AdventistHealth

[redacted]

[redacted]

Sex: Female

Adm Date: 6/6/2024 Dis Date: 6/6/2024

Anatomic Pathology

ACCESSION: [redacted]

COLLECTED DATE/TIME: 6/6/2024 17:00 PDT
RECEIVED DATE/TIME: 6/6/2024 19:23 PDT

Surgical Pathology Final Report – 6/11/2024 12:04 PDT – Auth (Verified)

DIAGNOSIS

1. Skin nodule from left mastectomy site 2 cm below medial inferior mammary fold scar, punch biopsy:
-Moderately differentiated adenocarcinoma consistent with infiltrating lobular carcinoma ,involving dermis and subcutaneous tissue
-No epidermal tumor identified
-No definitive dermal lymphatic invasion identified
-Findings supported by immunohistochemistry

2. Skin nodule from left mastectomy site, 1 cm below medial inferior mammary fold scar, punch biopsy:
-Moderately differentiated adenocarcinoma consistent with infiltrating lobular carcinoma, involving dermis
-No epidermal tumor identified
-Negative for dermal lymphatic invasion
-Findings supported by immunohistochemistry

3. Skin nodule from left mastectomy site, 3 cm from medial scar, punch biopsy:
-Moderately differentiated adenocarcinoma consistent with infiltrating lobular carcinoma involving dermis
-No epidermal tumor identified
-Negative for dermal lymphatic invasion
-Findings supported by immunohistochemistry

4. Skin nodule left lower outer quadrant, punch biopsy:

Copy To:

[redacted]

Attending Physician(s): [redacted]
Admitting Physician:
Ordering Physician: [redacted]
Print Dt/Tm: [redacted]

Primary Care Physician(s):

Report Request ID: [redacted]

Adventist Health

[redacted]

[redacted]

Sex: Female

Adm Date: 6/6/2024 Dis Date: 6/6/2024

Anatomic Pathology

ACCESSION: [redacted]

COLLECTED DATE/TIME: 6/6/2024 17:00 PDT
RECEIVED DATE/TIME: 6/6/2024 19:23 PDT

DIAGNOSIS
-Moderately differentiated adenocarcinoma consistent with infiltrating lobular carcinoma involving dermis
-No epidermal tumor identified
-Negative for dermal lymphatic invasion
-Findings supported by immunohistochemistry

MMC
Verified:06/11/24 12:04 PDT [redacted]

Performed at: Adventist Health Glendale Laboratory, [redacted]

Comment
No previous history on this patient is present in our files. Please contact the laboratory if a breast prognostic panel is desired on the current specimen.

Clinical Information
Pre-Operative Diagnosis: Left breast infiltrating lobular cancer now has multiple skin nodules

Specimen/Site
1 Skin punch biopsy left mastectomy site skin nodule 2 cm. below the medial IMF scar
2 Skin punch biopsy of left mastecomy site skin nodule 1 cm below the medial IMF scar
3 Skin punch biopsy of left mastectomy site skin nodule 3 cm from medial scar
4 Skin punch biopsy of left mastectomy site skin nodule lower outer quadrant

Gross Description
1. Received in formalin labeled with 2 patient identifiers and "left 2 cm below medial IMF

Copy To:

[redacted]

Attending Physician(s): [redacted]
Admitting Physician:
Ordering Physician: [redacted]
Print Dt/Tm: [redacted]

Primary Care Physician(s):

Report Request ID: [redacted]

AdventistHealth

[redacted]

[redacted]

[redacted]

Sex: Female

Adm Date: 6/6/2024 Dis Date: 6/6/2024

Anatomic Pathology

ACCESSION: [redacted]

COLLECTED DATE/TIME: 6/6/2024 17:00 PDT
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Gross Description
scar "is a punch biopsy of gray-tan skin which measures 0.2 x 0.3 cm and is entirely embedded in 1A.

