COLLEGE of AMERICAN PATHOLOGISTS

Master

Cytopathology Checklist

CAP Accreditation Program

College of American Pathologists
325 Waukegan Road
Northfield, IL 60093-2750
www.cap.org

10.24.2022

Disclaimer and Copyright Notice

CAP inspections are performed with the edition of the Checklists mailed to a facility at the completion of the application or reapplication process, not necessarily those currently posted on the website. The checklists undergo regular revision and a new edition may be published after the inspection materials are sent.

For questions about the use of the Checklists or Checklist interpretation, email accred@cap.org or call 800-323-4040 or 847-832-7000 (international customers, use country code 001).

The Checklists used for inspection by the College of American Pathologists' Accreditation Programs have been created by the CAP and are copyrighted works of the CAP. The CAP has authorized copying and use of the checklists by CAP inspectors in conducting laboratory inspections for the Council on Accreditation and by laboratories that are preparing for such inspections. Except as permitted by section 107 of the Copyright Act, 17 U.S.C. sec. 107, any other use of the Checklists constitutes infringement of the CAP's copyrights in the Checklists. The CAP will take appropriate legal action to protect these copyrights.

Cytopathology Checklist

TABLE OF CONTENTS

ON-LINE CHECKLIST AVAILABILITY AND RESOURCES

Participants of the CAP accreditation programs may download the checklists from the CAP website (cap.org) by logging into e-*LAB* Solutions Suite. 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.

A repository of questions and answers and other resources is also available in e-LAB Solutions Suite under Accreditation Resources, Checklist Requirement Q & A.

SUMMARY OF CHECKLIST EDITION CHANGES
Cytopathology Checklist
10/24/2022 Edition

The information below includes a listing of checklist requirements with significant changes in the current edition and previous edition of this checklist. The list is separated into three categories:

1. New
2. Revised:
   - Modifications that may require a change in policy, procedure, or process for continued compliance; or
   - A change to the Phase
3. Deleted/Moved/Merged:
   - Deleted
   - Moved — Relocation of a requirement into a different checklist (requirements that have been resequenced within the same checklist are not listed)
   - Merged — The combining of similar requirements

NOTE: The requirements listed below are from the Master version of the checklist. The customized checklist version created for inspections and self-evaluations may not list all of these requirements.

Previously Cited Checklist Requirements

- The **inspector's version** of the checklist contains a listing of previously cited checklist requirements. Specific information on those citations, including the inspection date and inspector comments, is included following each related requirement within the checklist.
- Laboratories can access data on previously cited deficiencies by logging into e-LAB Solutions Suite on cap.org and going to Accreditation Reports - Inspection Summation Report.

NEW Checklist Requirements

Requirement	Effective Date
CYP.04510	09/22/2021
CYP.04520	09/22/2021
CYP.04540	09/22/2021
CYP.04550	09/22/2021
CYP.07666	09/22/2021

REVISED Checklist Requirements

Requirement	Effective Date
CYP.01900	10/24/2022
CYP.04150	09/22/2021
CYP.04310	09/22/2021
CYP.04330	09/22/2021
CYP.04340	09/22/2021
CYP.04370	09/22/2021
CYP.04530	10/24/2022
CYP.06450	10/24/2022
CYP.06475	10/24/2022
CYP.07100	09/22/2021
CYP.07452	09/22/2021
CYP.07543	10/24/2022
CYP.07600	10/24/2022
CYP.07650	10/24/2022
CYP.07670	09/22/2021
CYP.07692	09/22/2021
CYP.07700	10/24/2022
CYP.08500	09/22/2021
CYP.08575	09/22/2021
CYP.09700	10/24/2022
CYP.09910	10/24/2022
CYP.09920	10/24/2022
CYP.09930	10/24/2022
CYP.09940	10/24/2022

DELETED/MOVED/MERGED Checklist Requirements

Requirement	Effective Date
CYP.06800	10/23/2022

INTRODUCTION

This checklist is used in conjunction with the All Common and Laboratory General Checklists to inspect a cytopathology laboratory section or department.

Laboratories that do not file slides on-site (eg, "read-only" laboratories) must retain a sample of 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 minimum, include all slides accessioned over a continuous two-week period within the previous two years.

If telepathology is used by the pathologist or cytotechnologist to review slides or images for primary diagnosis of cytology or real time evaluation of FNA specimens for adequacy or triaging, refer to the Telepathology section of the Laboratory General Checklist for additional requirements. Telepathology occurs when a pathologist views digitized or analog video or still image(s), and renders an interpretation that is included in a formal diagnostic report or recorded in the patient record. This also includes the review of images by a cytotechnologist when a judgment of adequacy is recorded in the patient record.

