7) Bui MM, Riben MW, Allison KH, et al. Quantitative Image Analysis of Human Epidermal Growth Factor Receptor 2 Immunohistochemistry for Breast Cancer Guideline from the College of American Pathologists. 2018. *Arch Pathol Lab Med.* doi: 10.5858/arpa.2018-0378-CP.

***REVISED** 12/26/2024*

**ANP.22970 Annual Result Comparison - Breast Carcinoma** **Phase II**

**For HER2 and ER immunohistochemical (IHC) tests performed on breast carcinoma that provide independent predictive information, the laboratory at least annually compares its patient results with published benchmarks.**

*NOTE: For estrogen receptor studies: in general, the overall proportion of ER-negative breast cancers (invasive and DCIS) should not exceed 30%. The proportion is somewhat lower in postmenopausal than premenopausal women (approximately 20% vs. 35%). The proportion of ER-negative cases is considerably lower in well-differentiated carcinomas (<10%) and certain special types of invasive carcinomas (<10% in lobular, tubular, and mucinous types). Investigation is warranted if the proportion of ER-negative cases varies significantly from the published benchmarks.*

*For HER2 studies, the overall proportion of HER2 positive breast cancers is 10-25%. Laboratories must monitor their results. Investigation is warranted if the proportion of HER2 positive cases varies significantly from published data.*

**Evidence of Compliance:**

✓ Records of annual result comparison

REFERENCES

1) Wolff AC, Somerfield MR, Dowsett M, et al. Human Epidermal Growth Factor Receptor 2 Testing in Breast Cancer: American Society of Clinical Oncology/College of American Pathologist Guideline Update. *Arch Pathol Lab Med.* Published online June 7, 2023. doi: 10.5858/arpa.2023-0905-SA
2) Allison KH, Hammond ME, Dowsett M, et al. Estrogen and progesterone receptors in breast cancer: American Society of Clinical Oncology/College of American Pathologists Guideline update [published online ahead of print January 2020] *Arch Pathol Lab Med.* doi: 10.5858/arpa.2019-0904-SA.
3) Fitzgibbons PL, Murphy DA, Hammond ME, *et al.* Recommendations for validating estrogen and progesterone receptor immunohistochemistry assays. *Arch Pathol Lab Med* 2010;134:930-935
4) Dunnwald LK, Rossing MA, Li CI. Hormone receptor status, tumor characteristics, and prognosis: a prospective cohort of breast cancer patients. *Breast Cancer Research* 2007;9:R6
5) Rüschoff J, Lebeau A, Kreipe H, et al. Assessing HER2 testing quality in breast cancer: variables that influence HER2 positivity rate from a large, multicenter, observational study in Germany. *Mod Pathol.* 2017;30:217-26.

***NEW** 12/26/2024*

**ANP.22975 Immunohistochemical (IHC) Predictive Marker Interpretation** **Phase I**

**Each pathologist interpreting IHC predictive markers participates in an annual analyte-specific quality assessment for each of the following predictive markers, as applicable:**

- **Breast HER2**
- **Breast ER**
- **Gastric HER2**
- **Lung highly sensitive ALK**
- **Lung PD-L1 tumor proportion score (TPS)**

*NOTE: This requirement applies to all pathologists in the laboratory that interpret one or more of these markers, whether in laboratories that perform both staining and interpretation or interpretation only. An individual pathologist need participate only once for each predictive marker used by that pathologist in patient care evaluation, regardless of the number of locations where the pathologist performs interpretations.*

*The quality assessment for each predictive marker must include a comparison of each pathologist's interpretation against the intended results. The laboratory director must define criteria for acceptable results and ensure follow up on each unacceptable result.*

*Examples of how this requirement can be met include the use of:*

- *IHC proficiency testing (PT) stained slides or images used **after** the deadline for submission of results to the PT provider*
- *Educational, peer-based, interpretation-based programs that provide stained slides or images (eg, CAP HER2 and ER Immunohistochemistry Interpretation Only Program [HER1])*
- *Laboratory-developed programs for sharing stained slides or images.*

**Evidence of Compliance:**

✓ Records of annual assessment of each pathologist for predictive marker interpretation (performed on site or at another laboratory), where applicable

*****REVISED** 12/26/2024***

**ANP.22978 Validation/Verification - Predictive Marker Testing** **Phase II**

**Predictive marker testing by immunohistochemistry (IHC) and/or in situ hybridization (eg, FISH, CISH, SISH) is validated/verified and records of validation/verification are retained.**

*NOTE: For validation of **laboratory-developed or modified FDA-cleared/approved predictive assays**, the validation must be performed on a minimum of 40 cases (20 positive and 20 negative samples).*

*For verification of **unmodified FDA-cleared/approved predictive assays**, the laboratory must follow the instructions provided by the manufacturer. If the instructions do not list a minimum number of samples for assay verification, the verification must be performed on a minimum of 20 positive and 20 negative tissues.*

*If the laboratory director determines that fewer validation/verification cases are sufficient for a specific marker (eg, a rare antigen, tissue, gene, or probe), the rationale for that decision must be recorded. Positive cases in the validation/verification set should span the expected range of clinical results (expression levels). Only definitively positive and negative cases may be used for validation/verification.*

*The validation/verification data must clearly show the degree of concordance between assays or methods. Minimum acceptable concordance levels for IHC tests are 90% for positive and negative results.*

*The characteristics of the cases used for validation/verification should be similar to those seen in the laboratory's patient population (ie, core biopsy vs. open biopsy, primary vs. metastatic tumor, etc.).*

*Samples used for validation/verification must be handled in conformance with the guidelines in this checklist. Laboratories should use tissues that have been processed using the same fixative and methods as cases that will be tested clinically.*

*If significant changes are made to the testing methods (eg, antibody clone, antigen retrieval protocol or detection system, probe or pretreatment protocol), revalidation/verification is required.*

*This requirement is applicable to both new and existing assays. If review of the initial validation/ verification does not meet the current standard, it must be supplemented and brought into compliance. It is possible to do this retroactively by review and documentation of past proficiency testing challenges or by sending unstained slides from recent cases to a referral laboratory for correlation. If no records exist from the initial validation/verification, the assay must be fully revalidated/verified.*

**Evidence of Compliance:**

✓ Records of validation/verification data including criteria for concordance

REFERENCES

1) Wolff AC, Somerfield MR, Dowsett M, et al. Human Epidermal Growth Factor Receptor 2 Testing in Breast Cancer: American Society of Clinical Oncology/College of American Pathologist Guideline Update. *Arch Pathol Lab Med.* Published online June 7, 2023. doi: 10.5858/arpa.2023-0905-SA
2) Fitzgibbons PL, Murphy DA, Hammond ME, Allred DC, Valenstein P. Recommendations for validating estrogen and progesterone receptor immunohistochemistry assays. *Arch Pathol Lab Med* 2010; 134:930-935.
3) Wolff AC, Hammond ME, Hicks DG, *et al.* Recommendations for human epidermal growth factor receptor 2 testing in breast cancer; American Society of Clinical Oncology/College of American Pathologists. *Arch Pathol Lab Med* 2014;138(2):241-256