COLLEGE of AMERICAN PATHOLOGISTS

December 2024 Changes

Anatomic Pathology Checklist

CAP Accreditation Program

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Using the Changes Only Checklist

This document contains new checklist requirements, major and minor requirement revisions, and changes to explanatory text**. Changes appear in a track changes format that compares the previous checklist edition to the December 26, 2024 edition.** Requirements with significant revisions will display a "Revised" flag. These changes may affect your laboratory operations. Requirements with minor revisions will not display a "Revised" flag. They are editorial changes that are not likely to affect your laboratory operations.

Information regarding requirements that are new or have been combined, moved, resequenced or deleted, as applicable, appears in table format below.

2024 CHECKLIST EDITION CHANGES
NEW, DELETED, MERGED, AND MOVED REQUIREMENTS *

2023 Requirement		Action Taken	2024 Requirement	
		New	ANP	10290
		New	ANP	22560
		New	ANP	22975
		New	ANP	29680
		New	ANP	29720
		New	ANP	33110

*Deleted – Removed the requirement from the checklist edition
*Merged – Combined the requirement with a similar requirement in the same or different checklist
*Moved – Relocated the requirement to another checklist or resequenced it within the same checklist

ON-LINE CHECKLIST DOWNLOAD OPTIONS

Participants of the CAP accreditation programs may download the checklists ~~from the CAP website (cap.org)~~ by logging into cap.org and going to e-LAB Solutions Suite - Accreditation Checklists. They are available in different checklist types and formatting options, including:

- Master — contains ALL of the requirements and instructions available in PDF, Word/XML or Excel formats
- Custom — customized based on the laboratory's activity (test) menu; available in PDF, Word/XML or Excel formats
- Changes Only — contains only those requirements with significant changes since the previous checklist edition in a track changes format to show the differences; in PDF version only. Requirements that have been moved or merged appear in a table at the end of the file.

INTRODUCTION

This checklist is used in conjunction with the All Common (COM) and Laboratory General Checklists to inspect an anatomic pathology laboratory section or department.

Do NOT use this Checklist if the laboratory does NOT perform any on-site preparation or examination of anatomic pathology specimens, but refers all submitted material to an outside laboratory, or if the laboratory's involvement in anatomic pathology is limited to filing of reports and/or slides.

Laboratories that do not file slides on-site (eg, "read-only" laboratories) must retain a sample of cases and all associated slides on-site for review by the inspector on all days when the laboratory is subject to its regular on-site inspection. The sample must, at a minimum, include all cases and associated slides accessioned over a continuous 2-week period within the previous 2 years.

*If telepathology is used by the pathologist to review slides or images for primary diagnosis, frozen section diagnosis, formal second-opinion consultations, ancillary techniques in which the pathologist participates in interpretation of images, or real-time evaluation of FNA specimens for triaging and preliminary diagnosis, refer to the Telepathology and Remote Data Assessment section of the Laboratory General Checklist for additional requirements. Telepathology occurs when a pathologist views digitalized or analog video or still image(s), or other data files (eg, flow cytometry files) at an off-site or remote location and an interpretation is rendered that is included in a formal diagnostic report or recorded in the patient record. The Telepathology and Remote Data Assessment section of the Laboratory General Checklist is not applicable if the image(s) and/or data files are generated and interpreted **within the same laboratory** using the laboratory's validated software.*


Policy/Procedure icon - The placement of this icon next to a checklist requirement indicates that a written policy or procedure is required to demonstrate compliance with the requirement. The icon is not intended to imply that a separate policy or procedure is required to address individual requirements. A single policy or procedure may cover multiple checklist requirements.

***Laboratories not subject to US regulations:** Checklist requirements apply to all laboratories unless a specific disclaimer of exclusion is stated in the checklist. When the phrase "FDA-cleared/approved test (or assay)" is used within the checklist, it also applies to tests approved by an internationally recognized regulatory authority (eg, CE-marking).*

SURGICAL PATHOLOGY

QUALITY MANAGEMENT

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

ANP.10290 **Instructions for Body Handling** **Phase II**

There are documented instructions covering such items as receipt, storage, and release of bodies.

NOTE: In some institutions, such policies and procedures may reside in the nursing or security manuals. In such cases, the laboratory must have copies of the manuals available at the time of inspection.

This requirement is not applicable if the laboratory is not responsible for handling bodies.

SURGICAL SPECIMEN EXAMINATION

***REVISED** 12/26/2024*

ANP.11610 **Gross Examination - Qualifications to Assist with Grossing** **Phase II**

For laboratories subject to US regulations, individuals other than a pathologist or pathology resident (or an individual who meets the grossing subspecialty qualifications listed under ANP.11600) who assist in gross examinations meet high complexity testing

personnel qualifications. For laboratories not subject to US regulations, such individuals are qualified under national, state or provincial, and local regulations, as applicable.

