hormonal treatment of breast carcinoma but does not apply to estrogen receptor testing used solely to assist in determining the primary site of origin of a metastatic neoplasm.

The current CAP guidelines (https://www.cap.org/protocols-and-guidelines/current-cap-guidelines) relating to predictive marker testing (eg, ASCO/CAP HER2 and ER testing in breast cancer) may be found at cap.org in the Protocols and Guidelines section. The guidelines are periodically updated based on new evidence. Laboratories should review updated predictive marker guidelines and promptly implement changes for items relating to requirements in the checklists (eg, validation, fixation, scoring criteria).

Inspector Instructions:

	• Predictive markers policies and procedures • Sampling of patient reports for completeness, including ASCO/CAP scoring when applicable • Records of annual benchmark comparison for breast predictive markers, if applicable to the patient population tested • Records of annual analyte-specific quality assessment, as applicable • Sampling of predictive marker assay validation, verification, and revalidation/verification studies
	• What is your laboratory's course of action when negative HER2 and/or negative ER by immunocytochemical results are obtained and the fixation was not appropriate? • How did you validate/verify the most recently added predictive marker on your test menu?

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

CYP.04510 Report Elements **Phase II**

For immunocytochemical tests that provide independent predictive information, the patient report includes information on specimen processing, the antibody clone, and the scoring method used.

NOTE: The laboratory processing the cytology specimen must record the cold ischemia time (if applicable) and the length of time in fixative. If the cytopathology laboratory refers immunocytochemistry or ISH studies, this information must be provided to the laboratory(ies) performing these studies.

For immunocytochemical studies used to provide predictive information independent of diagnosis or other cytopathologic findings (eg, estrogen receptors and HER2 in breast carcinoma, PD-L1 and lung adenocarcinoma predictive immunostains), the laboratory must include the following information in the patient report:

1. *The type of specimen fixation and processing (eg, formalin-fixed paraffin-embedded sections, air-dried imprints, etc.)*
2. *The antibody clone and general form of detection system used (eg, 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/or scoring system (eg, percent of stained cells, staining pattern)*
4. *Laboratory interpretation of predictive marker testing 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 and ER 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

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

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