K140465

MAR 2 0 2014

VENTANA®
A Member of the Roche Group

510(k) Summary

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of 21 CFR 807.92.

Submitter Name	Ventana Medical Systems, Inc. Digital Pathology
Address	203 Ravendale Drive Mountain View, CA 94043
Contact	Mr. Mort Minaee Phone: (408) 207-4201 FAX: (408) 207-4299 Email: mort.minaee@ventana.roche.com
Date Prepared	February 21, 2014
Proprietary Name	Virtuoso™ System for IHC ER (SP1)
Common Name	Digital pathology and image analysis system for immunochemistry-stained slides
Classification Name	Immunohistochemistry reagents and kits
Product Codes	NOT, NQN, OEO, 21 CFR § 864.1860
Predicate Devices	Virtuoso™ IHC ER (SP1) [Benchmark XT Stainer] K130515
Establishment Registration	Ventana Medical Systems Inc., Mountain View, California, #3007207919.

1. DEVICE DESCRIPTION

General Description

The Virtuoso™ System is an instrument-plus-software system designed to assist the qualified pathologist in the consistent assessment of protein expression in immunohistochemically stained histologic sections from formalin-fixed, paraffin-embedded normal and neoplastic tissues. The system consists of a slide scanner (iScan), computer, monitor, keyboard, mouse, image analysis algorithms for specific immunohistochemical markers, and software with a Windows web browser-based user interface. Virtuoso is a web-based, end-to-end, digital pathology software solution that allows pathology laboratories to acquire, manage, view, analyze, share, and report digital images of pathology specimens. Using the Virtuoso software, the pathologist can view digital images, add annotations, make measurements, perform image analysis, and generate reports.

Hardware: The iScan slide scanning device captures digital images of formalin-fixed, paraffin-embedded tissues that are suitable for storage and viewing. The device includes a digital slide scanner, racks for loading glass slides, computer, scanner software, keyboard, mouse and monitor.

Software: The Virtuoso software is designed to complement the routine workflow of a qualified pathologist in the review of immunohistochemically stained histologic slides. It allows the user to select fields of view (FOVs) in the digital image for analysis and provides quantitative data on these FOVs to assist with interpretation. The software makes no independent interpretations of the data and requires competent human intervention for all steps in the analysis process.

Additional Materials Required:

- Ventana CONFIRM™ anti-Estrogen Receptor (ER) (SP1) Rabbit Monoclonal Primary Antibody
- Ventana Benchmark ULTRA stainer
- Reagents for visualization, such as DAB chromogen
- Associated materials for completing immunohistochemical staining according to the appropriate package insert
- Color printer if user wishes to print color copies

Device Quality Control

The quality of results depends on the laboratory following the quality control instructions recommended in the labeling of the immunohistochemistry (IHC) reagents. The software also performs a quality check on the digital images to determine if they are suitable for further analysis using "Image Quality Assessment" algorithms.

Modes of Operation

- Manual scoring of IHC ER stained slide images on a computer monitor (digital read).
- Computer scoring of IHC ER stained slide images performed by ER Image Analysis Application with manual verification by the pathologist.

Summary of Procedure

Samples are obtained as formalin-fixed, paraffin-embedded tissue blocks. Histologic sections are prepared and mounted onto glass slides. Slides are reacted with the ER (SP1) primary antibody, and are then visualized using DAB on the Benchmark ULTRA stainer. Prepared slides are loaded into the Virtuoso system scanner and scanned. Control slides should also be scanned and reviewed before scoring the slides. The resulting digital images are reviewed by the pathologist on a computer monitor, and appropriate fields of view (FOVs) are then selected for analysis by the Virtuoso software. The Virtuoso software produces a quantitative score for the FOV and an aggregate score over all the FOVs for the whole slide. The pathologist has the choice of accepting the result or overriding with his/her own score for some or all FOVs.