NOTE: Individuals assisting with grossing may perform physical examination/description of tissue specimens, including color, weight, measurement or other characteristics of the tissue, or other mechanical procedures (eg, dissection) under appropriate supervision. The laboratory director may delegate the grossing of specimens to non-pathologist individuals, but is responsible for determining whether an individual's education, training and experience meet the required qualifications.

For laboratories subject to US regulations, these individuals must be qualified as high complexity testing personnel under the CLIA regulations. The minimum training/experience required of such personnel is:

1. *An earned associate degree in a laboratory science (chemical or biological science) or medical laboratory technology, obtained from an accredited institution, OR*
2. *Education/training equivalent to the above that includes the following:*

    - *60 semester hours or equivalent from an accredited institution. This education must include 24 semester hours of medical laboratory technology courses, OR 24 semester hours of science courses that includes six semester hours of chemistry, six semester hours of biology, and 12 semester hours of chemistry, biology or medical laboratory technology in any combination, AND*
    - *Laboratory training including either completion of a clinical laboratory training program approved or accredited by the ~~ABHES, NAACLS, or other organization approved by HHS~~Accrediting Bureau of Health Education Schools (ABHES), or the Commission on Accreditation of Allied Health Education Programs (CAAHEP) (note that this training may be included in the 60 semester hours listed above), OR at least three months of recorded laboratory training in each specialty in which the individual performs high complexity testing.*

If there are more stringent state or local regulations for grossing qualifications, they must be followed. Additional educational pathways for qualifying as high complexity testing personnel may be found in the CAP Personnel Guidance Document located in e-LAB Solutions Suite on cap.org (log-in required) under Accreditation Resources - Accreditation Checklists.

For US Department of Defense laboratories, effective May 29, 2014, newly hired high complexity testing personnel must have either:

- *A minimum of an associate degree in a biological or chemical science or medical laboratory technology from an accredited institution **AND** be certified by the ASCP, AMT or other board or registry deemed comparable by OASD(HD) or their designee Center for Laboratory Medicine Services (CLMS) as an MLT or MT/MLS; OR*
- *Successfully completed an official U.S. military medical laboratory procedures training course of at least 50 weeks duration and currently hold the military enlisted occupational specialty of medical laboratory specialist (laboratory technician).*

Evidence of Compliance:

✓ Records of qualifications including degree or transcript and work history in related field

REFERENCES

1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. ~~2003(Oct 1):1070-1071 [~~2023(Dec 28):[42CFR493.1489~~], 1071-1072 [42CFR493.1491]~~].
2) California Business and Professions Code §1269.3.

SURGICAL PATHOLOGY REPORTS

***REVISED** 12/26/2024*

ANP.12500 Record and Material Retention - Surgical Pathology **Phase II**

Surgical pathology records and materials are retained for an appropriate period.

NOTE 1: The retention policy must address protecting and preserving the integrity and retrieval of surgical pathology materials and records.

Policies for retention of records and materials must comply with national, federal, state (or provincial), and local laws and regulations, and with the retention periods listed in the table below, whichever is most stringent.

Type of Record/Material	Retention Period
Accession log records	2 years
Wet tissue (stock bottle)	2 weeks after final report
Paraffin blocks (including cell blocks)	10 years Refer to Note 2 below, paragraphs #2 and #3, for deceased patient material
Immunohistochemistry batch control slides	2 years
~~Glass~~Surgical pathology glass slides	10 years - slides must remain readable for this period
Surgical pathology reports *	10 years
Reports of outside consultations on laboratory cases (whether or not requested by the laboratory)	10 years after the date that the original report was issued
Fluorochrome-stained slides	At the discretion of the laboratory director
Images or permanent slides of ISH studies	10 years for neoplastic disorders 20 years for constitutional disorders (Subject to ~~Notes~~Note 4 ~~and 5~~ below)
Images for Circulating Tumor Cells	10 years
Digital images used for primary diagnosis	10 years if original glass slides are not available; may not replace glass slides
Datasets from In-Vivo Microscopy (IVM) or Ex Vivo Microscopy (EVM) systems used to aid in interpretation or diagnosis	10 years - data must be retrievable for this period (Subject to Note ~~6~~5 below)

** Pathology reports may be retained in either paper or electronic format. If retained in electronic format alone, the reports must include a secure pathologist electronic signature. Images of paper reports, such as microfiche or PDF files are acceptable.*

NOTE 2: Paraffin blocks used for patient diagnostic, prognostic and/or predictive purposes must be kept for at least 10 years and be stored in a manner that preserves their identity and integrity. Tissue blocks must be stored in a temperature-controlled, pest-free environment to maintain tissue integrity. The CAP recommends (but does not require) ambient temperatures in block storage areas to be less than 27°C.