2. Received in formalin labeled with 2 patient identifiers and "left 1 cm below medial IMF scar" is a gray-tan punch biopsy surfaced by apparent skin which measures 0.2 x 0.1 cm and is entirely embedded in cassette 2A

3. Received in formalin labeled with 2 patient identifiers and "left 3 cm from medial scar" is a 0.6 x 0.2 cm punch biopsy which is gray-tan and is entirely embedded in cassette 3A

4. Received in formalin labeled with 2 patient identifiers and "left lower outer quadrant" is a 0.3 x 0.1 cm pale-tan punch biopsy fragment which is entirely embedded in cassette 4A.

Specimens excised: 06/06/2024 16:10

Specimens placed in neutral buffered formalin 06/06/2024 16:12

Time out of Formalin: 06/09/2024 20:30

MMC:JRS

Special Stains
Immunohistochemistry reveals the following findings:
CD31(Parts 1A, 2A, 3A, 4A): Highlights dermal lymphatics without intralymphatic carcinoma identified
Estrogen receptor(Parts 1A, 2A, 3A, 4A): Highlights tumor cell nuclei; NO intraepidermal carcinoma identified

The above immunohistochemical test(s) may involve analyte specific reagents (ASR's). These tests were developed and the performance characteristics determined by Adventist Health White Memorial

Copy To:

[redacted]

Attending Physician(s): [redacted]
Admitting Physician:
Ordering Physician: [redacted]
Print Dt/Tm: [redacted]

Primary Care Physician(s):

Report Request ID: [redacted]

AdventistHealth

[redacted]

[redacted]

[redacted]

Sex: Female

Adm Date: 6/6/2024 Dis Date: 6/6/2024

Anatomic Pathology

ACCESSION: [redacted]

COLLECTED DATE/TIME: 6/6/2024 17:00 PDT
RECEIVED DATE/TIME: 6/6/2024 19:23 PDT

Special Stains
Histology Laboratory. It has not been cleared or approved by the US Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary. This test is used for clinical purposes. It should not be regarded as investigational or for research.

Appropriate controls are examined and show the expected reactivity

Additional Pathologist Review
The case has been reviewed in consultation by an additional intradepartmental pathologist, who concurs with the above findings.

Copy To:

[redacted]

Attending Physician(s): [redacted]
Admitting Physician:
Ordering Physician: [redacted]
Print Dt/Tm: [redacted]

Primary Care Physician(s):

Report Request ID: [redacted]

Glendale Adventist Medical Center

Adventist Health

Histology Image Analysis
IHC Quantitative Breast Panel

Client [redacted]
Adventist Health Glendale

[redacted]

CC 6

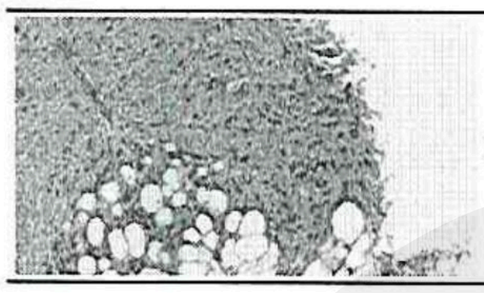
Patient Name: **Abrams, Roxann L**
Patient DOB / Sex: [redacted] **F**
Specimen Type: [redacted]
Body Site: [redacted]
Specimen ID: **15-GS-24-3651.1A/GS-24-3651.1A**
MRN: [redacted]
Other Patient ID / Acct #: [redacted]
Reason for Referral: [redacted]

Ordering Physician(s): [redacted]
Treating Physician(s): [redacted]
Accession / CaseNo: [redacted]
Collection Date: [redacted]
Received Date: [redacted]
Report Date: [redacted]

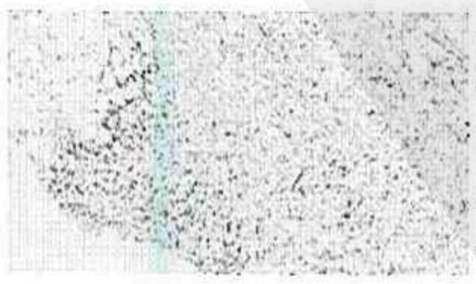
Comments:
Refer to separate report for results of HER2 FISH testing.