2. INDICATIONS 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 ER (SP1) 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 estrogen receptor (ER) protein in formalin-fixed, paraffin-embedded neoplastic tissue. This device is an accessory to Ventana Medical Systems, Inc. CONFIRM™ anti-Estrogen Receptor (ER) (SP1) Rabbit Monoclonal Primary Antibody assay. The CONFIRM™ anti-Estrogen Receptor (ER) (SP1) 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). For prescription use only.

Note: The IHC ER (SP1) 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 ER 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-Estrogen Receptor (ER) (SP1) Rabbit Monoclonal Primary Antibody used to assure the validity of the Virtuoso System for IHC ER Digital Read and Image Analysis scores.

3. TECHNOLOGICAL CHARACTERISTICS

The following chart describes similarities and differences between the two test systems.

Characteristic	Virtuoso™ IHC ER (SP1) [Benchmark ULTRA Stainer]	Virtuoso™ IHC ER (SP1) [Benchmark XT Stainer] K130515
Intended Use/Indications for 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. The Virtuoso™ System for IHC ER (SP1) 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 estrogen receptor (ER) protein in formalin-fixed, paraffin-embedded neoplastic tissue. This device is an accessory to Ventana Medical Systems, Inc. CONFIRM™ anti-Estrogen Receptor (ER) (SP1) Rabbit Monoclonal Primary Antibody assay. The CONFIRM™ anti-Estrogen Receptor (ER) (SP1) 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). For Prescription Use Only.	SAME SAME SAME
Specimen Type	Formalin-fixed, paraffin-embedded tissue stained by immunohistochemical technique	Same
System Operation (Digital Read and Image Analysis)	Histologic observation by a pathologist through the viewer and image analysis systems	Same
Hardware and Software	Ventana iScan slide scanner, computer, color monitor, proprietary software for ER (SP1)	Same
Platform Components	mouse, keyboard, windows web browser.	Same
Primary Antibody (Assay) Reagent	Ventana CONFIRM™ anti-Estrogen Receptor (ER) (SP1) Rabbit Monoclonal Primary Antibody	Same
Ancillary Reagents/Stainers	DAB universal chromogen kits, Slides stained with Benchmark ULTRA stainer	DAB universal chromogen kits, Slides stained with Benchmark XT stainer
Localization of IHC positive stain	Nucleus	Same
Interpretation	Interpretation is performed by the pathologist.	Same

4. NON-CLINICAL PERFORMANCE EVALUATION

See k130515

5. CLINICAL PERFORMANCE EVALUATION

The objective of the clinical study was to establish agreement (concordance) of the Virtuoso System Digital Read and Image Analysis applications relative to the reference method of manual microscopy in the detection and semi-quantitative measurement of ER protein in formalin-fixed, paraffin-embedded neoplastic tissue using ER (SP1) reagents and immunohistochemically stained on the BenchMark ULTRA automated slide staining device and scanned on iScan Coreo.

125 cases were available from the original study and were evaluated per inclusion/exclusion criteria. 14 cases were ineligible for the study due to the following reasons: Run control slides and original tissue blocks unavailable (9 cases), Original cases stained on the BenchMark XT platform instead of BenchMark ULTRA platform (6 cases) and Broken or cracked slide (2 cases).

The Virtuoso System for IHC ER (SP1) with the Benchmark ULTRA stainer was clinically validated via a concordance study where 111 cases were evaluated three ways by one pathologist at one site in a blinded fashion. Each case was scored (1) manually with a routine microscope, (2) as a digital image, and (3) by way of the image analysis application using a different order of slide presentation for each round. The manual score (reference result) was compared to both the digital read result and the image analysis result.

For the 111 evaluable cases, the overall percent agreement rate, defining negative and positive at the 1% positive staining cutoff, was 98.2% The PPA and NPA rates were 98.6% and 97.6%, respectively. Table 1 below provides a summary of the results. This study objective was met, as the acceptance criterion of 75% minimum total agreement between the digital read and manual read was met.