***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).*

GENERAL CYTOPATHOLOGY

This Checklist is intended for laboratories that perform on-site preparation and/or interpretation of cytologic specimens. These include GYNECOLOGIC (cervicovaginal), and/or NON-GYNECOLOGIC (exfoliated specimens from other sites, fluids, and aspirates) cytopathology. If the laboratory does NOT perform any on-site examination of cytopathology specimens, but refers all submitted material to an outside laboratory, do NOT use this Checklist. Do NOT use this Checklist if the laboratory's involvement in cytopathology is limited to filing of reports and/or slides.

Cytopathology inspectors must be pathologists or cytotechnologists who have extensive experience in the practice of cytology, are knowledgeable about current CAP Checklist and CLIA requirements, and have completed appropriate inspector training prior to inspecting.

Regardless of the size of the laboratory, the Inspector should spend at least several hours inspecting the cytopathology laboratory. The on-site inspection will require review of case (slide) material, direct observation of technical procedures, and careful review of quality management monitors.

Laboratories that are doing histology processing of cell blocks and tissues must be inspected with the Anatomic Pathology Checklist.

INTERLABORATORY COMPARISONS

NOTE: Peer interlaboratory comparison programs provide valuable educational opportunities based on peer performance comparisons in both technical and interpretive arenas. While not completely emulating

cytopathology preparation and interpretation, participation in such programs enables a laboratory to compare its performance to peer laboratories.

Inspector Instructions:

READ	• Sampling of interlaboratory comparison program policies and procedures • Sampling of interlaboratory comparison program records including participation, retesting and remedial training, if applicable
ASK	• What type of remedial training do you provide when an individual has an unacceptable score on PT?
DISCOVER	• Select an example of unacceptable interlaboratory comparison results (if applicable) and follow records from original testing to retesting and remedial training, if necessary. Determine if practice matches policies and procedures.

CYP.00125 PT Participation - Gynecologic Cytopathology **Phase II**

For laboratories subject to US regulations that perform gynecologic cytopathology, the laboratory and all individuals who examine gynecologic preparations participate in the CAP Gynecologic Cytology PT Program (PAP PT) or another proficiency testing program in gynecologic cytopathology approved by the Centers for Medicare and Medicaid Services (CMS).

NOTE: This checklist requirement applies only to US laboratories and other laboratories subject to CLIA regulations. Laboratories must retain records of PT performance for at least 2 years. Records must be kept for each individual participating in annual PT, including identification of those who are retested; records of remedial training; records of imposition of limitations on slide examination; and records of re-examination of slides, as required by CLIA.

Evidence of Compliance:

- ✓ Records that the laboratory is enrolled and all currently employed personnel have successfully completed PT **AND**
- ✓ Records of retesting, remedial training and imposition of limitations, if applicable **AND**
- ✓ Records of notification to the PT provider and CMS for any PAP testing personnel who left employment prior to completion of annual PT

REFERENCES
1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Extension of certain effective dates for clinical laboratory requirements and personnel requirements for cytologists. *Fed Register.* 1994(Dec 6):62609 [42CFR493.855]

CYP.00150 Educational Participation - Gynecologic Cytopathology **Phase I**

For laboratories subject to US regulations that perform gynecologic cytopathology, the laboratory participates in the educational component of the CAP Gynecologic Cytology PT Program (PAP PT) or another educational peer-comparison program in gynecologic cytopathology.

NOTE: Interlaboratory comparison programs in cytopathology provide valuable educational opportunities for peer performance comparisons in both technical and diagnostic arenas. While not completely emulating cervicovaginal cytopathologic preparation and interpretation,

participation in the PAP program enables a laboratory to compare its performance to benchmarks derived from a database of peer laboratories.

Evidence of Compliance:

- ✓ Records of enrollment and participation in the educational component of the CAP PAP PT program **OR**
- ✓ Records of enrollment and participation in another educational gynecologic cytopathology peer-comparison program **OR**
- ✓ Records for participation in a laboratory-developed program by circulating gynecologic case material with other laboratories