Results

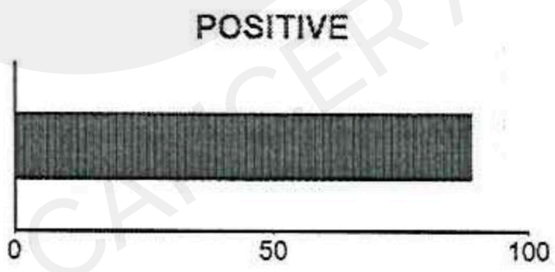
Specimen ID: [redacted]



H&E Image for Reference only

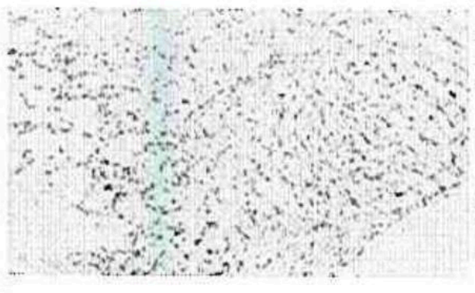


ER: POSITIVE
Tumor Stained: 89%
Intensity: 3+
Allred Score: 8
Internal Control: Absent

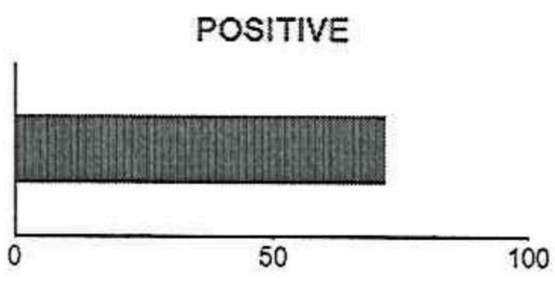


Reference Ranges	
Positive	**>10%**
Low Positive	**1-10%**
Negative	**<1%**

Allred Score Reference Ranges	
0	No effect
2 - 3	Small chance of benefit
4 - 6	Moderate chance of benefit
7 - 8	Good chance of benefit



PgR: POSITIVE
Tumor Stained: 72%
Intensity: 3+
Allred Score: 8
Internal Control: Absent



Reference Ranges	
Positive	**>/=1%**
Negative	**<1%**

Allred Score Reference Ranges	
0	No effect
2 - 3	Small chance of benefit
4 - 6	Moderate chance of benefit
7 - 8	Good chance of benefit

HER2 Breast:

HER2 staining was performed utilizing the FDA approved Ventana Pathway anti-HER-2/neu antibody (clone 4B5) staining procedure of FFPE specimens using a multimer-based detection system on the Ventana Ultra. Scoring is performed using the 2023 ASCO/CAP HER2 breast guidelines (1). Known artifacts such as edge artifact, tissue retraction and tissue crush may give the false impression of over expression. Care should be taken to avoid assessing these areas, especially in needle core biopsies which generally harbor all of these artifacts (2). Only membrane staining should be assessed in the invasive component of the specimen. The 2023 ASCO/CAP guideline recommendations state that a new HER2 test may be ordered on the excision specimen if the initial HER2 test result in a core needle biopsy specimen of a primary breast cancer is negative and any of the following is observed: the tumor is grade 3, the amount of invasive tumor on the core is small, the resection specimen contains high-grade carcinoma that is morphologically distinct from that in the core, the core biopsy result is equivocal for HER2 after testing by both ISH and IHC, or there is doubt about the specimen handling of the core biopsy (long ischemic time, short time in fixative, different fixative) or the test is suspected by the pathologist to be negative on the basis of testing error.

