MAR - 5 2012

K111869

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# SECTION 7
# 510(k) SUMMARY

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92. The assigned 510(k) number is K111869.


**807.92 (a)(1): Name:** Ventana Digital Pathology
**Address:** 919 Hermosa Court
Sunnyvale, CA 94085

**Phone:** (408) 207-4200
**FAX:** (408) 207-4299
**Contact:** Mr. Indu Lakshman


**807.92 (a)(2): Device name- trade name and common name, and classification**

**Trade name:** Virtuoso™ System for IHC PR (1E2)

**Common Name:** Digital pathology and image analysis system for immunochemistry-stained slides

**Classifications:** 21 CFR § 864.1860- Immunohistochemistry reagents and kits

**Product Codes**: NQN, OEO

**807.92 (a)(3): Identification of the legally marketed predicate devices**

The Virtuoso System for IHC PR (1E2) is substantially equivalent to the ScanScope® System for ER and PR (Aperio Technologies, Inc., Vista, CA) cleared under premarket notification K073677 on August 1, 2008. Both devices are digital pathology and image analysis systems for the consistent assessment of pathology interpretations using immunohistochemically stained slides (in this case, stained for ER expression), and both systems include slide scanner hardware, and software that both automates the procedural steps and performs the analyses.

**807.92 (a)(4): 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 algorithm for specific immunohistochemical marker, and software with a Windows web

**Revised Page 1 to correct Product Codes**

specific immunohistochemical marker, 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™ PR (1E2) rabbit monoclonal primary antibody reagent
- Reagents for visualization, such as universal DAB universal 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.

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 PR (1E2) primary antibody,, and are then visualized using DAB. Prepared slides are loaded into the Virtuoso system scanner and scanned. 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.



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**807.92 (a)(5): Intended 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 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.



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**807.92 (a)(6): Technological Similarities and Differences to the Predicate Devices**

The similarities and differences between the two test systems are described below.

| Characteristic | Virtuoso™ IHC PR (1E2) | ScanScope® XT System- K073677 |
|---|---|---|
| Intended Use/Indications for Use | This device is intended for in vitro diagnostic (IVD) use.<br>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.<br>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 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). | This device is intended for in vitro diagnostic (IVD) use.<br>The ScanScope System is an automated digital slide creation, management, viewing, and analysis system. It is intended for IVD use as an aid to the pathologist in the display, detection, counting, and classification of tissues and cells of clinical interest based on particular color, intensity, size, pattern, and shape.<br>The IHC ER and PR Image Analysis applications are intended for use as an aid to the pathologist in the detection and quantitative measurement of ER and PR in formalin-fixed, paraffin-embedded normal and neoplastic tissue. ER and PR are indicated for use as an aid in the management, prognosis, and predication of therapy outcomes of breast cancer. |
| 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 | BioImagene (now Ventana) iScan slide scanner, computer, color monitor, and Virtuoso™ proprietary software for PR (1E2) | Automated digital slide scanner, computer, color monitor, keyboard, image analysis software and digital pathology information management software. |
| Primary Antibodies (Assay) Reagents | Ventana CONFIRM™ PR (1E2) | Dako monoclonal mouse anti-human: ERα(1D5) and PR (PgR 636) |
| Localization of IHC positive stain | Nucleus | Nucleus |
| Results Reported | Percent positive nuclei | Percent positive nuclei and intensity score |
| Interpretation | Interpretation is performed by the pathologist. | Same |



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**807.92 (b)(1/2): Brief Description of Clinical Data (Non-clinical data N/A)**

The Virtuoso System for IHC PR (1E2) was clinically validated via two studies. The first (primary) study evaluated overall system performance in terms of: (1) agreement between the reference manual method (with a traditional microscope) and both the digital read (DR) and image analysis (IA) applications of the Virtuoso system, (2) intra-pathologist/inter-day reproducibility of the two Virtuoso applications, and (3) inter-pathologist reproducibility of the two Virtuoso applications.

In the second study, scanner precision was evaluated in an isolated fashion via a cross-over design from the primary study. In this second study, a subset of the clinical cases (n = 40) was scanned two more times with two different scanners at two separate locations. This study evaluated scanner precision of the image analysis application only for both inter-scanner precision and intra-scanner/inter-day precision, as the image analysis application is the more objective of the two applications and is not affected by memory bias as would be the case with human interpretations. The data from both studies are summarized below.