Paraffin blocks may be released for research purposes if all of the following criteria are met:

1. *For laboratories subject to US regulations, formal written authorization is obtained in accordance with the requirements of HIPAA if identifiable patient information is released.*
2. *The laboratory retains sufficient blocks to support the diagnosis for the full 10-year period. After a patient has been deceased for two years, only one block containing normal tissue (if it exists) needs to be retained for the full 10-year period.*
3. *Provision is made for retrieval by the laboratory of any blocks or material that remain after use in research, if the blocks or material are needed for diagnostic, legal, or other legitimate purposes. After a patient has been deceased for two years, only one block containing normal tissue (if it exists) must be retrievable for the full 10-year period.*
4. *In the event of limited material (eg, only one diagnostic block), tissue microarray (TMA) cores or portions of the block may be released for research or clinical trials, as long as the original lab retains control or access to the diagnostic material if clinically needed.*
5. *The laboratory meets other relevant requirements including but not limited to the requirements of the institution, the directives of any applicable institutional review board (IRB) or similar entity; and state and local laws and regulations.*

The restriction on release of blocks does not prohibit release of blocks for purposes of treatment, diagnosis, prognosis, etc., for patients on research protocols as long as release is consistent with patient privacy regulations (eg, HIPAA) and applicable state and local regulations; and there is IRB approval, as applicable.

NOTE 3: Given that patient survival rates are increasing and the continued emergence of treatment based on biomarker testing, which at times may be required on the original tissue, it is recommended that, whenever feasible, tissue block retention from patients with diagnosed malignancies be retained beyond the 10 year requirement.

NOTE 4: There is no retention requirement for images of ~~glass~~ slide preparations when the source slides remain readable for the required retention period. If slides are expected to become unreadable before the end of the required retention periods (for example, FISH slides), then images that adequately represent findings on the slides must be retained.

~~NOTE 5: For an~~If representative images of chromosome ISH ~~assay~~slides are retained, those with a normal result~~, retain~~ must include an image of at least one cell illustrating the normal probe signal pattern~~. For an ISH assay~~, and those with an abnormal result~~, retain~~ must include images of at least two cells illustrating each relevant abnormal probe signal pattern.

NOTE ~~6~~5: In Vivo Microscopy (IVM) and Ex Vivo Microscopy (EVM) systems include confocal microscopy, optical coherence tomography, multiphoton microscopy, optical spectroscopy/spectroscopic imaging, and similar technologies. These systems may be used by physicians during procedures (IVM) or by the laboratory in the evaluation of specimens that have been removed from the patient (EVM). The dataset refers to digitized or analog video or still images or other data (eg, spectroscopic data) generated by an IVM or EVM system. If such data is used to aid in interpretation or diagnosis, record retention requirements apply. Stored data should include, at a minimum, the data used to aid in interpretation or diagnosis.

NOTE ~~7~~6: Refer to GEN.20425 for record and material retention requirements for laboratories that cease operations.

REFERENCES

1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24): [42CFR493.~~1273(b)] and [42CFR493.~~1105~~]~~].
2) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2023(Dec 28): [42CFR493.1273(b)].
~~2~~3) Pantanowitz L, Dickinson K, Evans AJ, et al. ATA guidelines for telepathology. *Telemed JE Health.* 2014;20(11):1049-56.
~~3~~4) 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.
~~4~~5) National Cancer Institute. NCI Best Practices for Biospecimen Resources. B.6.6 Biospecimen Storage. March 2016.

HISTOLOGY LABORATORY

GENERAL QUALITY CONTROL

Special Stains/Studies **Phase II**

ANP.21395

For special stains, including histochemical stains, and studies using immunologic and ISH methodology, positive and negative controls are verified and recorded as acceptable prior to or concurrent with the reporting of patient results and records retained.

NOTE: Controls must be verified and recorded as acceptable by a pathologist or designee (provided the designee meets high complexity testing qualifications).

Positive tissue controls must contain the component specific to the special stain that is being applied to the specimen.

Immunohistochemical tests using polymer-based detection systems (biotin-free) are sufficiently free of background reactivity to obviate the need for a negative reagent control and such controls may be omitted at the discretion of the laboratory director following appropriate validation. ~~The Centers for Medicare and Medicaid Services (CMS) recognizes the use of polymer-based detection systems (biotin free) may preclude the use of a negative reagent control. However, there have been no changes to the histopathology regulations. The CMS will be looking into an alternate QC method for these types of stains.~~

If interpretation of the special stain or study is performed by a different laboratory, there must be a procedure for the laboratory performing the stain or study to verify the acceptability of the controls before transfer, if the controls are not sent with the patient slides (regardless of the outside laboratory's accrediting organization). Records of this verification must be readily available to the laboratory performing the interpretation.