Table 1: 2X2 Agreement Table, ER Clinical Assessment Digital Read vs. Manual Read

	Manual Microscopic Read		
Digital Read	**Positive**	**Negative**	**Total**
Positive	69	1	70
Negative	1	40	41
Total	70	41	111
Positive Percent Agreement (PPA) n/N (%) (95% CI)	69/70 (98.6) (92.3-99.7)		
Negative Percent Agreement (NPA) n/N (%) (95% CI)	40/41 (97.6) (87.4-99.6)		
Overall Percent Agreement (OPA) n/N (%) (95% CI)	109/111 (98.2) (93.7-99.5)		

Positive=a clinical score of ≥1%; Negative= a clinical score of 0-0.99%.
All confidence intervals are 2-sided 95% confidence intervals calculated using the score method.

For the 111 evaluable cases, the overall percent agreement rate, as defined above, was 91.0%. The PPA and NPA rates were 91.4% and 90.2%, respectively. Table 2 below provides a summary of the results. This study objective was also met as the acceptance criterion of 75% minimum total agreement between the image analysis read and manual read was met.

Table 2: 2X2 Agreement Table, ER Clinical Assessment Image Analysis vs. Manual Read

	Manual Microscopic Read		
Image Analysis Read	**Positive**	**Negative**	**Total**
Positive	64	4	68
Negative	6	37	43
Total	70	41	111
Positive Percent Agreement (PPA) n/N (%) (95% CI)	64/70 (91.4) (82.5-96.0)		
Negative Percent Agreement (NPA) n/N (%) (95% CI)	37/41 (90.2) (77.5-96.1)		
Overall Percent Agreement (OPA) n/N (%) (95% CI)	101/111 (91.0) (84.2-95.0)		

6. CONCLUSIONS

Concordance studies were performed for the Virtuoso System for IHC ER (SP1) with the Benchmark ULTRA stainer. The overall concordance between the Virtuoso digital read and the manual method was 98.2%. Overall concordance between the Virtuosos image analysis and the manual method was 91.0%. The test system was shown to be safe and effective for its intended use.

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

March 20, 2014

VENTANA MEDICAL SYSTEMS, INC.
MORTEZZA MINAEE
SENIOR DIRECTOR, REGULATORY AFFAIRS
203 RAVENDALE DRIVE
MOUNTAIN VIEW CA 94043

Re: K140465
Trade/Device Name: Virtuoso™ System for IHC (SP1) with Benchmark ULTRA stainer
Regulation Number: 21 CFR 864.1860
Regulation Name: Immunohistochemistry reagents and kits
Regulatory Class: II
Product Code: NQN, OEO, NOT
Dated: February 21, 2014
Received: February 24, 2014

Dear Mr. Minaee:

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 Small Manufacturers, International and Consumer Assistance 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 Small Manufacturers, International and Consumer Assistance 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

for

Maria M. Chan, Ph.D.
Director
Division of Immunology and Hematology Devices
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)*

k140465

Device Name
Virtuoso System for IHC ER (SP1)

Indications for Use *(Describe)*

Intended Use and Indications 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 ER (SP1) 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 estrogen receptor (ER) protein in formalin-fixed, paraffin-embedded neoplastic tissue. This device is an accessory to the CONFIRM anti-Estrogen Receptor (ER) (SP1) Rabbit Monoclonal Primary Antibody Assay. The CONFIRM anti-Estrogen Receptor (ER) (SP1) Rabbit Monoclonal Primary Antibody 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 ER (SP1) 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 ER 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- Estrogen Receptor (ER) (SP1) Rabbit Monoclonal Primary Antibody assay used to assure the validity of the Virtuoso System for IHC ER Digital Read and Image Analysis scores. The actual correlation of CONFIRM anti-Estrogen Receptor (ER) (SP1) Rabbit Monoclonal Antibody to clinical outcome has not been established. This device is intended for IHC slides stained on the BenchMark XT and BenchMark ULTRA stainers.

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

This section applies only to requirements of the Paperwork Reduction Act of 1995.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 79 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."