**Agreement/Concordance**

a. Virtuoso Digital Read vs Manual Method

Each pathologist's Virtuoso digital read results were compared to their manual results. The data were categorized as "neg" and "pos" using classifications of less than 1% to describe negative, and 1% or greater (Categories 1 and 2 in table) to describe positive. (Category 1 was assigned to positivity of 1-10%, and Category 2 was assigned to positivity of >10%.) The overall agreements, across the three sites were 95%, 97%, and 92%. The overall, negative, and positive percent agreements, with the 95% confidence intervals (CI) around the percent agreements, are shown below.

**PR Agreements: Digital Read vs Manual (manual = true score)**

| Confusion Matrix | | Digital | | | | | |
|---|---|---|---|---|---|---|---|
| | | Site 1 (n = 112) | | Site 2 (n = 114) | | Site 3 (n = 116) | |
| | | Neg | Pos | Neg | Pos | Neg | Pos |
| Manual | Neg (0) | 50 | 3 | 51 | 0 | 52 | 1 |
| | Pos (1+, 2+) | 3 | 56 | 3 | 60 | 8 | 55 |
| | % Agreement | 95% | | 97% | | 92% | |
| | (95% CI) | (89% - | 98%) | (93% - | 99%) | (86% - | 96%) |
| Negative % Agreement | | 94% | | 100% | | 98% | |
| (95% CI) | | (85% - | 98%) | (93% - | 100%) | (90% - | 100%) |
| Positive % Agreement | | 95% | | 95% | | 87% | |
| (95% CI) | | (86% - | 98%) | (87% - | 98%) | (77% - | 93%) |



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b. Virtuoso Image Analysis vs Manual Method

The same analysis as performed for digital read was performed for image analysis. The overall agreements across the three sites were 92%, 97%, and 92%. The data tables, along with negative and positive percent agreements, plus the 95% CIs, are presented below.

**PR Agreement: Image Analysis vs Manual (manual = true score)**

| Confusion Matrix | | Image Analysis | | | | | |
|---|---|---|---|---|---|---|---|
| | | Site 1 (n = 112) | | Site 2 (n = 115) | | Site 3 (n = 114) | |
| | | Neg | Pos | Neg | Pos | Neg | Pos |
| Manual | Neg (0) | 50 | 2 | 51 | 2 | 51 | 1 |
| | Pos (1+, 2+) | 7 | 53 | 2 | 60 | 8 | 54 |
| | % Agreement | 92% | | 97% | | 92% | |
| | (95% CI) | (85% - | 96%) | (91% - | 99%) | (86% - | 96%) |
| Negative % Agreement | | 96% | | 96% | | 98% | |
| (95% CI) | | (87% - | 99%) | (87% - | 99%) | (90% - | 100%) |
| Positive % Agreement | | 88% | | 97% | | 87% | |
| (95% CI) | | (78% - | 94%) | (89% - | 99%) | (77% - | 93%) |

**Reproducibility**

a. Intra-Pathologist/Inter-Day (pair-wise comparisons, Session 1 vs Session 2, Session 1 vs Session 3, Session 2 vs Session 3)

*Digital Read*

The agreements between each of the three comparisons across three sessions with the same pathologist are shown below. The total agreements ranged from 85% to 90%, as shown below (with 95% CIs).

**PR Reproducibility**

| Intra-Pathologist Digital | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Confusion Matrix | | | Session 2 | | Session 3 | | Session 3 | |
| | | | Neg | Pos | Neg | Pos | Neg | Pos |
| | | | 19 | 20 | 21 | 18 | 21 | 18 |
| Session 1 | Neg | 20 | 17 | 2 | 18 | 1 | | |
| | Pos | 20 | 2 | 18 | 3 | 17 | | |
| Session 2 | Neg | 19 | | | | | 17 | 2 |
| | Pos | 20 | | | | | 4 | 16 |
| % Agreement | | | 90% | | 90% | | 85% | |
| (95% CI) | | | (76% - | 96%) | (76% - | 96%) | (70% - | 93%) |



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*Image Analysis*

The agreements between each of the three comparisons across three sessions with the same pathologist are shown below. The agreements ranged from 95% to 97%, as shown below (with 95% CIs).