Evidence of Compliance:

✓ Records for verification of control acceptability (prior to completion of associated cases)

REFERENCES
1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24):7166 [42CFR493.1256(f)]
2) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24):3708 [42CFR493.1256(d)(6)]
3) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. ~~2003(Jan 24~~2023(Dec 28): [42CFR493.1273(a),(f~~)~~)].
4) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register.* 2003(Jan 24):~~7166~~ [42CFR493.1256(e)(2~~)~~ ~~and [42CFR493.1273(a)~~].

IMMUNOHISTOCHEMISTRY

***REVISED** 12/26/2024*

ANP.22550 QC - Antibodies **Phase II**

Positive ~~tissue~~ controls are used for each antibody.

NOTE: Positive controls assess the performance of the ~~primary antibody. They are performed on sections~~immunohistochemistry assay (including impact of ~~tissue known to contain the target~~ fixation and antigen~~, using the same epitope~~ retrieval) and can assess the sensitivity of the assay. They should, whenever possible, be subjected to the same processing, antigen retrieval, and immunostaining ~~protocols~~protocol as ~~the~~ patient tissue.

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

~~Ideally, the~~ For tissue-based positive controls, the ideal control ~~tissue would be~~is of the same specimen type as the patient test specimen (eg, small biopsy, large tissue section, cell block), and ~~would be~~is processed and fixed in the same manner (eg, formalin-fixed, alcohol-fixed, decalcified) as the patient specimen. However, for most laboratories, 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 laboratory to maintain a bank of formalin-fixed tissue samples as its positive controls; these controls can be used for patient specimens that are of different type, or fixed/processed differently, providing that the laboratory can show that these patient 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 laboratory manual must clearly state the manner in which internal positive controls are used.

A positive control ~~section~~ included on the same slide as the patient tissue is optimal practice because it helps identify failure to apply primary antibody or other critical ~~reagent~~reagents to the patient 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 ~~control tissues possess~~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:

✓ Patient reports or worksheet with control results **AND**
✓ Immunohistochemical-stained slides with positive ~~tissue~~ controls

REFERENCES

~~1) O'Leary TJ. Standardization in immunohistochemistry. *Appl Immunohistochem Molecul Morphol* 2001;9:3-8~~
~~2~~1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register.* ~~2003(Jan 24~~2023(Dec 28): [42CFR493.1273(a)~~)~~)].
~~3~~2) 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~~3) Cheung CC, Taylor CR, Torlakovic EE. An Audit of Failed Immunohistochemical Slides in a Clinical Laboratory: The Role of On-Side Controls. *Appl Immunohistochem Mol Morphol.* 2017;25(5):308-312.
~~5~~4) 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.
5) Clinical and Laboratory Standards Institute (CLSI). *Quality Assurance for Design Control and Implementation of Immunohistochemistry Assays.* 2nd ed. CLSI document I/LA28. Clinical and Laboratory Standards Institute, Wayne, PA; 2011.
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*

ANP.22560 Synthetic and Commercial Control Range Establishment or Verification Phase II

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

NOTE: The laboratory 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.

Evidence of Compliance:
✓ Records for control range establishment or verification of each lot, as applicable

REFERENCES
1) Clinical and Laboratory Standards Institute (CLSI). *Evaluation of Precision of Quantitative Measurement Procedures. Approved Guideline.* 3rd ed. CLSI document EP05-A3. Clinical and Laboratory Standards Institute, Wayne, PA; 2014.
2) Clinical and Laboratory Standards Institute (CLSI). *Statistical Quality Control for Quantitative Measurement Procedures, Principles and Definitions.* 4th ed. CLSI guideline C24. Clinical and Laboratory Standards Institute, Wayne, PA; 2016.

***REVISED** 12/26/2024*

ANP.22750 ~~Antibody~~ Validation/Verification - Non-Predictive Antibody Marker Testing Phase II

The laboratory has records of validation/verification of new antibodies, including introduction of a new clone, prior to use for patient diagnosis or treatment.

NOTE: The performance characteristics of each assay must be appropriately validated/verified before being placed into clinical use. The initial goal is to establish the optimal antibody titration, detection system, and antigen retrieval protocol. Once optimized, a panel of tissues must be tested to determine the assay's sensitivity and specificity. The scope of the validation/verification is at the discretion of the laboratory director and will vary with the antibody.

Means of validation/verification may include, but are not limited to: 1) correlating the results using the new antibody with the morphology and expected results; 2) comparing the results using the new antibody with the results of prior testing of the same tissues with a validated/verified assay in the same laboratory; 3) comparing the results using the new antibody with the results of testing the same tissue in another laboratory with a validated/verified assay; or 4) comparing the results using the new antibody with previously validated/verified non-IHC tests or testing previously graded tissue challenges from a formal proficiency testing program.

For an initial validation/verification, laboratories should achieve at least 90% overall concordance between the new test and the comparator test or expected results.

