

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION  
DECISION SUMMARY  
ASSAY ONLY TEMPLATE**

**A. 510(k) Number:**

K062615

**B. Purpose for Submission:**

Marketing product in the U.S.

**C. Measurand:**

Progesterone Receptor on formalin-fixed paraffin-embedded breast cancer specimens

**D. Type of Test:**

Immunohistochemical

**E. Applicant:**

Vision BioSystems

**F. Proprietary and Established Names:**

Vision BioSystems Progesterone Receptor PGR Clone 16

Novocastra™ Ready-To-Use Primary Antibody (Catalog No: RTU-PGR-312)

Novocastra™ Liquid Mouse Monoclonal Antibody (Catalog No: NCL-L-PGR-312)

Novocastra™ Lyophilized Mouse Monoclonal Antibody (Catalog No: NCL-PGR-312)

Origin™ Ready-To-Use Primary Antibody (Catalog No: ORG-8821)

Bond™ Ready-To-Use Primary Antibody (Catalog No: PA0312)

**G. Regulatory Information:**

1. Regulation section:

21 CFR §864.1860 Immunohistochemistry reagents and kits

2. Classification:

Class II

3. Product code:

MXZ

4. Panel

Pathology (88)

**H. Intended Use:**

1. Intended use(s):

Vision BioSystems Progesterone Receptor Clone 16 (PGR Clone 16) Mouse Monoclonal antibody is intended for laboratory use to qualitatively identify by light microscopy, progesterone receptor (PGR) antigen in sections of formalin fixed paraffin embedded tissue. PGR Clone 16 specifically binds to the PGR antigen located in the nucleus of PGR positive normal and neoplastic cells.

Novocastra™ antibodies are intended for manual use. Origin™ antibodies are optimized for use with the Ventana® Medical Systems, NexES® and BenchMark™ Immunohistochemistry Staining Systems in combination with Ventana® Detection Kits. Bond™ Ready-to-Use Primary Antibodies are optimized for use on the Vision BioSystems Bond-max™ system.

2. Indication(s) for use:

PGR Clone 16 is indicated as an aid in the management, prognosis and prediction of therapy outcome of breast cancer. The clinical interpretation of any staining or its absence should be complemented by morphological studies using proper controls and should be evaluated within the context of the patient's clinical history and other diagnostic tests by a qualified pathologist.

3. Special conditions for use statement(s):

Prescription use only.

4. Special instrument requirements:

Origin™ antibodies are optimized for use with the Ventana® Medical Systems, NexES® and BenchMark™ Immunohistochemistry Staining Systems in combination with Ventana® Detection Kits.

Bond™ Ready-to-Use Primary Antibodies are optimized for use on the Vision BioSystems Bond-max™ system

## **I. Device Description:**

Vision BioSystems PR 16 is a monoclonal antibody that specifically binds to the progesterone receptor antigen located in the nuclear region of a variety of normal and neoplastic tissues routinely processed and paraffin-embedded. PGR Clone 16 is intended for use in standard immunohistochemical staining procedures to allow for visualization of the targeted antigen by the sequential application of the PGR Clone 16 primary antibody, visualization reagent, and chromogen, resulting in a visible reaction at the antigen site. Results are evaluated using a light microscope. The antibodies are available as ready-to-use, concentrated, lyophilized, a version optimized for use with the Ventana Medical Systems Automated Stainers and a version for use with Vision BioSystems Bond-max™ System.

Novocastra™ Ready-To-Use Primary Antibody (manual) is a mouse anti-human monoclonal antibody produced as a tissue culture supernatant. This product is supplied in a ready-to-use format presented in 5% horse serum in PBS containing 12mM sodium azide as a preservative. The total antibody concentration is greater than or equal to 1.8 mg/L as determined by ELISA.

Novocastra™ Liquid Primary Antibody (manual) is a mouse anti-human monoclonal antibody produced as a liquid tissue culture supernatant containing 15mM sodium azide as a preservative. The total antibody concentration is greater than or equal to 1.8 mg/L as determined by ELISA.

Novocastra™ Lyophilized Primary Antibody (manual) is a mouse anti-human monoclonal antibody produced as a lyophilized tissue culture supernatant containing 15mM sodium azide as a preservative. The user is required to reconstitute the contents of the vial with sterile distilled water prior to use. The total antibody concentration is greater than or equal to 324.0 mg/L as determined by ELISA.

Vision BioSystems Bond™ Ready-To-Use Primary Antibody (automated for Bond-max™ System) is a mouse anti-human monoclonal antibody produced as a tissue culture supernatant. This product is supplied in a ready-to-use format and in Tris buffered saline with carrier, containing 0.35% ProClin™ 950 as a preservative. The total protein concentration is approximately 10 mg/mL and the antibody concentration is greater than or equal to 0.72 mg/L as determined by ELISA.

Origin™ Ready-To-Use Primary Antibody (automated for Ventana Medical Systems Automated Stainers) is a mouse anti-human monoclonal antibody. This product is supplied in a ready-to-use format and in phosphate buffer pH 7.3 with 3 mg/ml carrier protein and 0.05% ProClin™ 300 as a preservative. The antibody concentration is greater than or equal to 1.8 mg/L as determined by ELISA.