References:

1. Wolff AC, Hammond MEH, Allison KH, et al. Human Epidermal Growth Factor Receptor 2 Testing in Breast Cancer: American Society of Clinical Oncology/College of American Pathologists Clinical Practice Guideline Focused Update. Arch Pathol Lab Med. 2023. 147 (9):993-1000.
2. VENTANA PATHWAY anti-HER-2/neu (4B5) package insert

Ki67:

Zeta clone MIB1 was used to detect Ki67 in formalin-fixed paraffin-embedded tissue sections. A multimer-technology based system was used for detection.

AR:

Cell Marque SP107 clone was used to detect Androgen Receptor in formalin-fixed paraffin-embedded tissue sections. A polymer technology based system was used for detection.

Stain	CPT Code	Quantity
[redacted]	[redacted]	[redacted]

Electronic Signature

[redacted] M.D.,Pathologist

The Accessioning Component, Technical Component Processing and Analysis of this test was completed at NeoGenomics California, 31 Columbia, Aliso Viejo, CA / 92656 / 866-776-5907 / CLIA # 05D1021650 / Laboratory Director(s): Vladislav Chizhevsky, M.D. The Professional Component of this test was completed at Adventist Health Glendale, 1509 Wilson Terrace Pathology Department, Glendale, CA 91206 / Phone: (818) 409-8320 / Fax: (818) 956-7662.

The performance characteristics of the IHC/ISH assays have been validated on formalin-fixed paraffin embedded tissues only. This test was developed and its performance characteristics determined by NeoGenomics Laboratories, Inc. It has not been cleared or approved by the U.S. Food and Drug Administration. This test is used for clinical purposes. It should not be regarded as investigational or for research. This laboratory is certified under the Clinical Laboratory Improvement Amendments (CLIA) as qualified to perform high complexity clinical laboratory testing. For the classification of IHC antibodies, please contact the Client Services team.

Images that may be included within this report are representative of the patient but not all testing in its entirety and should not be used to render a result.

The CPT codes provided with our test descriptions are based on AMA guidelines and are for informational purposes only. Correct CPT coding is the sole responsibility of the billing party. Please direct any questions regarding coding to the payer being billed.

Ki67:
Ki-67 is a nuclear protein found in cells in all phases of the cell cycle, except the resting phase (phase G0), and is useful as a marker of cell proliferation. The percentage of Ki-67 positive tumor cells is used to stratify patients into good and poor prognostic groups, but there is lack of consensus guidelines for scoring and best cutoffs for prognosis. Studies that have evaluated proliferation index using Ki-67 by IHC in breast cancer have shown a significant correlation between high proliferation rates and shorter disease free and overall survival.

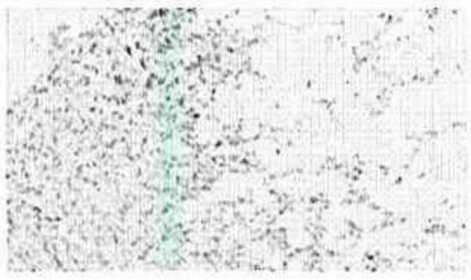
Scoring and interpretation : The Ki-67 proliferation index is assessed by counting at least three regions, and is reported as percent positive cells based on nuclear expression. The cut-off to define a high Ki-67 proliferation index is not well-established or universally agreed upon. In our laboratory, we use a scoring criteria of <20% of tumor cells with unequivocal nuclear staining of any intensity (>/=1+) is considered diagnostic negative for Ki-67 expression and >/= 20% of tumor cells with unequivocal nuclear staining of any intensity (>/=1+) is considered diagnostic positive for Ki-67 expression with a minimum of 200 viable tumor cells. The scoring criteria of "no Ki-67 expression" versus "Ki-67 expression" represent the level of Ki-67 expression based on these established cut-offs and do not apply to the overall number of positive cells or guidelines for prognostic purposes. The New York State Department of Health has not evaluated any test claims nor reviewed the accuracy of this test.

