

If digital image analysis is used, additional requirements in the Digital Image Analysis section also apply.

****REVISED** 08/24/2023**

CYG.47880 Report Elements

Phase I

For in situ hybridization (ISH) tests that provide independent predictive information, the patient report includes information on specimen processing, the probe, and the scoring method used.

NOTE: The following information must be included in the patient report:

1. The type of specimen fixation and processing (eg, formalin-fixed paraffin-embedded sections, air-dried imprints)
2. The probe and, if applicable, the detection system used (ie, LSAB, polymer, proprietary kit, vendor name, etc.; information on the type of equipment used is not necessary)
3. Criteria used to determine a positive vs. negative result and scoring system (eg, manual or automated)
4. Laboratory interpretation of predictive marker testing (ISH) is reported according to the manufacturer's instructions, or when available, following the structure, format, and criteria set forth in the current [CAP guidelines](#) relating to predictive marker testing (eg, ASCO/CAP HER2 testing in breast cancer and CAP/ASCP/ASCO HER2 in gastroesophageal carcinoma).
5. Limitations relating to suboptimal preanalytical factors that may impact results, such as prolonged cold ischemia time, unknown ischemia time, or over- or under-fixation.

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) 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) 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**

CYG.48399 Validation/Verification - Predictive Marker Testing

Phase II



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

*NOTE: For validation of **laboratory-developed and modified FDA-cleared/approved HER2 (ERBB2) breast 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 HER2 (ERBB2) breast 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.*

*For **other predictive marker assays**, the laboratory director must determine the appropriate number of positive and negative samples to be used to adequately validate/verify the test. In general, laboratories should consider using higher numbers of test cases when assessing laboratory-developed tests or modified FDA-cleared/approved tests than is necessary for unmodified FDA-cleared/approved tests for the same analyte. For genetic abnormalities where positive cases are rare, the laboratory director may determine that fewer validation cases are necessary. However, the rationale for using fewer cases must be recorded.*

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.