**PR Reproducibility**

| Intra-Pathologist Image Analysis | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Confusion Matrix | | | Session 2 | | Session 3 | | Session 3 | | |
| | | | Neg | Pos | Neg | Pos | Neg | Pos | |
| | | | 17 | 22 | 18 | 21 | 18 | 21 | |
| Session 1 | Neg | 18 | 17 | 1 | 17 | 1 | | | |
| | Pos | 21 | 0 | 21 | 1 | 20 | | | |
| Session 2 | Neg | 17 | | | | | 17 | 0 | |
| | Pos | 22 | | | | | 1 | 21 | |
| % Agreement | | | 97% | | 95% | | 97% | | |
| (95% CI) | | | (87% - | 100%) | (83% - | 99%) | (87% - | 100%) | |

b. Inter-Pathologist (pair-wise comparisons, Pathologist 1 vs Pathologist 2, Pathologist 1 vs Pathologist 3, Pathologist 2 vs Pathologist 3)

*Manual Read*

The three manual readings across the three pathologists were compared to each other. The agreements ranged from 92% to 97%, indicating minimal variation among the three pathologists.

**PR Manual Read, Inter-Pathologist**

| Inter-Pathologist Manual | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Confusion Matrix | | | Site 2 | | Site 3 | | Site 3 | | |
| | | | Neg | Pos | Neg | Pos | Neg | Pos | |
| | | | 55 | 64 | 56 | 63 | 56 | 63 | |
| Site 1 | Neg | 56 | 53 | 3 | 51 | 5 | | | |
| | Pos | 62 | 1 | 61 | 4 | 58 | | | |
| Site 2 | Neg | 55 | | | | | 51 | 3 | |
| | Pos | 64 | | | | | 4 | 60 | |
| % Agreement | | | 97% | | 92% | | 94% | | |
| (95% CI) | | | (92% - | 99%) | (86% - | 96%) | (88% - | 97%) | |



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*Digital Read*

The reproducibility in the Virtuoso digital readings among the three pathologists is shown below, along with the 95% CIs. The percent total agreements ranged from 92% to 97%.

**PR Digital Read, Inter-Pathologist**

| Inter-Pathologist Digital | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Confusion Matrix | | | Site 2 | | Site 3 | | Site 3 | | |
| | | | Neg | Pos | Neg | Pos | Neg | Pos | |
| | | | 54 | 60 | 60 | 56 | 60 | 56 | |
| Site 1 | Neg | 53 | 51 | 1 | 50 | 2 | | | |
| | Pos | 59 | 2 | 57 | 7 | 52 | | | |
| Site 2 | Neg | 54 | | | | | 50 | 2 | |
| | Pos | 60 | | | | | 6 | 54 | |
| % Agreement | | | 97% | | 92% | | 93% | | |
| (95% CI) | | | (92% - | 99%) | (85% - | 96%) | (87% - | 96%) | |

*Image Analysis*

The reproducibility in the Virtuoso image analysis interpretations among the three pathologists is shown below, along with the 95% CIs. The percent agreements ranged from 92% to 95%.

**PR Image Analysis, Inter-Pathologist**

| Inter-Pathologist Image Analysis | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Confusion Matrix | | | Site 2 | | Site 3 | | Site 3 | | |
| | | | Neg | Pos | Neg | Pos | Neg | Pos | |
| | | | 53 | 62 | 60 | 55 | 60 | 55 | |
| Site 1 | Neg | 57 | 50 | 6 | 54 | 2 | | | |
| | Pos | 55 | 0 | 55 | 3 | 52 | | | |
| Site 2 | Neg | 53 | | | | | 52 | 1 | |
| | Pos | 62 | | | | | 8 | 54 | |
| % Agreement | | | 95% | | 95% | | 92% | | |
| (95% CI) | | | (89% - | 97%) | (90% - | 98%) | (86% - | 96%) | |

Scanner Precision

Forty (40) cases representing the useful categories of <1%, 1-10%, and 10% positive staining for PR were scanned on three different scanners at three different sites to assess inter-scanner precision, and the same three FOVs (total = 120) were captured and evaluated each time by the image analysis application. Limiting the



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study to image analysis only ensured that only scanner precision was under evaluation, as all other factors were kept constant. Similarly, these same 40 and three FOVs per case were scanned on three different days by the same scanner to assess intra-scanner/inter-day precision.

