- *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