The validation/verification data must clearly show the degree of concordance between the assays or methods. Acceptable concordance levels should be defined by the laboratory and follow the current CAP guidelines if available.

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 changes are made to the testing methods (eg, probe, pretreatment protocol), the laboratory director is responsible for determining the extent of the performance verification or revalidation needed based on the scope of the changes in the test method.

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.

This checklist requirement applies to laboratories that perform the technical portion of the testing process.

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 Pathologists Guideline Update. *Arch Pathol Lab Med.* Published online June 7, 2023. doi: 10.5858/arpa.2023-0905-SA.

CYG.48932 Fixation - HER2 (ERBB2) Breast Predictive Marker Testing Phase I

If the laboratory assesses HER2 (ERBB2) gene amplification by in situ hybridization (ISH) for breast predictive marker testing, the laboratory monitors cold ischemia time (one hour or less) and appropriate specimen fixation time.

NOTE: The CAP strongly recommends that specimens subject to HER2 (ERBB2) testing be placed in fixative within one hour of biopsy or resection (cold ischemia time) and remain in 10% neutral buffered formalin for at least six hours and up to 72 hours (formalin fixation time) at room temperature. Refer to ANP.22983 for ideal fixation parameters.

If specimens are fixed in a solution other than 10% neutral buffered formalin, the laboratory must perform a validation study showing that results are concordant with results from formalin-fixed tissues.

Laboratories testing specimens obtained from another institution must have a policy that addresses cold ischemia time and time of fixation. This information may be obtained by using the laboratory requisition form. Laboratories must communicate with the submitting service to facilitate appropriate specimen handling and proper recording of fixation parameters (refer to ANP.22983 for details).

Evidence of Compliance:

✓ Records of action taken when cold ischemia and fixation times are consistently outside of required parameters or are not available to the laboratory

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) Compton CC, Robb, JA, Anderson MW, et al. Preanalytics and Precision Pathology: Pathology Practices to Ensure Molecular Integrity of Cancer Patient Biospecimens for Precision Medicine. *Arch Pathol Lab Med.* 2019;143(11):1346-63.