References:
1. Ki-67LDT as a predictive assay in therapy; A correlation study comparing NeoGenomics LDT to Agilent Ki-67 pharmDx assay. NeoGenomics White Paper. 2022.

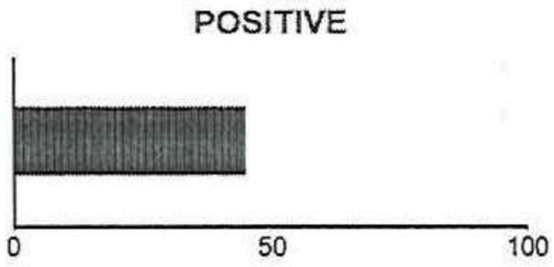
AR:
Androgen receptor is an intracellular protein which belongs to a large family of hormone-induced transcription factors. Androgen receptor mediates the biological actions of physiological androgens such as testosterone and 5 a-dihydrotestosterone, which are essential for differentiation, development and maintenance of the male reproductive organs. AR is responsible for the regulation of the growth of the prostate epithelial cells. In untreated prostate carcinoma, androgen receptor positive cells are more likely to be responsive to hormonal therapy. In patients with hormone refractory prostate carcinoma, the presence of androgen receptor has a negative prognostic impact (1). Androgen signaling pathway also may play a critical role in normal and malignant breast tissue. In particular, AR is expressed in normal breast epithelial cells and in approximately 70% to 90% of invasive breast carcinomas. In addition, 25% to 82% of metastatic breast tumors that are ER-negative and PR-negative express a significant amount of AR. Among women with ER-positive breast cancers, AR expression has been associated with a decrease in cancer-related mortality (2). Androgen receptor expression also aids in diagnosis of salivary duct carcinoma and has been described in cancers from other sites, including liver and pancreas. The New York State Department of Health has not evaluated any test claims nor reviewed the accuracy of this test.
References:
1. Grossmann ME, Huang H, Tindall DJ. Androgen receptor signaling in androgen-refractory prostate cancer. J Natl Cancer Inst. 2001;93(22):1687-97.
2. Hu R, Dawood S, et al. Androgen receptor expression and breast cancer survival in postmenopausal women. Clin Cancer Res. 2011;17(7):1867-74.

Methodology:
ER:
Leica clone 6F11 was used to detect Estrogen Receptor in formalin-fixed paraffin-embedded tissue sections. A polymer-technology based system was used for detection.

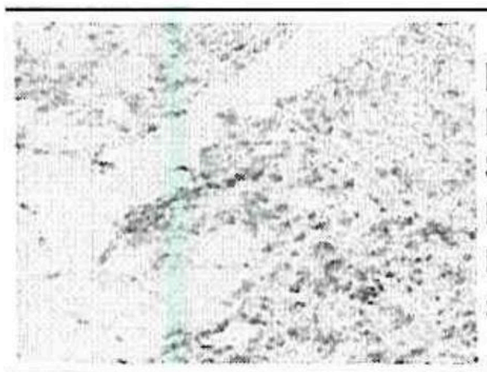
PgR:
Progesterone Receptor is performed as a lab developed test (LDT) using Leica clone 16 in formalin-fixed paraffin-embedded tissue sections. A polymer technology based system was used for detection.



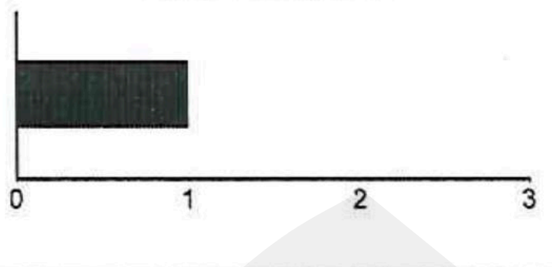
AR: POSITIVE
Tumor Stained: 45%
Intensity: 2+
Internal Control: Present, Positive