REFERENCES

1) Davey DD, *et al.* Improving accuracy in gynecologic cytology: results of the College of American Pathologists interlaboratory program in cervicovaginal cytology (PAP). *Arch Pathol Lab Med.* 1993;117:1193-1198
2) Plott E. Cytology proficiency testing research and development at the Centers for Disease Control, 1967-1992. *Lab Med.* 1994;25:224-229
3) Wood D, Thompson DW. Proficiency testing in gynecologic cytology: the Ontario experience of a voluntary organization. *Lab Med.* 1994;25:240-244
4) Bonfiglio TA, Somark TM. ASCP educational and proficiency testing programs in cytopathology. *Lab Med.* 1994;25:245-247
5) Davey DD, Fidler WJ. The College of American Pathologists interlaboratory comparison program in cervicovaginal cytology. *Lab Med.* 1994;25:248-252
6) Nielsen ML. Cytopathology laboratory improvement programs of the College of American Pathologists. Laboratory accreditation program (CAP LAP) and performance improvement program in cervicovaginal cytology (CAP PAP). *Arch Pathol Lab Med.* 1997;121:256-259
7) Woodhouse SL, *et al.* Interobserver variability in subclassification of squamous intraepithelial lesions. Results of the College of American Pathologists interlaboratory comparison program in cervicovaginal cytology. *Arch Pathol Lab Med.* 1999;123:1079-1084
8) Keenlyside RA, *et al.* Do proficiency test results correlate with the work performance of screeners who screen Papanicolaou smears? *Am J Clin Pathol.* 1999;112:769-776
9) Jones BA, Davey DD. Quality management in gynecologic cytology using interlaboratory comparison. *Arch Pathol Lab Med.* 2000;124:672-681
10) Colgan TJ, *et al*. Reparative changes and the false-positive/false-negative Papanicolaou test: A study from the College of American Pathologists interlaboratory comparison program in cervicovaginal cytology. *Arch Pathol Lab Med*. 2001;125:123-140
11) Nakhleh RE, Fitzgibbons PL, *eds.* Quality management in anatomic pathology. Promoting patient safety through systems improvement and error reduction. Northfield, IL: College of American Pathologists, 2005

CYP.00170 Educational Participation - Gynecologic Cytopathology — Phase II

For laboratories not subject to US regulations that perform gynecologic cytopathology, the laboratory participates in the educational component of the CAP PAP Education Program or another interlaboratory peer-comparison educational program in gynecologic cytopathology.

NOTE: Participation in the PAP Education program enables a laboratory to compare its performance to benchmarks derived from a national database of peer laboratories.

Evidence of Compliance:

- ✓ Records of enrollment and participation in the educational component of the CAP PAP PT program **OR**
- ✓ Records of enrollment and participation in another educational gynecologic cytopathology peer-comparison program **OR**
- ✓ Records for participation in a laboratory-developed program by circulating gynecologic case material with other laboratories

REFERENCES

1) Davey DD, *et al.* Improving accuracy in gynecologic cytology: results of the College of American Pathologists interlaboratory program in cervicovaginal cytology (PAP). *Arch Pathol Lab Med.* 1993;117:1193-1198
2) Plott E. Cytology proficiency testing research and development at the Centers for Disease Control, 1967-1992. *Lab Med.* 1994;25:224-229
3) Wood D, Thompson DW. Proficiency testing in gynecologic cytology: the Ontario experience of a voluntary organization. *Lab Med.* 1994;25:240-244
4) Bonfiglio TA, Somark TM. ASCP educational and proficiency testing programs in cytopathology. *Lab Med.* 1994;25:245-247
5) Davey DD, Fidler WJ. The College of American Pathologists interlaboratory comparison program in cervicovaginal cytology. *Lab Med.* 1994;25:248-252
6) Nielsen ML. Cytopathology laboratory improvement programs of the College of American Pathologists. Laboratory accreditation program (CAP LAP) and performance improvement program in cervicovaginal cytology (CAP PAP). *Arch Pathol Lab Med.* 1997;121:256-259
7) Woodhouse SL, *et al.* Interobserver variability in subclassification of squamous intraepithelial lesions. Results of the College of American Pathologists interlaboratory comparison program in cervicovaginal cytology. *Arch Pathol Lab Med.* 1999;123:1079-1084
8) Keenlyside RA, *et al.* Do proficiency test results correlate with the work performance of screeners who screen Papanicolaou smears? *Am J Clin Pathol.* 1999;112:769-776

9) Jones BA, Davey DD. Quality management in gynecologic cytology using interlaboratory comparison. *Arch Pathol Lab Med.* 2000;124:672-681
10) Colgan TJ, *et al*. Reparative changes and the false-positive/false-negative Papanicolaou test: A study from the College of American Pathologists interlaboratory comparison program in cervicovaginal cytology. *Arch Pathol Lab Med*. 2001;125:123-140
11) Nakhleh RE, Fitzgibbons PL, *eds.* Quality management in anatomic pathology. Promoting patient safety through systems improvement and error reduction. Northfield, IL: College of American Pathologists, 2005

CYP.00190 Educational Participation - Non-gynecologic Cytopathology **Phase I**

For laboratories that perform non-gynecologic cytopathology, the laboratory participates in an interlaboratory peer-comparison educational program in NON-GYNECOLOGIC cytopathology (eg, CAP Interlaboratory Comparison Program in Non-Gynecologic Cytopathology NGC).