*For validation~~/verification of a~~ of **laboratory-developed or modified FDA-cleared/approved nonpredictive** ~~assay~~**assays**, the validation~~/verification should test~~ must be performed on a minimum of 10 positive and 10 negative tissues.*

*For verification of **unmodified FDA-cleared/approved nonpredictive 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 10 positive and 10 negative tissues.*

If the laboratory director determines that fewer validation/verification cases are sufficient for a specific marker (eg, a rare antigen or tissue), the rationale for that decision needs to be recorded. Positive cases in the validation/verification set should span the expected range of clinical results (expression level), especially for those markers that are reported quantitatively.

For p16/Ki67 dual stain testing performed on gynecologic cytopathology specimens using FDA cleared/approved kits, the laboratory must verify that test performance is consistent with the manufacturer's validation data.

When possible, laboratories should use tissues that have been processed using the same fixative and processing methods as cases that will be tested clinically. If IHC is regularly done on specimens that are not fixed or processed in the same manner as the tissues used for validation/verification (eg, alcohol fixed cell blocks, cytologic smears, formalin post fixed tissue, or decalcified tissue), the laboratory should test a sufficient number of such tissues to ensure that assays consistently achieve expected results. The laboratory director is responsible for determining the number of positive and negative cases and the number of ~~predictive and nonpredictive~~ markers to test.

Refer to the subsection "Predictive Markers" for specific validation/verification requirements for tests that provide independent predictive information (eg, HER2 and ER testing in breast carcinoma).

Evidence of Compliance:

✓ Records of validation/verification, if applicable

REFERENCES

1) Hsi ED. A practical approach for evaluating new antibodies in the clinical immunohistochemistry laboratory. *Arch Pathol Lab Med.* 2001;125:289-294
2) Clinical and Laboratory Standards Institute (CLSI). *Quality Assurance for Design Control and Implementation of Immunohistochemistry Assays; Approved Guideline—* - *Second Edition.* CLSI document I/LA28-~~A2 (ISBN 1-56238-745-6).~~ Clinical and Laboratory Standards Institute, ~~940 West Valley Road, Suite 1400,~~ Wayne, ~~Pennsylvania 19087 USA,~~PA; 2011.
3) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register.* 2003(Jan 24):~~7166~~ [42CFR493.1256(e)(2)~~] and [42CFR493.1273(a)~~].
4) ~~Fitzgibbons PL, Bradley LA, Fatheree LA, et al. Principles of Analytic Validation of Immunohistochemical Assays. *Arch Pathol Lab Med.* doi: 10.5858/arpa.2013-0610-CP.~~Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register.* 2023(Dec 28): [42CFR493.1273(a)].
5) Allen M. Gown, MD. Diagnostic Immunohistochemistry: What Can Go Wrong and How to Prevent it. *Arch Pathol Lab Med*. 2016;140(9):893-898.
6) Uhlen M, Bandrowski A, Carr S, et al. A proposal for validation of antibodies. *Nat Methods.* 2016; 13(10):838-7.
7) ~~Fitzgibbons PL, Bradley LA, Fatheree LA~~Goldsmith JD, Troxell M, Roy-Chowdhuri S, et al. ~~College of American Pathologists Pathology and Laboratory Quality Center.~~ Principles of analytic validation of immunohistochemical assays~~. Guideline from the Pathology and Laboratory Quality Center.~~ guideline update. *Arch Pathol Lab Med.* ~~2014;138(11):1432-43.~~2024. https://doi.org/10.5858/arpa.2023-0483-CP

IN SITU HYBRIDIZATION (ISH)

***REVISED** 12/26/2024*

ANP.22965 Image and Slide Retention - ISH **Phase II**

Photographic or digitized images or permanent slides are retained of all in situ hybridization (ISH) assays for an appropriate period.

NOTE: Images or permanent slides of ISH assays for neoplastic disorders must be retained for 10 years; images or permanent slides of ISH assays for constitutional disorders must be retained for 20 years. ~~For an ISH assay with a normal result, retain an image of at least one cell illustrating the normal probe signal pattern. For an ISH assay with an abnormal result, retain images of at least two cells illustrating each relevant abnormal probe signal pattern.~~

There is no retention requirement for retaining images of slide preparations when the source slides remain readable for the required retention period. If slides are expected to become unreadable before the end of the required retention periods (for example, FISH slides), then images of the slides must be retained.

If representative images of chromosome ISH slides are retained, those with a normal result must include an image of at least one cell illustrating the normal probe signal pattern, and those with an abnormal result must include images of at least two cells illustrating each relevant abnormal probe signal pattern.

REFERENCES
1) American College of Medical Genetics Laboratory. Standards and guidelines for clinical genetics laboratories, 2021 edition.