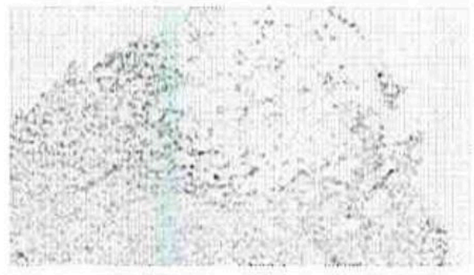
Reference Ranges	
Positive	>1%
Negative	</=1%



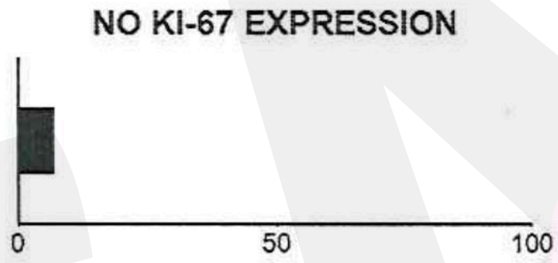
HER2 Breast: NEGATIVE/ LOW
Score: 1+
Percentage of Cells with Uniform Intense Complete Membrane Staining: **0%**



Reference Ranges	
Positive	3+
Equivocal/ Low	2+
Negative/ Low	1+
Negative	0



Ki67: NO KI-67 EXPRESSION
Tumor Stained: 7%
Intensity: 3+



Reference Range: Average Scoring	
Ki-67 Expression	>/=20%
No Ki-67 Expression	<20%

Tissue Fixative:

Specimens for predictive IHC and/or FISH testing should be submitted following CAP guidelines: Incisional and excisional biopsy samples should have a cold ischemia time of no longer than 1 hour and be fixed in 10% neutral buffered formalin (NBF) for intervals ranging from at least 6 hours to no more than 72 hours when testing. The fixative, fixation time and/or cold ischemic time do not meet the CAP guidelines. A negative result can be a potential false negative due to the possibility of prolonged cold ischemic time, inadequate fixative and/or fixation time. Results should be interpreted with caution.

Cytology specimens should also be fixed in 10% NBF. Please note that body fluid cytology specimens do not have specific cold ischemic time documentation requirements in this setting and are an exception to this statement.

Cold Ischemic Duration: 2 min(s)
Fixative: 10% Neutral Buffered Formalin
Fixation Duration: 76 hours

Intended Use:

Whole slide image capture was performed with the Aperio ScanScope and quantitative computer-assisted image analysis using Indica Labs software.
The digitized slide(s) was/were adequate for quantitative image analysis. All controls were reviewed and showed appropriate positive and negative immunoreactivity.

ER:
ER belongs to a superfamily of nuclear hormone receptors and is expressed in about 85% of invasive breast cancers. There are two known isoforms of estrogen receptor; ERα and ERß. It is a weak prognostic factor but a strong predictive factor for response to endocrine therapies, both in adjuvant and metastatic settings. The primary indication to assess ER in breast cancer is to predict response to hormonal therapies such as tamoxifen, other selective estrogen receptor modulators (SERMs) and aromatase inhibitors. The College of American Pathologists (CAP) and American Society of Clinical Oncology (ASCO) have recommended that ER should be measured in all primary breast cancers using validated biochemical or immunohistochemical methods. ER has also recently been shown to predict for benefit from tamoxifen in patients with ductal carcinoma in situ (DCIS).
Scoring/interpretation: ER staining is scored in our laboratory as the percentage of positive staining tumor nuclei on the examined slide. We use a cut-off level of 1-10% for low positive and >10% for positive as per 2020 ASCO/CAP guidelines (PMID: 31928354). Analyzed sections should be from specimens fixed in formalin for a minimum of 6 to 8 hours and no more than 72 hours in accordance with CAP/ ASCO published guidelines. An optional Allred Score may be provided which can be used to evaluate ER (Allred DC, Harvey JM, Berardo M, and Clark GM. Prognostic and predictive factors in breast cancer by immunohistochemical analysis. Mod Pathol 11: 155-168, 1998). The New York State Department of Health has not evaluated any test claims nor reviewed the accuracy of this test. The performance characteristics of these assays have not been validated on decalcified specimens. Results should be interpreted with caution given the likelihood of false negativity on decalcified specimens. Repeat testing on a different block or resection of specimen should be considered for the following scenarios: in the instance where estrogen receptor result is negative and progesterone receptor result is positive; estrogen and progesterone receptor results are negative or estrogen receptor is low positive (1-10%) in breast specimen, in the absence of internal controls; weak staining or staining of few cells in a small sample (<100 tumor cells), or when ER/PR results are negative in tumor subtypes that are typically positive, such as invasive tubular, lobular, mucinous and low grade invasive breast carcinomas.