Evidence of Compliance:

- ✓ Records of enrollment and participation in the educational component of the CAP NGC program **OR**
- ✓ Records of enrollment and participation in another educational non-gynecologic cytopathology peer-comparison program **OR**
- ✓ Records for participation in a laboratory-developed program by circulating non-gynecologic case material with other laboratories

QUALITY MANAGEMENT

Quality management in cytopathology should address both negative and abnormal/positive cases. The program must include both rescreening and hierarchic case review, as well as correlation of cytological and available histological material. In addition, the laboratory should participate in interlaboratory comparison, self-assessment and performance improvement programs. There must be records of intra- and extra-departmental consultation, as appropriate. Results of QM surveillance should be shared with the responsible pathologist(s) and cytotechnologist(s).

Inspector Instructions:

- How are disparities between histological and cytological findings addressed?
- Under what circumstances do you issue a corrected, addendum, or amended report?

CYP.01650 Cytopathology Exclusion **Phase I**

The institution defines specimens that may be excluded from routine submission to the cytology department for examination.

NOTE: This policy may be made in conjunction with the hospital administration and appropriate medical staff departments. The laboratory director should have participated in or been consulted by the medical staff in deciding which cytology specimens are to be sent to the laboratory for examination.

This checklist item is not applicable if 1) All specimens are submitted to pathology, or 2) The laboratory is not part of an institution that provides cytologic services.

(No policy is needed for fluids such as urines and CSF that do not routinely undergo cytologic examination.)

CYP.01900 Disparity Resolution **Phase II**

If significant disparities exist between histological and cytological findings, these are resolved in a confidential peer-reviewed quality management report, or in an addendum or in the patient report.

NOTE: For requirements specific to gynecologic cytopathology, also refer to the Gynecologic Cytopathology section of this checklist.

CYP.02100 Consultation Report Retention **Phase I**

Records of intra- and extra-departmental consultations are retained.

NOTE: The retention requirement for reports (10 years) applies to records of consultations.

REFERENCES
1) Abt AB, *et al.* The effect of interinstitution anatomic pathology consultation on patient care. *Arch Pathol Lab Med.* 1995;119:514-517

QUALITY CONTROL

SPECIMEN COLLECTION AND RECEIPT

Inspector Instructions:

READ	• Sampling of specimen collection and handling policies and procedures
ASK	• What is your course of action when you receive unacceptable cytopathology specimens? • When are FNA slides labeled? What identifiers are placed on the slides and containers? • What procedures do you have in place to prevent errors in ID, site and testing?

CYP.03366 FNA Error Prevention **Phase II**

The pathologist performing FNA procedures verifies patient identification using at least two patient identifiers, the procedure site, and the procedure to be performed.

REFERENCES
1) Clinical and Laboratory Standards Institute. *Fine Needle Aspiration Biopsy (FNAB) Techniques; Approved Guideline.* 2nd ed. CLSI Document GP20-A2. Clinical and Laboratory Standards Institute, Wayne, PA; 2003.

CYP.03800 Physician Notification **Phase II**

The laboratory notifies submitting physicians when unacceptable specimens are received.

Evidence of Compliance:

✓ Records of physician notification (eg, follow-up correspondence, records of telephone calls or written reports)

REFERENCES
1) Nakhleh RE, Fitzgibbons PL, *eds.* Quality management in anatomic pathology. Promoting patient safety through systems improvement and error reduction. Northfield, IL: College of American Pathologists, 2005

2) Solomon D, *et al*. The 2001 Bethesda system. Terminology for reporting results of cervical cytology. *JAMA.* 2002:287:2114-2119
3) Solomon D, Nayar, R, *eds.* The Bethesda system for reporting cervical/vaginal cytologic diagnoses: Definitions, criteria, and explanatory notes for terminology and specimen adequacy. New York, NY: Springer-Verlag; 2nd edition, 2004

CYP.03850 Cytology Assessment Record **Phase I**

If a statement of adequacy, preliminary diagnosis, or recommendations for additional studies is provided at the time of cytology sample collection, records of that statement are retained.

NOTE: Records might include a note in the patient's medical record or in the final cytopathology report.

CYTOLOGY STAINS AND SLIDE PREPARATIONS

Inspector Instructions:

	• Records of annual assessment of stain quality • Sampling of stain policies and procedures • Sampling of records of daily review of technical quality of cytologic preparations with corrective action of unacceptable stain quality
	• Sampling of stains (labeling) • Sampling of slides (labeling)
	• How do you assess the quality of cytopathology stains? • Who performs the daily review of the quality of cytological preparations? • What is your course of action when stain quality is unacceptable? • How frequently do you change stains? Under what circumstances do you filter stains? • How do you assign expiration dates for laboratory-prepared stains and solutions? If you extend expiration dates, how do you do so?
	• Scan several slides; check stain quality and labeling. Ensure that stain quality is acceptable.

CYP.04100 Staining Solutions **Phase II**

Staining solutions are filtered, covered when not in use, and changed in accordance with a defined schedule.

