based on final results, concordance between sites was 83.3%.

Scan-to-scan variation with the Ikoniscope® oncoFISH her2 system was performed at one (1) clinical site. One daily panel of slides was re-scanned two (2) additional times on different days with the Ikoniscope yielding results from three (3) Ikoniscope® oncoFISH her2 runs. The table below (Table 3) lists the oncoFISH her2 ratio results with the mean, standard deviation (SD) and percent coefficient of variation (%CV) for the three scans of the same six (6) specimens.

Table 3. Scan-to-Scan Variation Results

Specimen	N	Ikoniscope oncoFISH her2 HER2/CEP17 ratio		
		Mean	SD	%CV
1	3	1.63	0.05	3.06
2	3	1.63	0.07	4.79
3	3	1.31	0.08	6.54
4	3	1.45	0.167	11.49
5	3	10.36	0.56	5.49
6	3	1.66	0.1	6

- c. *Linearity:*
Not Applicable
- d. *Carryover:*
Not Applicable
- e. *Interfering Substances:*
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.