

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY**

A. 510(k) Number:

k122143

B. Purpose for Submission:

Device modification. Clearance for use with the Benchmark ULTRA™ stainer.

C. Manufacturer and Instrument Name:

Ventana Medical Systems, Inc., Virtuoso™ System for IHC Progesterone Receptor (PR)
(Clone 1E2)

D. Type of Test or Tests Performed:

Computer-assisted image analysis scoring and manual scoring of digital images of PR immunohistochemistry stained slides.

E. System Descriptions:

1. Device Description:

No change. See k111869.

2. Principles of Operation:

No change. See k111869.

3. Modes of Operation:

No change. See k111869.

4. Specimen Identification:

No change. See k111869.

5. Specimen Sampling and Handling:

No change. See k111869.

6. Calibration:

Calibration is performed at installation and annually by a Ventana Medical Services Inc. field service technician.

7. Quality Control:

No change. See k111869.

8. Software:

FDA has reviewed applicant's Hazard Analysis and Software Development processes for this line of product types:

Yes or No

F. Regulatory Information:

1. Regulation section:

21 CFR §864.1860, Immunohistochemistry reagents and kits

2. Classification:

Class II

3. Product code:

NQN – Microscope, automated, image analysis, immunohistochemistry, operator intervention, nuclear intensity and percent positivity

NOT – Microscope, Automated, Image Analysis, Operator Intervention

OEO – Automated Digital Image Manual Interpretation Microscope

4. Panel:

Pathology (88)

G. Intended Use:

1. Indication(s) for Use:

The Virtuoso™ system provides automated digital slide creation, management, analysis, and viewing. It is intended for in vitro diagnostic use as an aid to the pathologist in the display, detection, counting, review and classification of tissues and cells of clinical interest based on particular morphology, color, intensity, size, pattern and shape.

The Virtuoso™ System for IHC PR (1E2) is for digital read and image analysis applications. This particular Virtuoso™ system is intended for use as an aid to the

pathologist in the detection and semi-quantitative measurement of progesterone receptor (PR) protein in formalin-fixed, paraffin-embedded normal and neoplastic tissue. This device is an accessory to the Ventana Medical Systems, Inc. CONFIRM™ anti-Progesterone Receptor (PR) (1E2) Rabbit Monoclonal Primary Antibody assay. The CONFIRM™ anti-Progesterone Receptor (PR) (1E2) Rabbit Monoclonal Primary Antibody assay is indicated for use as an aid in the assessment of breast cancer patients for whom endocrine treatment is being considered (but is not the sole basis for treatment).

Note: The IHC PR (1E2) Digital Read and Image Analysis applications are adjunctive computer-assisted methodologies for the qualified pathologist in the acquisition and measurement of images from microscope glass slides of breast cancer specimens stained for the presence of PR protein. The pathologist should verify agreement with the Image Analysis software application score. The accuracy of the test results depends on the quality of the immunohistochemical staining. It is the responsibility of a qualified pathologist to employ appropriate morphological studies and controls as specified in the instructions for the CONFIRM™ anti-Progesterone Receptor (PR) (1E2) Rabbit Monoclonal Primary Antibody used to assure the validity of the Virtuoso System for IHC PR Digital Read and Image Analysis scores. The actual correlation of CONFIRM™ anti-PR antibody to clinical outcome has not been established.

2. Special Conditions for Use Statement(s):

For prescription use only.

Indicated for use with either the Benchmark XT or ULTRA™ stainers.

* A precautionary statement indicating that this device has not been tested, or its safety and effectiveness validated, when used with a personal computer (PC) from home was included in the Limitations section of the device package insert.

H. Substantial Equivalence Information:

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

Ventana Virtuoso™ System for IHC PR (1E2) for use with the Benchmark XT stainer (k111869)

2. Comparison with Predicate Device:

Similarities		
Item	Device Ventana Virtuoso™ System for IHC PR (1E2) with the Benchmark ULTRA™ stainer	Predicate Ventana Virtuoso™ System for IHC PR (1E2) with the Benchmark XT stainer
Intended Use	This device is intended for in vitro diagnostic (IVD) use. The Virtuoso™ System provides automated digital slide creation, management, analysis, and viewing. It is intended for IVD use as an aid to the pathologist in the display, detection, counting, review and classification of tissues and cells of clinical interest based on particular morphology, color, size, intensity, pattern, and shape.	Same
Sample type	Formalin-fixed, paraffin embedded tissue stained by IHC.	Same
Device components	Automated digital slide scanner, computer, color monitor, and image analysis software and digital pathology information management software.	Same
Primary Antibody (Assay) Reagent	Ventana CONFIRM™ PR (1E2)	Same

Differences		
Item	Device Ventana Virtuoso™ System for IHC PR (1E2) with the Benchmark ULTRA™ stainer	Predicate Ventana Virtuoso™ System for IHC PR (1E2) with the Benchmark XT stainer
Stainer	Benchmark ULTRA™ Features 30 slide positions and 35 reagents. The Benchmark ULTRA™ is a continuous access stainer, capable of random access processing.	Benchmark XT™ Single drawer of 30 slide positions and 35 reagents.

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

None.

J. Performance Characteristics:

1. Analytical Performance:

a. Accuracy:

The performance of the Virtuoso™ System for PR (1E2) when used in conjunction with the Benchmark ULTRA™ stainer was validated by assessing the positive percent agreement (PPA), negative percent agreement (NPA), and overall percent agreement (OPA) between the reference manual method (with a traditional microscope) and both the digital read (DR) and image analysis (IA) applications of the Virtuoso™ system. A total of 120 patient slides were scored as positive or negative for PR status using the percent positive staining cutoff of <1% for the distinction between positive and negative staining. The agreements with the 95% confidence intervals (CI) around the agreements are shown below. All confidence intervals are 2-sided 95% confidence intervals calculated using the score method.

Table 1:
Digital Read vs. Manual Scoring

Digital Read	Manual Microscopic Read		
	Positive	Negative	Total
Positive	68	1	69
Negative	4	40	44
Total	72	41	113
PPA n/N (%) (95% CI)	68/72 (94.4) (86.6-97.8)		
NPA n/N (%) (95% CI)	40/41 (97.6) (87.4-99.6)		
OPA n/N (%) (95% CI)	108/113 (95.6) (90.1-98.1)		

Table 2:
Image Analysis vs. Manual Scoring

Digital Read	Manual Microscopic Read		
	Positive	Negative	Total
Positive	71	1	72
Negative	3	39	42
Total	74	40	114
PPA n/N (%) (95% CI)	71/74 (95.9) (88.7-98.6)		
NPA n/N (%) (95% CI)	39/40 (97.5) (87.1-99.6)		
OPA n/N (%) (95% CI)	110/114 (96.5) (91.3-98.6)		

Agreement between digital reads and image analysis to manual scoring was assessed using two Ventana DAB detection kits (iVIEW™ vs. ultraView™). Reanalysis of the results summarized in the two tables above by stratification by detection kit also yielded acceptable results.

b. Precision/Reproducibility:

Not applicable.

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.