Evidence of Compliance:

✓ Records of solution changes at defined intervals

REFERENCES
1) Clinical and Laboratory Standards Institute. *Cervicovaginal Cytology Based on the Papanicolaou Technique; Approved Guideline*; 3rd ed. CLSI document GP15-A3. Clinical and Laboratory Standards Institute, Wayne, PA, 2008.

*****REVISED** 09/22/2021***

CYP.04150 Cross-Contamination **Phase I**

The laboratory prevents cross-contamination of cytologic specimens during processing and staining.

NOTE: Procedures must prevent cross-contamination between the following:

- *Gynecologic and non-gynecologic specimens.*
- *Non-gynecologic cases that have high potential for cross-contamination from other non-gynecologic specimens.*

Methods to prevent cross-contamination between specimens may include cytocentrifuge, filter, and monolayer preparations. Direct smears made from the sediment of highly cellular cases should be stained after the other cases, and the staining fluids must be changed or filtered between each of the highly cellular cases. One procedure to detect highly cellular specimens is to use a toluidine blue, or other rapid stain, on a wet preparation. One procedure to detect possible contamination is to insert a clean blank slide in each staining run and examine it for contamination.

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):7169 [42CFR493.1274(b)(2-3)]

CYP.04300 Cytologic Preparation Technical Quality **Phase II**

The pathologist or supervisory-level cytotechnologist performs daily review of the technical quality of cytologic preparations.

NOTE: The technical quality of cytologic preparations must be checked daily (on days processing occurs). This includes checking all stains for predicted staining characteristics each day of use. This check must include all of the types of preparations seen that day such as cytospins, cell blocks, and liquid-based preparations.

If preparation and staining is performed by a different laboratory, there must be a procedure for the laboratory performing the preparation and staining to verify the acceptability of the quality of preparations and the acceptability of controls (if needed) before transfer. Records of this verification must be readily available to the laboratory performing interpretations. There should also be a mechanism for feedback from the interpreting laboratory to the laboratory that prepared the slides of any issues with the preparations.

Evidence of Compliance:

✓ Records of daily review of cytologic preparations

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): [42CFR493.1256(e)(2)]

IMMUNOCYTOCHEMISTRY (ICC)

This section is intended for cytology only laboratories performing immunocytochemistry (ICC) within the cytology laboratory. This section does not apply to cytology laboratories for which all ICC is performed in a general anatomic pathology immunohistochemistry laboratory that is inspected using the Anatomic Pathology Checklist. ***Cytology laboratories that are doing histology processing of cell blocks and tissues must be inspected with the Anatomic Pathology Checklist.***

Please refer to the Definition of Terms section in the All Common (COM) Checklist for definitions of analytical validation and analytical verification.

Inspector Instructions:

	• Sampling of ICC policies and procedures • Sampling of new antibody validation/verification records • Sampling of new reagents/shipment confirmation of acceptability records • Sampling of antibody QC records • Sampling of buffer pH records • Sampling of batch control records
	• Sampling of slides (quality)
	• How does your laboratory validate/verify new antibodies? • How does your laboratory confirm the acceptability of new reagent lots? • How does your laboratory distinguish non-specific false-positive staining from endogenous biotin?

***REVISED** 09/22/2021*

CYP.04310 Specimen Modification **Phase II**

If the laboratory performs immunochemical staining on specimens other than formalin-fixed, paraffin-embedded cellular material, the laboratory defines appropriate modifications, if any, for other specimen types.

NOTE: Such specimens include air-dried touch imprints, air-dried and/or alcohol fixed smears, cytocentrifuge or other liquid-based preparations, and cellular materials 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 (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, 2011.

CYP.04320 Buffer pH **Phase II**

The pH of the buffers used in immunocytochemistry is routinely monitored.

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

Evidence of Compliance:

✓ Records of buffer pH within defined limits

***REVISED** 09/22/2021*

CYP.04330 QC - Antibodies **Phase II**

Positive controls are used for each antibody.

NOTE: Positive controls assess the performance of the primary antibody. They are performed on sections of tissue or cells known to contain the target antigen, using the same epitope retrieval and immunostaining protocols as the patient specimen. 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 (but not essential to satisfy this requirement), the positive control would be the same specimen type/fixative as the patient test specimen (eg, air-dried touch imprints, air-dried and/or alcohol fixed smears, cytocentrifuge or other liquid-based preparations, and cellular materials fixed in alcohol blends or other fixatives). 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) have equivalent immunoreactivity to routinely processed, formalin-fixed tissue.

A separate tissue section may be used as a positive control, but cytology specimens may 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 specimen is optimal practice because it helps identify failure to apply primary antibody or other critical reagent to the patient test slide; however, one separate positive control per staining run for each antibody in the run (batch control) may be sufficient provided that the control slide is closely scrutinized by a qualified reviewer.

Ideally, positive controls possess low levels of antigen expression, as is often seen in neoplasms. 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.

