

Assisting with your efforts to be ASCO/CAP Compliant

Ventana's Fully Integrated Breast Panel System

HER-2/ <i>neu</i> (4B5)	This antibody is intended for <i>in vitro</i> diagnostic use. Ventana Medical Systems, Inc.'s (Ventana) PATHWAY anti-HER-2/ <i>neu</i> (4B5) Rabbit Monoclonal Primary Antibody (PATHWAY HER-2 (4B5)) is a rabbit monoclonal antibody intended for laboratory use for the semi-quantitative detection of HER-2 antigen in sections of formalin-fixed, paraffin-embedded normal and neoplastic tissue on a Ventana automated immunohistochemistry slide staining device.
ER (SP1)	CONFIRM anti-Estrogen Receptor (ER) (SP1) Primary Antibody is a rabbit monoclonal antibody (IgG) that is intended for laboratory use for the qualitative detection of estrogen receptor (ER) antigen in sections of formalin-fixed, paraffin-embedded tissue on a Ventana automated slide stainer and has been optimally diluted for use with iVIEW DAB Detection Kit.
PR (1E2)	CONFIRM anti-PR (1E2) Primary Antibody is intended for laboratory use for the qualitative detection of progesterone receptor (PR) antigen in sections of formalin-fixed, paraffin-embedded tissue on a Ventana automated slide stainer with Ventana detection kits and ancillary reagents.
Ki-67 (30-9)	CONFIRM anti-Ki-67 (30-9) Primary Antibody is directed against C-terminal portion of Ki-67 antigen, and is intended for use to identify stained proliferating cells by light microscopy in sections of formalin-fixed, paraffin-embedded tissue on a Ventana automated slide stainer.
HER2 4 in 1 Control Slides	PATHWAY HER2 4 in 1 Control Slides consist of formalin fixed, paraffin embedded, cultured human breast cell lines and are intended to be used as assayed, semi-quantitative quality control material, in conjunction with PATHWAY HER2 (4B5) primary antibody, for use in monitoring the performance of the immunohistochemical anti- <i>c-erbB-2</i> /HER-2 staining process on a Ventana automated slide stainer.

Sensitive

Rabbit Monoclonals	ER (SP1) #790-4324 IVD	PR (1E2) #790-2223 IVD
	Ki-67 (30-9) #790-4286 IVD	HER-2/<i>neu</i> (4B5) #790-100 PMA (U.S. ONLY)
Control	HER-2 4-in-1 Control Slides #781-2991	

Standardized

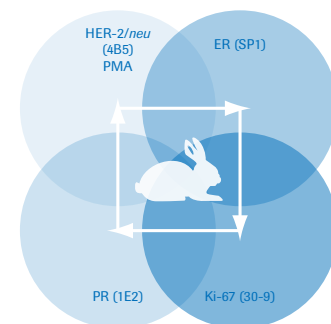
Slide preparation automation with BenchMark XT
#N750-BMKXT-FS

Objective

Image Analysis and integrated patient report from VIAS [510(k)]
#VIAS-799-CLICK-115

Efficient

BenchMark XT, VIAS, and VANTAGE
#1339800



Breast Panel System

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Summary of the ASCO/CAP HER2 Testing Guidelines

A complete copy of the guidelines may be found on the ASCO and CAP websites: www.asco.org and www.cap.org

Tissue Handling Standardization

- 10% neutral buffered formalin—optimal fixation times: 6 to 48 hours and should be documented on the pathology report.
- Alternative fixative (e.g. PREFER, Alcoholic Formalin, etc.) must be validated against the results of the identical specimen fixed in 10% NBF.
- Cut sections stored longer than 6 weeks are not optimal for testing and should be re-cut.

Method Validation Requirements

- Testing must be initially validated using 25-100 formalin-fixed samples using standard operating procedures.
 - Parallel testing by an alternative method within your lab (e.g. FISH, SISH) is acceptable.
 - Parallel by identical method in another lab with the same validated assay is also acceptable.
 - Positive and negative HER2 categories must be 95% concordant with the validated comparison method.
- Validation should be performed twice a year (external proficiency exam testing meets this requirement).
- Laboratory/Lab Director is ultimately responsible for validation. Assay procedures must be standardized.
 - Any deviations from the standardized procedure must be validated.
 - Any changes from procedure must be documented on the report.
- Optimal performance is easily obtained using automated platforms. Personnel must have their competency assessed at regular intervals.

Standardized Control Materials

- Cell line controls or tumor blocks with well defined negative, equivocal and positive expression need to be used. If controls do not show usual results, the assay must be repeated rather than interpreted.
- Controls need to be used by the laboratory with each run of tests.

Image Analysis

- Image analysis is an effective tool for achieving consistent interpretation of HER2. Pathologists must confirm the image result.
- Image analysis must be validated before implementation.
- Image analysis must be calibrated regularly.
- Quantitative image analysis is encouraged for cases with weak membrane staining (1-2+) to improve consistency of interpretation.

Reporting

- Only evaluate invasive breast cancer or the invasive component of the breast cancer
- More than 30% of the tumor must show circumferential membrane staining for positive results

Positive Score: IHC 3+	FISH >6.0 gene copy	FISH HER2/CEP17 ratio >2.2
Equivocal Score: IHC 2+	FISH 4.0-6.0 gene copy	FISH HER2/CEP17 ratio 1.8-2.2
Negative Score: IHC 0 or 1+	FISH <4.0 gene copy	FISH HER2/CEP17 ratio <1.8

- If cytoplasmic staining obscures membrane staining, repeat assay or do FISH.
- For an IHC equivocal result, the specimen must be retested with a validated assay for gene amplification.
- Reject if lobules or normal ducts show obvious staining.
- Report should include:
 - Specimen site and type, and specimen fixation time.
 - Antibody clone/vendor/method used and if FDA approved (if modified, it should be stated and a statement that the lab takes responsibility for test performance)
 - Image analysis results- Controls-protein expression
 - Adequacy of sample for evaluation—results % invasive tumor cell showing complete staining.
 - Uniformity—present/absent, dark circumferential staining—present/absent.

Proficiency Assessment

- Participation in an external proficiency exam with at least two testing events/year. Satisfactory performance requires at least 90% correct responses on graded challenges for either test.
- Unsatisfactory performance will require the laboratory to respond according to accreditation agency program requirements