PgR:
PgR belongs to a superfamily of nuclear hormone receptors. ER induces PgR expression, and therefore PgR status serves as an indicator of an intact ER pathway. There are two known isoforms of PgR: PRa and PRß. The current assays in clinical breast cancer measure both isoforms. PgR is expressed in about 60-70% of invasive breast cancers. The College of American Pathologists (CAP) and American Society of Clinical Oncology (ASCO) have recommended that PgR should be measured in all primary invasive breast cancers using validated biochemical or immunohistochemical methods; testing of PgR is optional for newly diagnosed ductal carcinoma in situ. PgR levels may help to stratify outcomes in ER-positive breast cancer patients, with data supporting that cases with lower or negative PgR expression may have a worse prognosis. Per CAP guidelines, although controversial as a result category, confirmed ER-negative/PgR positive samples may represent a rare biologic phenotype that may be offered endocrine therapies, although due to the rarity of this result group, there are limited data to support this. Scoring/interpretation: PgR immunostaining is scored in our laboratory as the percentage of positive staining tumor nuclei on the examined slide. We use a cut-off level of 1% in our laboratory based on comparison of our results to that of a clinically validated PgR assay, as determined by two large clinical studies. Analyzed sections should be from specimens fixed in formalin for a minimum of 6 to 8 hours and no more than 72 hours in accordance with CAP/ASCO published guidelines. An optional Allred Score may be provided which can be used to evaluate PgR stains (Allred DC, Harvey JM, Berardo M, and Clark GM. Prognostic and predictive factors in breast cancer by immunohistochemical analysis. Mod Pathol 11: 155-168, 1998). The New York State Department of Health has not evaluated any test claims nor reviewed the accuracy of this test. The performance characteristics of these assays have not been validated on decalcified specimens. Results should be interpreted with caution given the likelihood of false negativity on decalcified specimens.

HER2 Breast:
HER2, a member of the epidermal growth factor receptor family, is a transmembrane protein with tyrosine kinase activity. Gene amplification and protein overexpression of HER2 have been found in a variety of tumors, including breast carcinomas. The expected overexpression rate varies based on the grade and type of breast cancer. Patients with breast cancers that are HER2 IHC 3+ or IHC 2+/ISH amplified may be eligible for several therapies that disrupt HER2 signaling pathways. Invasive breast cancers that test 'HER2-negative' (IHC 0, 1+ or 2+/ISH not-amplified) are more specifically considered "HER2-negative for protein overexpression/gene amplification" since non-overexpressed levels of the HER2 protein may be present in these cases. Patients with breast cancers that are HER2 IHC 1+ or IHC 2+/ISH not amplified (so-called HER2 Low) may be eligible for a treatment that targets non-amplified/non-overexpressed levels of HER2 expression for cytotoxic drug delivery (IHC 0 results do not result in eligibility currently). The New York State Department of Health has not evaluated any test claims nor reviewed the accuracy of this test. The performance characteristics of this assay have not been validated on decalcified specimens. Results should be interpreted with caution given the likelihood of false negativity on decalcified specimens. Antigenicity of cut tissue sections may diminish over time and is compromised within 6 weeks after cutting from the paraffin block.