Evidence of Compliance:

- ✓ Patient reports or worksheet with control results **AND**
- ✓ Immunochemical-stained slides with positive controls

REFERENCES

1) O'Leary TJ. Standardization in immunohistochemistry. *Appl Immunohistochem Molecul Morphol* 2001;9:3-8
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): [42CFR493.1273(a)]
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 Nol 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.

*****REVISED** 09/22/2021***

CYP.04340 QC - Antibodies **Phase II**

Appropriate negative controls are used.

NOTE: Negative controls must assess the presence of nonspecific staining in patient specimens as well as the specificity of each antibody with the exception listed below. 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.

For laboratories using older biotin-based detection systems, it is important to use a negative reagent control to assess nonspecific or aberrant staining in patient specimens related to the antigen retrieval conditions and/or detection system used. A separate section of patient specimen is processed using the same reagent and epitope retrieval protocol as the patient test slide, except that the primary antibody is omitted, and replaced by any one of the following:

- *An unrelated antibody of the same isotype as the primary antibody (for monoclonal primary antibodies)*
- *An unrelated antibody from the same animal species as the primary antibody (for polyclonal primary antibodies)*
- *The negative control reagent included in the staining kit*
- *The diluent/buffer solution in which the primary antibody is diluted*

In general, a separate negative reagent control should be run for each specimen being immunostained; however, for cases in which there is simultaneous staining of multiple specimens from the same specimen with the same antibody, performing a single negative control on one of the specimens may be sufficient provided that all such specimens are fixed and processed identically. This exception does not apply to stains on different types of tissues or those using different antigen retrieval protocols or antibody detection systems. The laboratory director must determine which cases will have only one negative reagent control, and this must be specified in the department's procedure manual.

The negative reagent control would ideally control for each reagent protocol and antibody retrieval condition; however, large antibody panels often employ multiple antigen retrieval procedures. In such cases, a reasonable minimum control would be to perform the negative reagent control using the most aggressive retrieval procedure in the particular antibody panel. Aggressiveness of antigen retrieval (in decreasing order) is as follows: pressure cooker; enzyme digestion; boiling; microwave; steamer; water bath. High pH retrieval should be considered more aggressive than comparable retrieval in citrate buffer at pH 6.0.

Immunochemical 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.

It is also important to assess the specificity of each antibody by a negative cellular/tissue control, which must show no staining of cells/tissues known to lack the antigen. The negative control is processed using the same fixation, epitope retrieval and immunostaining protocols as the patient tissue. Unexpected positive staining of such tissues indicates that the test has lost specificity, perhaps because of improper antibody concentration or excessive antigen retrieval. Intrinsic properties of the test tissue may also be the cause of "non-specific" staining. For example, cells/ tissues with high endogenous biotin activity such as liver or renal tubules may simulate positive staining when using a detection method based on biotin labeling.

A negative cellular sample or tissue control must be processed for each antibody in a given run. Any of the following can serve as a negative cellular/tissue control:

1. *Multitissue blocks. These can provide simultaneous positive and negative tissue controls, and are considered “good practice” (see below).*
2. *The positive control slide or patient test slides, if these slides contain cellular or tissue elements that should not react with the antibody.*
3. *A separate negative cytologic preparation or tissue control slide.*

The type of negative cellular/tissue control used (ie, separate sections, internal controls or multitissue blocks) must be specified in the laboratory manual.

Multitissue blocks or tissue microarrays (TMAs) can have a major role in maintaining quality. When used as a combined positive and negative tissue control as mentioned above, they can serve as a permanent record of the sensitivity and specificity of every stain, particularly when mounted on the same slide as the patient tissue. When the components are chosen appropriately, multitissue blocks may be used for many different primary antibodies, decreasing the number of different control blocks needed by the laboratory. Multitissue blocks are also ideal

for determining optimal titers of primary antibodies since they allow simultaneous evaluation of many different pieces of tissue. Finally, they are a useful and efficient means to screen new antibodies for sensitivity and specificity or new lots of antibody for consistency, which should be done before putting any antibody into diagnostic use.

Evidence of Compliance:

- ✓ Patient reports or worksheet with control results **AND**
- ✓ Immunochemical-stained slides with appropriate negative controls

