

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

A. 510(k) Number:

K060227

B. Purpose for Submission:

Marketing product in U.S.

C. Measurand:

Estrogen 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 Estrogen Receptor Clone 6F11 (manual)

Origin™ Mouse Monoclonal Antibody, Estrogen Receptor Clone 6F11 (automated)

G. Regulatory Information:

1. Regulation section:

21 CFR §864.1860 Immunohistochemistry reagents and kits

2. Classification:

Class II

3. Product code:

MYA

4. Panel:

Pathology 88

H. Intended Use:

1. Intended use(s):

Vision Biosystems Estrogen Receptor Clone 6F11 is intended for laboratory use to qualitatively identify by light microscopy, estrogen receptor (ER) antigen in sections of formalin fixed, paraffin embedded tissue. Estrogen Receptor Clone 6F11 specifically binds to the ER antigen located in the nucleus of ER positive normal and neoplastic cells.

Origin™ Mouse Monoclonal Antibody, Estrogen Receptor Clone 6F11 is intended for laboratory use to qualitatively identify by light microscopy, estrogen receptor (ER) antigen in sections of formalin fixed, paraffin embedded tissue. Estrogen Receptor Clone 6F11 specifically binds to the ER antigen located in the nucleus of ER positive normal and neoplastic cells.

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

2. Indication(s) for use:

ER 6F11 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):

N/A

4. Special instrument requirements:

Ventana® Medical Systems, NexES® and BenchMark™ Immunohistochemistry Automated Staining Systems

I. Device Description:

Vision BioSystems ER 6F11 is a monoclonal antibody that specifically binds to the estrogen receptor antigen located in the nuclear region of a variety of normal and neoplastic tissues routinely processed and paraffin-embedded. ER 6F11 is intended for use in standard immunohistochemical staining procedures to allow for visualization of the targeted antigen by the sequential application of the ER 6F11 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, and a version optimized for use with the Ventana Medical Systems Automated Stainers.

Vision BioSystems ER 6F11 (RTU-ER-6F11) (Ready-to-use) contains 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 protein concentration is 1.0-8.0 g/L. Refer to the vial label for batch specific IG and total protein concentrations.

Origin™ ER6F11 (ORG-8871) (Automated) is a ready-to-use mouse monoclonal antibody presented in phosphate buffer pH 7.3 with 3 mg/ml carrier protein and 0.05% ProClin® 300.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Ventana Confirm Anti-Estrogen Receptor (6F11) Primary Antibody

Dako Monoclonal Mouse-Anti Human Estrogen Receptor, Clone 1D5

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

K984567

K993957

3. Comparison with predicate:

Similarities			
Item	Device	Predicate K984567	Predicate K993957
Antibody type	Monoclonal	same	same
Intended use	Semi-quantitative detection of ER	same	same
Technology	Immunohistochemistry	same	same
Differences			
Item	Device	Predicate	Predicate
Clone (ER)	6F11	6F11	1D5
Staining	Manual & Automated	Automated only	Manual & Automated

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

“Guidance for Industry: Guidance for Submission of Immunohistochemistry Applications to the FDA”

“Guidance for Industry and FDA Staff- Use of Symbols on Labels an in Labeling of In Vitro Diagnostic Devices Intended for Professional Use”

CEN 13640, “Stability Testing of In Vitro Diagnostic Reagents”

L. Test Principle:

Vision BioSystems Estrogen Receptor Clone 6F11 , specifically binds to estrogen 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. Immunohistochemistry is a well established, widely accepted laboratory methodology. The specific antibody is localized by a biotin conjugated secondary antibody formulation that recognizes mouse immunoglobulins. This step is followed by the addition of an avidin/streptavidin enzyme conjugate that binds to the biotin present on the secondary antibody. The specific antibody-secondary antibody-avidin/streptavidin enzyme complex is then visualized with a precipitating enzyme reaction product, which is readily detected by light microscopy.

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:*

A total of 92 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.

f. *Assay cut-off:*

A positive staining result is defined as more than 10% of tumor cells with stained nuclei of any intensity.

2. Comparison studies:

a. *Method comparison with predicate device:*

Estrogen receptor status was evaluated in 592 cases using routinely prepared paraffin-embedded tissue samples from primary breast carcinomas with ER 6F11 and anti-ER 1D5. 435 cases were positive with 1D5 and 438 were positive with 6F11. Overall, 1D5 and ER6F11 showed a 97.5% concordance rate.¹

Comparative studies of ER 6F11 and the predicate ER 1D5 with 55 cases showed 69% scoring positive with ER6F11 and 60% scoring positive with ER 1D5. There was 90.1% (50/55) concordance between the two methods.²

¹Kaplan, P.A. et. al. 1D5 and 6F11 an immunohistochemical comparison of two monoclonal antibodies for the evaluation of estrogen receptor status in primary breast carcinoma. Am J Clin Pathol 2005: 276-280.

²Bevitt DJ, Milton ID, Piggot N et al. New monoclonal antibodies to oestrogen and progesterone receptors effective for paraffin section immunohistochemistry. Journal of Pathology 1997; 183(2), 228-232.

b. *Matrix comparison:*

N/A

3. Clinical studies:

a. *Clinical Sensitivity:*

N/A

b. *Clinical specificity:*

N/A

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

4. Clinical cut-off:

N/A

5. Expected values/Reference range:

N/A

N. Proposed Labeling:

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

O. Conclusion:

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