PREDICTIVE MARKERS

~~*This checklist*~~*The term predictive marker as used in this section* ~~*applies only*~~*refers to immunohistochemical (IHC), immunocytochemical, and in situ hybridization (ISH)* ~~*tests used to predict responsiveness to a specific treatment*~~*biomarkers used independent of* ~~*other histopathologic*~~*histologic findings to identify individuals who are more likely to experience a favorable or unfavorable effect from a specific (targeted) therapy, compared to individuals with the same diagnosis lacking the biomarker. Rather than confirming a specific diagnosis (such as B-cell lymphoma or gastrointestinal stromal tumor), these* ~~*tests should differentiate predicted*~~*biomarkers predict responsiveness to a* ~~*targeted therapy*~~*specific treatment among cases of the same diagnosis. For example, this section applies to estrogen receptor testing used to determine eligibility for 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 http://www.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).

If digital image analysis is used (eg, quantitative image analysis for HER2 by immunohistochemistry), additional requirements in the Digital Image Analysis section also apply.

ANP.22969 Report Elements Phase II

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

NOTE: The laboratory performing the gross examination of the specimen must record the cold ischemia time and the length of time in fixative. If the grossing laboratory refers IHC or ISH studies, this information must be provided to the laboratory(ies) performing these studies.

For IHC and ISH studies used to provide predictive information independent of diagnosis or other histopathologic findings (eg, ~~*hormone*~~*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. *For IHC studies, 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. *For ISH studies, 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)*
4. *Criteria used to determine a positive vs. negative result, and/or scoring system (eg, percent of stained cells, staining pattern)*
5. *Laboratory interpretation of predictive marker testing (IHC or 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 and ER testing in breast cancer and CAP/ASCP/ASCO HER2 in gastroesophageal carcinoma)

6. *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) Fisher ER, *et al.* Solving the dilemma of the immunohistochemical and other methods used for scoring ER and PR receptors in patients with invasive breast cancer. *Cancer.* 2005;103:164-73
2) Collins LC, *et al*. Bimodal frequency distribution of estrogen receptor immunohistochemical staining results in breast cancer: an analysis of 825 cases. *Am J Clin Pathol.* 2005;123:16-20
3) Allred DC, *et al.* ER expression is not bimodal in breast cancer. *Am J Clin Pathol.* 2005;124:474-5
4) 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
5) Allison KH, Hammond EH, Dowsett M, et al. Estrogen and Progesterone Receptor Testing in Breast Cancer: American Society of Clinical Oncology/College of American Pathologists Guideline Update *Arch Pathol Lab Med.* 2020; 144(5):545-63.
6) 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.
7) Bui MM, Riben MW, Allison KH, et al. Quantitative Image Analysis of Human Epidermal Growth Factor Receptor 2 Immunohistochemistry for Breast Cancer Guideline from the College of American Pathologists. 2018. *Arch Pathol Lab Med.* doi: 10.5858/arpa.2018-0378-CP.

*****REVISED** 12/26/2024***

ANP.22970 Annual Result Comparison - Breast Carcinoma Phase II

For HER2 and ER immunohistochemical (IHC) ~~and in situ hybridization (ISH) and ER IHC~~ tests performed on breast carcinoma that provide independent predictive information, the laboratory at least annually compares its patient results with published benchmarks~~, and evaluates interobserver variability among the pathologists in the laboratory~~.

NOTE: 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.

~~*Individuals interpreting the assay must also have their concordance compared with each other and this concordance should also be at least 95%.*~~

Evidence of Compliance:

✓ Records of annual result comparison ~~and evaluation of interobserver variability~~

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) Allison KH, Hammond ME, Dowsett M, et al. Estrogen and progesterone receptors in breast cancer: American Society of Clinical Oncology/College of American Pathologists Guideline update [published online ahead of print January 2020] *Arch Pathol Lab Med.* doi: 10.5858/arpa.2019-0904-SA.
3) Fitzgibbons PL, Murphy DA, Hammond ME, *et al.* Recommendations for validating estrogen and progesterone receptor immunohistochemistry assays. *Arch Pathol Lab Med* 2010;134:930-935
4) Dunnwald LK, Rossing MA, Li CI. Hormone receptor status, tumor characteristics, and prognosis: a prospective cohort of breast cancer patients. *Breast Cancer Research* 2007;9:R6

5) Rüschoff J, Lebeau A, Kreipe H, et al. Assessing HER2 testing quality in breast cancer: variables that influence HER2 positivity rate from a large, multicenter, observational study in Germany. *Mod Pathol.* 2017;30:217-26.