REFERENCES

1) Leong AS-Y, Cooper K, Leong FJW-M. Manual of Diagnostic Antibodies for Immunohistology. 2nd ed. London: Greenwich Medical Media; 2003
2) Dabbs DJ, ed. Diagnostic Immunohistochemistry: Theranostic and Genomic Applications. Philadelphia: Saunders/Elsevier; 2010
3) Burry RW. Specificity controls for immunocytochemical methods. *J Histochem Cytochem* 2000;48:163-166
4) Weirauch M. Multitissue control block for immunohistochemistry. *Lab Med.* 1999;30:448-449
5) Miller RT. Multitumor "sandwich" blocks in immunohistochemistry. Simplified method and preparation and practical uses. *Appl Immunohistochem* 1993;1: 156-159
6) Chan JKC, Wong CSC, Ku WT, Kwan MY. Reflections on the use of controls in immunohistochemistry and proposal for application of a multitissue spring-roll control block. *Ann Diagn Pathol* 2000;4: 329-336
7) 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(a)]
8) Torlakovic EE, Francis G, Garratt J, et al. International Ad Hoc Expert Panel. Standardization of negative controls in diagnostic immunohistochemistry recommendations from the international ad hoc expert panel. *Appl Immunohistochem Mol Morphol.* 2014;22(4):241-52.
9) Allen M, Gown, MD. Diagnostic Immunohistochemistry: What Can Go Wrong and How to Prevent it. *Arch Pathol Lab Med.* 2016;140(9):893-898.

CYP.04350 Endogenous Biotin — Phase I

If the laboratory uses an avidin-biotin complex (ABC) detection system (or a related system such as streptavidin-biotin or neutravidin-biotin), nonspecific false-positive staining from endogenous biotin is addressed.

NOTE: Biotin is a coenzyme present in mitochondria, and cells that have abundant mitochondria such as hepatocytes, kidney tubules and many tumors (particularly carcinomas) are rich in endogenous biotin. Biotin-rich intranuclear inclusions are also seen in gestational endometrium and in some tumors that form morules. If steps are not included in the immunostaining method to block endogenous biotin before applying the ABC detection complex, nonspecific false-positive staining may occur, particularly when using heat-induced epitope retrieval (which markedly increases the detectability of endogenous biotin). This artifact is often localized to tumor cells and may be easily misinterpreted as true immunoreactivity.

Blocking endogenous biotin involves incubating the slides with a solution of free avidin (which binds to endogenous biotin), followed by incubation with a biotin solution (which saturates any empty biotin-binding sites remaining on the avidin). Biotin-blocking steps should be performed immediately after epitope retrieval and before incubation with primary antibody.

REFERENCES

1) Miller RT, Kubier P. Blocking of endogenous avidin-binding activity in immunohistochemistry: the use of egg whites. *Appl Immunohistochem* 1997; 5: 63-66
2) Miller RT, Kubier P, Reynolds B, Henry T. Blocking of endogenous avidin-binding activity in immunohistochemistry: the use of skim milk as an economical and effective substitute for commercial biotin solutions. *Appl Immunohistochem & Molec Morphol* 1999;7:63-65
3) Allen M, Gown, MD. Diagnostic Immunohistochemistry: What Can Go Wrong and How to Prevent it. *Arch Pathol Lab Med.* 2016;140(9):893-898.

CYP.04360 Control Slide Review — Phase II

The laboratory director or designee reviews batch control slides for acceptability before reporting patient/client results.

NOTE: Records of this daily review must be retained and clearly show that positive and negative controls for all antibodies stain appropriately. Batch control records must be retained for two years.

Immunochemical 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.

The batch control slides must be readily available to pathologists who are signing out cases. The location of the slides should be stated in the procedure manual.

Evidence of Compliance:

✓ Records of control slide review

REFERENCES

1) Shellhorn N. IHC troubleshooting tips. Advance/Lab. 2000;9(1):33-37
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): [42CFR493.1273(f)]

*****REVISED** 09/22/2021***

CYP.04370 Antibody Validation/Verification - Non-Predictive Marker 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 cellular samples or 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 cellular samples or tissue in another laboratory with a validated/verified assay; or 4) comparing the results using the new antibody with previously validated/verified non-immunocytochemistry 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 nonpredictive assay, the validation/verification should test a minimum of 10 positive and 10 negative cellular samples or tissues. If the laboratory director determines that fewer validation/verification cases are sufficient for a specific marker (eg, a rare antigen or cell/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.

When possible, laboratories should use cellular samples or tissues that have been processed using the same fixative and processing methods as cases that will be tested clinically. If immunocytochemistry is regularly done on specimens that are not fixed or processed in the same manner as the tissues used for validation/verification (eg, air-dried touch imprints, air-dried and/or alcohol fixed smears, cytocentrifuge or other liquid-based preparations, and cellular materials fixed in alcohol blends or other fixatives), the laboratory should test a sufficient number of such cellular samples or tissues to ensure that assays consistently achieve expected results with the alternative fixative/processing conditions. 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" in the Anatomic Pathology Checklist 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, 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.
5) Uhlen M, Bandrowski A, Carr S, et al. A proposal for validation of antibodies. *Nat Methods.* 2016; 13(10):838-7.
6) Fitzgibbons PL, Bradley LA, Fatheree LA, 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. *Arch Pathol Lab Med.* 2014;138(11):1432-43.
7) Allen M, Gown, MD. Diagnostic Immunohistochemistry: What Can Go Wrong and How to Prevent it. *Arch Pathol Lab Med.* 2016;140(9):893-898.