Pairwise comparisons were performed between each of the three sites (inter-scanner), and between each of the three days (sessions, intra-scanner). The precision tables are found below.

**PR Inter-Scanner Agreement Rates (Site to Site)**

| Image Analysis | Virtuoso PR (1E2) Results- Site 2 | | | |
|---|---|---|---|---|
| **Virtuoso PR (1E2) Results- Site 1** | <1% | 1-10% | >10% | Total |
| <1% | 68 | 3 | 0 | 71 |
| 1-10% | 0 | 7 | 1 | 8 |
| >10% | 0 | 0 | 38 | 38 |
| Total | 68 | 10 | 39 | 117 |
| Overall Percent Agreement: 96.6% (113/117)<br>95% CI: (91.5% to 98.7%) | | | | |

| Image Analysis | Virtuoso PR (1E2) Results- Site 3 | | | |
|---|---|---|---|---|
| **Virtuoso PR (1E2) Results- Site 1** | <1% | 1-10% | >10% | Total |
| <1% | 71 | 0 | 0 | 71 |
| 1-10% | 2 | 6 | 0 | 8 |
| >10% | 0 | 1 | 37 | 38 |
| Total | 73 | 7 | 37 | 117 |
| Overall Percent Agreement: 97.4% (114/117)<br>95% CI: (92.7% to 99.1%) | | | | |

| Image Analysis | Virtuoso PR (1E2) Results - Site 3 | | | |
|---|---|---|---|---|
| **Virtuoso PR (1E2) Results- Site 2** | <1% | 1-10% | >10% | Total |
| <1% | 68 | 0 | 0 | 68 |
| 1-10% | 5 | 5 | 0 | 10 |
| >10% | 0 | 2 | 37 | 39 |
| Total | 73 | 7 | 37 | 117 |
| Overall Percent Agreement: 94.0% (110/117)<br>95% CI: (88.2% to 97.1%) | | | | |

**Conclusion (PR Inter-scanner)**

Overall inter-scanner percent agreements for the three categories ranged from 94.0% to 97.4% for all FOVs combined.



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**PR Intra-Scanner/Inter-Day Agreement Rates (Session-to-Session)**

| Image Analysis | Virtuoso PR (1E2) Results- Session 2 | | | |
|---|---|---|---|---|
| **Virtuoso PR (1E2) Results- Session 1** | <1% | 1-10% | >10% | Total |
| <1% | 68 | 0 | 0 | 68 |
| 1-10% | 2 | 8 | 0 | 10 |
| >10% | 0 | 1 | 38 | 39 |
| Total | 70 | 9 | 38 | 117 |
| Overall Percent Agreement: 97.4% (114/117)<br>95% CI: (92.7% to 99.1%) | | | | |

| Image Analysis | Virtuoso PR (1E2) Results- Session 3 | | | |
|---|---|---|---|---|
| **Virtuoso PR (1E2) Results- Session 1** | <1% | 1-10% | >10% | Total |
| <1% | 64 | 1 | 0 | 65 |
| 1-10% | 1 | 9 | 0 | 10 |
| >10% | 0 | 0 | 36 | 36 |
| Total | 65 | 10 | 36 | 111 |
| Overall Percent Agreement: 98.2% (109/111)<br>95% CI: (93.7% to 99.5%) | | | | |

| Image Analysis | Virtuoso PR (1E2) Results- Session 3 | | | |
|---|---|---|---|---|
| **Virtuoso PR (1E2) Results- Session 2** | <1% | 1-10% | >10% | Total |
| <1% | 65 | 2 | 0 | 67 |
| 1-10% | 0 | 8 | 1 | 9 |
| >10% | 0 | 0 | 35 | 35 |
| Total | 65 | 10 | 36 | 111 |
| Overall Percent Agreement: 97.3% (108/111)<br>95% CI: (92.4% to 99.1%) | | | | |

**Conclusion (PR Intra-scanner/Inter-day)**
Overall percent agreements for the three categories ranged 97.3% to 98.2% for all FOVs combined.