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

ANP.22975 **Immunohistochemical (IHC) Predictive Marker Interpretation** **Phase I**

Each pathologist interpreting IHC predictive markers participates in an annual analyte-specific quality assessment for each of the following predictive markers, as applicable:

- **Breast HER2**
- **Breast ER**
- **Gastric HER2**
- **Lung highly sensitive ALK**
- **Lung PD-L1 tumor proportion score (TPS)**

NOTE: This requirement applies to all pathologists in the laboratory that interpret one or more of these markers, whether in laboratories that perform both staining and interpretation or interpretation only. An individual pathologist need participate only once for each predictive marker used by that pathologist in patient care evaluation, regardless of the number of locations where the pathologist performs interpretations.

The quality assessment for each predictive marker must include a comparison of each pathologist's interpretation against the intended results. The laboratory director must define criteria for acceptable results and ensure follow up on each unacceptable result.

Examples of how this requirement can be met include the use of:
- *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~~ - Validation/Verification~~** **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: ~~Test~~For validation~~/verification~~ 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.

~~For HER2 and ER predictive marker testing performed on breast cancer specimens using laboratory-developed tests (LDTs) or modified FDA-cleared/approved tests, a minimum of 40~~

~~*positive and 40 negative samples must be used (according to ASCO/CAP Guidelines). Positive cases in the validation set should span the expected range of clinical results (expression levels). Only definitely positive and negative cases should be used for validation.*~~

The validation/verification data ~~should~~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, except for ER IHC methods which are 90% for positive and 95% for~~ 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
4) ~~Fitzgibbons PL, Bradley LA, Fatheree LA~~Goldsmith JD, Troxell M, Roy-Chowdhuri S, et al. ~~College of American Pathologists Pathology and Laboratory Quality Center.~~ Principles of analytic validation of immunohistochemical assays~~. Guideline from the Pathology and Laboratory Quality Center.~~: guideline update. *Arch Pathol Lab Med.* ~~2014;138(11):1432-43.~~2024. https://doi.org/10.5858/arpa.2023-0483-CP

DIGITAL IMAGE ANALYSIS

PERSONNEL

***REVISED** 12/26/2024*

ANP.23041 Testing Personnel Qualifications **Phase II**

Personnel who are responsible for evaluating the imaging system data are qualified as high-complexity testing personnel.

~~*NOTE:*~~*NOTE: Evaluation of imaging system data includes review of images and data to ensure that they met the quality standards to be readable/accessible for a pathologist to effectively use the images/data to render an interpretation/diagnosis. Refer to the Laboratory General Checklist for high complexity testing personnel (GEN.54750) and general supervisor (GEN.53600) qualifications. ~~A detailed listing of~~Detailed information on personnel qualifications can be found in the CAP Personnel Guidance Document located in e-LAB Solutions Suite on cap.org (log-in required) under Accreditation Resources - Accreditation Checklists.*

Evidence of Compliance:

✓ Records of qualifications including diploma, transcript(s), primary source verification report, equivalency evaluation, or current license (if required) **AND**

✓ Work history in related field

REFERENCES

1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. ~~2003(Oct 1):1070-1071 [~~2023(Dec 28):[42CFR493.1489]

CIRCULATING TUMOR CELL ANALYSIS (CTC)

PERSONNEL

***REVISED** 12/26/2024*

ANP.29630 Testing Personnel Qualifications **Phase II**

Personnel who operate the analyzer are qualified as high-complexity testing personnel.

NOTE: Refer to the Laboratory General Checklist for high complexity testing personnel (GEN.54750) and general supervisor (GEN.53600) qualifications. ~~A detailed listing of~~Detailed information on personnel qualifications can be found in the CAP Personnel Guidance Document located in e-LAB Solutions Suite on cap.org (log-in required) under Accreditation Resources - Accreditation Checklists.

Evidence of Compliance:

✓ Records of qualifications including diploma, transcript(s), primary source verification report, equivalency evaluation, or current license (if required)

✓ Work history in related field

REFERENCES

1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. ~~2003(Oct 1):1070-1071 [~~2023(Dec 28):[42CFR493.1489~~]~~.

FLOW CYTOMETRY DATA INTERPRETATION

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

ANP.29680 Cellular Viability **Phase II**

The laboratory ensures that the percentage of viable cells in each test specimen is provided by the laboratory performing the flow technical component, when applicable.

NOTE: Selective loss of cell subpopulations and/or the presence of dead cells may lead to spurious results. This does not mean that all specimens with low viability must be rejected. Finding an abnormal population in a specimen with poor viability may be valuable but the failure to find an abnormality should be interpreted with caution. If specimen viability is below the established laboratory minimum, test results may not be reliable and this should be noted in the test report. Routine viability testing may not be necessary. However, viability testing of specimens with a high risk of loss of viability, such as disaggregated lymph node specimens, is required.

REFERENCES

1) Clinical and Laboratory Standards Institute (CLSI). *Clinical Flow Cytometric Analysis of Neoplastic Hematolymphoid Cells; Approved Guideline—Second Edition*. CLSI document H43-A2. Clinical and Laboratory Standards Institute, Wayne, PA; 2007.