**J. Substantial Equivalence Information:**

1. Predicate device name(s):

Dako Mouse Anti-Human Progesterone Receptor Clone PgR 636

2. Predicate 510(k) number(s):

K020023

3. Comparison with predicate:

<b>Similarities</b>		
<b>Item</b>	<b>Device</b>	<b>Predicate</b>
Antibody type	Monoclonal mouse	same
Intended use	Semi-quantitative detection of ER	same
Technology	Immunohistochemistry	same

<b>Differences</b>		
<b>Item</b>	<b>Device</b>	<b>Predicate</b>
Immunogen	Formalin-fixed recombinant full-length A form of the human progesterone receptor	Prokaryotic recombinant protein corresponding to the N-terminal region of the A form of the human progesterone receptor
Clone	16	PGR 636

**K. Standard/Guidance Document Referenced (if applicable):**

“Guidance for Submission of Immunohistochemistry Applications to the FDA”

**L. Test Principle:**

Vision BioSystems Progesterone Receptor (Clone 16), specifically binds to progesterone receptor antigen located in the nuclear region of a variety of normal and neoplastic tissues. Immunohistochemical staining is performed on routinely processed, paraffin-embedded specimens allowing the qualitative identification by light microscopy of the antigens. Prior to staining, endogenous peroxidase activity is blocked and sections are subjected to epitope retrieval. The section is subsequently incubated with the primary antibody. For the Novacastra™ and Origin™ products, a

biotin-conjugated secondary antibody formulation that recognizes mouse immunoglobulins is used to detect the primary antibody. A streptavidin- or ABC-peroxidase conjugate is then applied and binds to the biotin present on the secondary antibody. For the Bond™ product, a polymer refine detection system is used. This system utilizes a controlled polymerization technology to prepare polymeric HRP-linker antibody conjugates. Sections are then incubated with the substrate/chromogen, 3,3'-diaminobenzidine (DAB). Reaction with the peroxidase produces a visible brown precipitate at the antigen site. Sections are counter stained with hematoxylin and cover slipped. Results are interpreted using a light microscope

#### **M. Performance Characteristics (if/when applicable):**

##### 1. Analytical performance:

a. *Precision/Reproducibility:*

b. *Linearity/assay reportable range:*

N/A

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

Positive and negative controls should be performed with each staining run. The pathologist is responsible for assuring that the assay is performing properly.

d. *Detection limit:*

N/A

e. *Analytical specificity:*

Novacastra™ Mouse Monoclonal Antibodies and Origin™ Ready-To-Use Primary Antibody: Specificity was evaluated on a range of normal tissues. Characteristic staining was observed in the nuclei of cells that express high levels of the protein: a proportion of endometrial, ovarian, and myometrial cells, and normal breast ductal cells. Negative tissues included adrenal, bone marrow, brain (cerebellum), brain (cerebrum), colon, esophagus, heart, kidney, liver, lung, mesothelial cells, parathyroid, peripheral nerve, salivary/submandibular gland, skeletal muscle, skin, small intestine, spleen, spinal cord, stomach, testis, thymus, and thyroid. Weak staining was observed in ovary stromal cells and occasional islet cells of the pancreas.

Bond™ Ready-To-Use Primary Antibody: An evaluation on a panel of normal tissues was conducted using the Bond™ Ready-To-Use Clone 16 primary antibody in conjunction with Bond™ Refine Detection System on the Vision BioSystems Bond-max™ slide staining system. A total of 85 formalin-fixed and paraffin-embedded tissues covering a wide range of normal human tissue types were tested with the ER antibody. The antibody demonstrated negative immunoreactivity with most tissues. Positive immunoreactivity was noted with some normal tissues which are typically positive, like uterus, ovary and ductal epithelial cells of the breast. Positive staining was also observed in ovary stromal cells, islet cells of the pancreas, the muscle layer of the small intestines and the capsular region of the testis.

*f. Assay cut-off:*

Slides are scored using the Quick Score System. The tumor is scored according to the proportion on cell nuclei stained (1-5) and the intensity of the staining (0-3). A score of 3 or over is classified as receptor positive.

2. Comparison studies:

*a. Method comparison with predicate device:*

The substantial equivalence studies were based on comparison to Dako PgR Clone 636. The comparison studies were conducted at two clinical sites for each configuration.

Novocastra Primary Antibody Configuration (NCL-L-PGR-312)

	NCL-L-PGR-312		
<b>PgR 636</b>	Positive	Negative	<b>Total</b>
Positive	113	0	<b>113</b>
Negative	3	73	<b>76</b>
Total	116	73	<b>189</b>

Total agreement was found to be 98% (186/189) with 95% CI (95%, 100%). Negative percent agreement is 96% (73/76), 95% CI (89%, 99%) and positive percent agreement 100% (113/113), 95% CI (97%, 100%).

Origin Configuration (ORG-8721)

	<b>ORG-8721</b>		
<b>PgR 636</b>	Positive	Negative	<b>Total</b>
Positive	110	8	<b>118</b>
Negative	5	82	<b>87</b>
Total	115	90	<b>205</b>

Total agreement was found to be 94% (192/205) with 95% CI (89%, 97%).  
Negative percent agreement is 94% (82/87), 95% CI (89%, 99%) and positive percent agreement 93% (110/118), 95% CI (87%, 97%).

Bond-max Configuration (PA0312)

	<b>NCL-L-PGR-312</b>		
<b>PgR 636</b>	Positive	Negative	<b>Total</b>
Positive	120	3	<b>123</b>
Negative	8	72	<b>80</b>
Total	128	75	<b>203</b>

Total agreement was found to be 95% (192/203) with 95% CI (91%, 97%).  
Negative percent agreement is 90% (72/80), 95% CI (93%, 99%) and positive percent agreement 98% (120/123), 95% CI (81%, 96%).

b. *Matrix comparison:*

N/A

3. Clinical studies:

a. *Clinical Sensitivity:*

b. *Clinical specificity:*

c. Other clinical supportive data (when a. and b. are not applicable):

4. Clinical cut-off:

5. Expected values/Reference range:

**N. Proposed Labeling:**

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

**O. Conclusion:**

1. The submitted information in this premarket notification is complete and supports a substantial equivalence decision.