Evidence of Compliance:

- ✓ Report template containing all required elements **AND**
- ✓ Copies of patient reports confirming inclusion of the required elements **AND**
- ✓ Established guidelines used by the laboratory

REFERENCES

1) Fischer AH, Schwartz MR, Moriarty AT, et al. Immunohistochemistry practices of cytopathology laboratories: a survey of participants in the College of American pathologists Nongynecologic Cytopathology Education Program. *Arch Pathol Lab Med.* 2014;138(9):1167-72.
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3) Collins LC, *et al*. Bimodal frequency distribution of estrogen receptor immunohistochemical staining results in breast cancer: an analysis of 825 cases. *Am J Clin Pathol.* 2005;123:16-20
4) Allred DC, *et al.* ER expression is not bimodal in breast cancer. *Am J Clin Pathol.* 2005;124:474-5
5) 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 Pathologists Guideline Update. *Arch Pathol Lab Med.* Published online June 7, 2023. doi: 10.5858/arpa.2023-0905-SA.
6) Allison KH, Hammond EH, Dowsett M, et al. Estrogen and Progesterone Receptor Testing in Breast Cancer: American Society of Clinical Oncology/College of American Pathologists Guideline Update *Arch Pathol Lab Med.* 2020; 144(5):545-63.
7) Bartley AN, Washington MK, Ventura CB, et al. HER2 Testing and Clinical Decision Making in Gastroesophageal Adenocarcinoma: Guideline from the College of American Pathologists, American Society for Clinical Pathology, and American Society of Clinical Oncology. *Arch Pathol Lab Med.* 2016:140(12):1345-1363.

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

CYP.04520 Annual Result Comparison - Breast Carcinoma **Phase I**

For HER2 and ER immunocytochemical tests performed on breast carcinoma that provide independent predictive information, the laboratory at least annually compares its patient results with published benchmarks, if applicable to the patient population tested.

NOTE: This checklist requirement is not applicable if the laboratory director determines that the population of breast carcinoma patients tested is not representative of the overall population of breast carcinoma patients.

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 Pathologists 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***

CYP.04525 Predictive Marker Interpretation **Phase I**

Each pathologist interpreting immunocytochemistry 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. This requirement can be met by the use of laboratory-developed programs for sharing stained cytology slides or images thereof.

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.

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***

CYP.04530 Validation/Verification - Predictive Marker Testing **Phase II**

Predictive marker testing by immunocytochemistry is validated/verified and records of validation/verification are retained.

*NOTE: For validation of **laboratory-developed or modified FDA-cleared/approved predictive assays**, validation must be performed on a minimum of 20 cases (10 positive and 10 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 10 positive and 10 negative cellular samples or tissues.*

If the laboratory director determines that fewer validation/verification cases are sufficient for a specific marker (eg, a rare antigen or tissue), 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 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 cellular samples or 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, or pretreatment protocol), revalidation/verification is required.