BAP.05338 Slide Quality **Phase II**

Slides are of sufficient quality for diagnosis.

NOTE: Histopathology slides must be of adequate technical quality to be diagnostically useful. Criteria to evaluate include adequate tissue fixation, processing, thickness of sections, absence of interfering tissue folds and tears, and good staining technique and coverslipping. For hematoxylin and eosin and other routine stains, the patient slide serves as the internal control to ensure adequate staining technique. The sections must be cut from sufficient depth in the block to include the entire tissue plane.

BAP.05342 Specimen Modification **Phase II**

If the biorepository performs immunohistochemical staining on specimens other than formalin-fixed, paraffin-embedded tissue, the written procedure defines appropriate modifications, if any, for specimen types.

NOTE: Such specimens include frozen sections, air-dried imprints, cytocentrifuge or other liquid-based preparations, decalcified tissue, and tissues fixed in alcohol blends or other fixatives.

REFERENCES
1) Perkins SL, Kjeldsberg CR. Immunophenotyping of lymphomas and leukemias in paraffin-embedded tissues. *Am J Clin Pathol* 1993:99(4):362-373
2) Clinical and Laboratory Standards Institute. *Quality Assurance for Design Control and Implementation of Immunohistochemistry Assays; Approved Guideline.* 2nd ed. CLSI Document I/LA28-A2. Clinical and Laboratory Standards Institute, Wayne, PA; 2011.

BAP.05345 Buffer pH **Phase II**

The pH of the buffers used in immunohistochemistry is monitored at defined intervals.

NOTE: pH must be tested when a new batch is prepared or received.

Evidence of Compliance:
- ✓ Records of initial and subsequent QC on each buffer

*****REVISED** 12/26/2024***
BAP.05348 QC - Antibodies **Phase II**

Positive controls are used for each antibody.

NOTE: Positive controls assess the performance of the immunohistochemistry assay (including impact of fixation and antigen retrieval) and can assess the sensitivity of the assay. They should, whenever possible, be subjected to the same processing, antigen retrieval, and immunostaining protocol as donor tissue.

Results of controls must be recorded, either in internal biorepository records, or in the donor report. A statement in the report such as, "All controls show appropriate reactivity" is sufficient.

For tissue-based positive controls, the ideal control is of the same specimen type as the donor test specimen (eg, small biopsy, large tissue section, cell block), and is processed and fixed in the same manner (eg, formalin-fixed, alcohol-fixed, decalcified) as the donor specimen. However, for most biorepositories, it is not practical to maintain separate positive control samples to cover every possible combination of fixation, processing and specimen type. Thus, it is reasonable for a biorepository to maintain a bank of formalin-fixed tissue samples as its positive controls; these controls can be used for donor specimens that are of different type, or fixed/ processed differently, providing that the biorepository can show that these donor specimens exhibit equivalent immunoreactivity. This can be accomplished by parallel testing a small panel

of common markers to show that specimens of different type, or processed in a different way (eg, alcohol-fixed cytology specimens, decalcified tissue) have equivalent immunoreactivity to routinely processed, formalin-fixed tissue.

A separate tissue section may be used as a positive control, but test sections often contain normal elements that express the antigen of interest (internal controls). Internal positive controls are acceptable for these antigens, but the biorepository manual must clearly state the manner in which internal positive controls are used.

A positive control included on the same slide as the donor tissue is optimal practice because it helps identify failure to apply primary antibody or other critical reagents to the donor test slide; however, one separate positive control per staining run for each antibody in the run (ie, batch control) may be sufficient provided that the control slide is closely scrutinized by a qualified reviewer.

Ideally, positive controls have low levels of antigen expression, as is often seen in neoplasms. Different expression level controls are suggested if related to companion diagnostic clinical decision points (ie, HER2; 0, 1+, 2+, 3+). Exclusive use of normal tissues that have high levels of antigen expression may result in failure to identify assays of insufficient sensitivity, leading to false-negative results.

Synthetic materials (eg, microbeads) and cell lines containing IHC analytes of interest may be run as controls in addition to positive tissue controls. Synthetic controls and cell lines should contain the target epitope of the IHC assay. Controls that assess the IHC protocol should be sensitive to the antigen retrieval step.

Synthetic and cell line-based controls can be particularly useful to assess assay performance at low expression levels, such as detecting low levels of expression in breast cancer. Synthetic and cell line-based controls are not ideal for optimizing digital pathology algorithms, which are optimally tuned to IHC expression in human tumors.

Evidence of Compliance:

- ✓ Donor reports or worksheet with control results **AND**
- ✓ Immunohistochemical-stained slides with positive controls

REFERENCES

1) Clinical and Laboratory Standards Institute. *Quality Assurance for Design Control and Implementation of Immunohistochemistry Assays; Approved Guideline - Second Edition*. CLSI document I/LA28-A2. Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA; 2011.
2) Allen M. Gown, MD. Diagnostic Immunohistochemistry: What Can Go Wrong and How to Prevent it. *Arch Pathol Lab Med*. 2016;140(9):893-898.
3) Cheung CC, D'Arrigo C, Dietel M, et al; From the International Society for Immunohistochemistry and Molecular Morphology (ISIMM) and International Quality Network for Pathology (IQN Path). Evolution of Quality Assurance for Clinical Immunohistochemistry in the Era of Precision Medicine: Part 4: Tissue Tools for Quality Assurance in Immunohistochemistry. *Appl Immunohistochem Mol Morphol.* 2017;25(4):227-230.
4) Cheung CC, Taylor CR, Torlakovic EE. An Audit of Failed Immunohistochemical Slides in a Clinical Laboratory: The Role of On-Slide Controls. *Appl Immunohistochem Mol Morphol.* 2017;25(5):308-312.
5) Torlakovic EE, Nielsen S, Francis G, et al. Standardization of positive controls in diagnostic immunohistochemistry: recommendations from the International Ad Hoc Expert Committee. *Appl Immunohistochem Mol Morphol.* 2015;23(1):1-18.
6) ISO 20166-4:2020 Molecular in vitro diagnostic examinations. Specifications for pre-examination processes for formalin-fixed and paraffin-embedded (FFPE) tissue. Part 4: in situ detection techniques. International Organization for Standardization. 2020.

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

BAP.05350 Synthetic and Commercial Control Range Establishment or Verification Phase II

If synthetic or commercial controls are used for quantitative testing, the biorepository establishes or verifies an acceptable control range for each lot of synthetic or commercial control material.

NOTE: The biorepository must verify control ranges supplied by the manufacturer if provided and establish an acceptable range by repetitive analysis if control ranges are not provided by the manufacturer.

Control values supplied by the manufacturer may be used without verification for qualitative (eg, positive or negative) testing.