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

ANP.29720 Rare Event Flow Cytometric Assays **Phase I**

For rare event flow cytometric assays, the lower limit of enumeration is included in the diagnostic report.

NOTE: When performing rare event flow cytometric assays (such as minimal residual disease (MRD) and/or high sensitivity PNH testing) on low cellularity samples, the number of events needed to achieve the laboratory's validated lower limit of enumeration/sensitivity may not be able to be collected. In these cases, laboratories must clearly state in the flow cytometric assay report that the sample was paucicellular and may thus have reduced analytical sensitivity.

AUTOPSY PATHOLOGY

AUTOPSY PERFORMANCE AND RECORDS

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

ANP.33110 Intra- and Extra-Departmental Consultations **Phase I**

The laboratory has a defined process for handling information from intra- and extra-departmental consultations in the deceased patient's final autopsy report.

NOTE: Intra-departmental consultations may be included in the deceased patient's final autopsy report or filed separately. The pathologist in charge of the autopsy must decide whether the results of intra-departmental consultations provide relevant information for inclusion in some manner in the autopsy report.

Records of extra-departmental consultations must be readily accessible within the pathology department. The method used to satisfy this requirement is at the discretion of the laboratory director and can be expected to vary according to the organization of the department. These consultations can be retained with the official autopsy reports or kept separately, so long as they can be readily linked.

Evidence of Compliance:

✓ Records of consultations included in the final report **OR**

✓ Records of consultations readily accessible within the pathology department

REFERENCES

1) Leslie KO, *et al*. Second opinions in surgical pathology. *Am J Clin Pathol.* 1996;106(suppl 1):S58-S64.
2) Tomaszewski JE, *et al*. Consensus conference on second opinions in diagnostic anatomic pathology. Who, what, and when. *Am J Clin Pathol.* 2000;114:329-335.
3) Hahm GK, *et al*. Quality assurance of second opinion in gastrointestinal and liver pathology. *Am J Clin Pathol.* 2000;114:631.
4) Renshaw AA, *et al*. Blinded review as a method of quality improvement in surgical pathology. *Arch Pathol Lab Med.* 2002;126:961-963.
5) Azam M, Nakhleh RE. Surgical pathology extradepartmental consultation practices. A College of American Pathologists Q-probes study of 2746 consultations from 180 laboratories. *Arch Pathol Lab Med.* 2002;126:405-412.
6) Cooper K, *et al.* Institutional consultations in surgical pathology. How should diagnostic disagreements be handled? *Arch Pathol Lab Med.* 2002;126:650-651.

***REVISED** 12/26/2024*

ANP.33120 Final Report TAT **Phase I**

The final autopsy report is produced within ~~60 working days~~three months from the date the autopsy is performed in 90% of the cases.

NOTE: The 90% threshold is used in recognition of the fact that occasional unusual cases may require ~~more than 60 days~~additional time for completion, particularly when external consultation is required.

If cases exceed ~~60 days~~three months, the reason for the delay should be recorded and records of ongoing review of this information by the director of the service retained.

Evidence of Compliance:

✓ Review of turnaround time data

REFERENCES

1) Caruso JL. Communication of Autopsy Results. In: Collins KA, ed. *Autopsy Pathology and Reporting.* 3rd ed. Northfield, IL: College of American Pathologists: 2017; chap 36.
2) Koponen MA. Autopsy Reporting. In: Collins KA, ed. *Autopsy Pathology and Reporting.* 3rd ed. Northfield, IL: College of American Pathologists: 2017; chap 33.
3) Cromwell S, et al. Improving Autopsy Report Turnaround Times by Implementing Lean Management Principles. *Pediatr Dev Pathol.* 2018; 21(1):41-47.
4) Siebert JR. Increasing the efficiency of autopsy reporting. Arch Pathol Lab Med. 2009 Dec; 133(12):1932-7.

FORENSIC AUTOPSY PATHOLOGY

GENERAL ISSUES - FORENSIC AUTOPSY

ANP.35000 Forensic Pathologist and Expert Consultants **Phase II**

The laboratory has access to a forensic pathologist and expert consultants, as appropriate for the following types of services:

- **Forensic neuropathology**
- **Forensic dentistry/odontology**
- **Forensic anthropology**
- **Radiology**

NOTE: References for specialties may be found on the following websites:

- *American Board of Forensic Anthropology: https://www.theabfa.org/active-diplomates-by-name*
- *American Board of Pathology: ~~http://www.abpath.org/index.php/verifying-certification~~http://www.abpath.org/verify-certification/*
- *American Board of Forensic Odontology: https://abfo.org/resources/member-directory/*
- *American Academy of Forensic Sciences: https://www.aafs.org/*
- *National Association of Medical Examiners: http://www.thename.org/*