**Additional Analyses:**
The precision data for the Virtuoso PR system also underwent analysis for percent coefficient of variation (%CV); this could be achieved as the system provides a quantitative output that is then interpreted as a semi-quantitative (<1%, 1-10%, >10%) output.

The results from the inter-scanner percent %CV analyses are presented in the table below. The %CVs were derived for each source of variability as the standard deviation (SD) for that source, divided by the mean, multiplied by 100%. %CVs of less than 10% are generally considered to demonstrate good precision. Across all 351 evaluable observations, the mean percent positivity for PR was 25.93%. The %CV for "sites" measures precision of the site-to-site scanning and, at 0.00%, demonstrates that scanning results were reproducible between sites. The %CV for "case" represents between-case biological variability, and the %CV for the residual term represents



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within-case, between-field biological variability, and as such, these sources of variability are outside the scope of scanner performance.

**PR Inter-Scanner %CV Analyses**

| Parameter | Statistic | FOVs |
|---|---|---|
| Percent Positivity (%) | N | 351 |
| | Mean | 25.926 |
| | Site (Scanner) SD | 0.000 |
| | Site (Scanner) %CV | 0.00 |
| | FOV SD | 39.112 |
| | FOV %CV | 150.86 |
| | Residual SD | 9.828 |
| | Residual %CV | 37.91 |

Results of the inter-day %CV analyses for PR are presented in the table below. Here, the %CV for "day" is shown to be 0.00%. Since it is impossible for a variance to be negative, the model sets the variance component to zero in those cases. Thus, a %CV of 0 should not be interpreted as a complete absence of variability for that particular source, but rather as variability that is negligible in magnitude. Thus, for the one site that repeated measurements on multiple days, reproducibility between days was shown to be extremely high. As before, the %CVs for "case" and for the residual term reflects the between-case and between-field biological heterogeneity, factors that are outside the scope of scanner performance.

**PR Intra-Scanner, Inter-Day %CV Analyses**

| Parameter | Statistic | All FOVs |
|---|---|---|
| Percent Positivity (%) | N | 345 |
| | Mean | 26.014 |
| | Day SD | 0.000 |
| | Day %CV | 0.00 |
| | FOV SD | 39.419 |
| | FOV %CV | 151.53 |
| | Residual SD | 9.678 |
| | Residual %CV | 37.20 |

**807.92 (b)(3): Conclusions from Clinical Testing**

Concordance, reproducibility, and precision studies were performed for the Virtuoso System for IHC PR (1E2). The test system was shown to be safe and effective for its intended use.



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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Ventana Medical Systems, Inc.
c/o Mr. Troy Quander
Vice President, Regulatory Affairs
1910 East Innovation Park Drive
Tucson, Arizona 85755

MAR 0 5 2012

Re: k111869
Trade/Device Name: Virtuoso™ System for IHC PR (1E2)
Regulation Number: 21 CFR §864.1860
Regulation Name: Immunohistochemistry reagents and kits
Regulatory Class: Class II
Product Code: NQN, OEO
Dated: January 17, 2012
Received: January 18, 2012

Dear Mr. Quander:

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.

If your device is classified (see above) into class II (Special Controls), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. 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); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820). This letter will allow you to begin marketing your device as described in your Section 510(k) premarket

notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Parts 801 and 809), please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 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/cdrh/industry/support/index.html.

Sincerely yours,

Maria M. Chan

Maria M. Chan, Ph.D.
Director
Division of Immunology and Hematology Devices
Office of *In Vitro* Diagnostic Devices
Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

# INDICATIONS FOR USE

**510(k) Number (if Known):** K111869

**Device Name:** Virtuoso™ System for IHC PR (1E2)

**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 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 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.

Prescription Use __X__ AND/OR Over-The-Counter Use ____
(Part 21 CFR 801 Subpart D) (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

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Concurrence of CDRH, Office of In Vitro Diagnostics (OIVD)

Division Sign-Off

Office of In Vitro Diagnostic
Device Evaluation and Safety

510(k) K111869