CYP.04380 New Reagent Lot Confirmation of Acceptability — Phase II

The performance of new lots of antibody and detection system reagents is compared with old lots before or concurrently with being placed into service.

NOTE: Parallel staining is required to control for variables such as disparity in the lots of detection reagents or instrument function. New lots of primary antibody and detection system reagents must be compared to the previous lot using at least one known positive control and one known negative control cellular samples or tissue. This comparison should be made on slides cut from the same control block.

Evidence of Compliance:

✓ Records of confirmation of new reagent lots

CYP.04390 Immunocytochemistry Assay Performance — Phase I

Laboratories confirm assay performance when conditions change that may affect performance.

NOTE: A change in antibody clone requires full revalidation/verification of the assay (equivalent to initial analytic validation/verification - see CYP.04370).

Laboratories must confirm assay performance with at least two known positive and two known negative cases when an existing validated/verified assay has changed in any of the following ways: antibody dilution, antibody vendor (same clone), or the incubation or retrieval times (same method).

A more extensive study to confirm acceptable assay performance in accordance with published guidelines must be performed when any of the following have changed: fixative type, antigen retrieval protocol (eg, change in pH, different buffer, different heat platform), antigen detection system, cytologic preparation/tissue processing or testing equipment, environmental conditions of testing (eg, laboratory relocation), or laboratory water supply. This study must include a representative sampling of the assays affected by the change and an appropriate number of positive and negative cases per assay, sufficient to confirm acceptable assay performance. The laboratory director is responsible for determining the extent of the study. The rationale for the assays selected and number of positive and negative cases checked per assay must be recorded.

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

REFERENCES
1) Fitzgibbons PL, Bradley LA, Fatheree LA, 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. *Arch Pathol Lab Med.* 2014; 138(11):1432-43.

CYP.04410 Slide Quality **Phase II**

The immunocytochemical stains produced are of acceptable technical quality.

NOTE: The inspector must examine examples of the immunochemical preparations offered by the laboratory. A reasonable sample might include 5-10 diagnostic antibody panels.

REFERENCES
1) Shellhorn N. IHC troubleshooting tips. *Advance/Lab*. 2000;9(1):33-37

PREDICTIVE MARKERS

This checklist section applies only to immunocytochemical tests used to predict responsiveness to a specific treatment independent of other cytopathologic findings. Rather than confirming a specific diagnosis (such as B-cell lymphoma or gastrointestinal stromal tumor), these tests should differentiate predicted responsiveness to a targeted therapy 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 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:

READ	• 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 • Sampling of predictive marker assay validation, verification, and revalidation/ verification studies
ASK	• 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?

*****NEW** 09/22/2021***

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, hormone 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 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) Fischer AH, Schwartz MR, Moriarty AT, et al. Immunohistochemistry practices of cytopathology laboratories: a survey of participants in the College of American pathologists Nongynecologic Cytopathology Education Program. *Arch Pathol Lab Med.* 2014;138(9):1167-72.
2) 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
3) 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
4) Allred DC, *et al.* ER expression is not bimodal in breast cancer. *Am J Clin Pathol.* 2005;124:474-5
5) Wolff AC, Hammond EH, Allison KH, et al. Human Epidermal Growth Factor Receptor 2 Testing in Breast Cancer: American Society of Clinical Oncology/College of American Pathologists Clinical Practice Guideline Focused Update. *Arch Pathol Lab Med.* 2018; 142(11):1364-82.
6) 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.
7) 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.

*****NEW** 09/22/2021***

CYP.04520 Annual Result Comparison - Breast Carcinoma **Phase II**

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, 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, Hammond EH, Allison KH, et al. Human Epidermal Growth Factor Receptor 2 Testing in Breast Cancer: American Society of Clinical Oncology/College of American Pathologists Clinical Practice Guideline Focused Update. *Arch Pathol Lab Med.* 2018; 142(11):1364-82.
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/REVISED** 10/24/2022***

CYP.04530 Predictive Marker Testing - Validation/Verification **Phase II**

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

NOTE: Test validation/verification must be performed on a minimum of 40 cases (20 positive and 20 negative samples). 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 must be recorded.

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 data should clearly show the degree of concordance between assays or methods. Minimum acceptable concordance levels 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, 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, Hammond EH, Allison KH, et al. Human Epidermal Growth Factor Receptor 2 Testing in Breast Cancer: American Society of Clinical Oncology/College of American Pathologists Clinical Practice Guideline Focused Update. *Arch Pathol Lab Med.* 2018; 142(11):1364-82.
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, 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. *Arch Pathol Lab Med.* 2014;138(11):1432-43.

*****NEW** 09/22/2021***

CYP.04540 Estrogen Receptor and HER2 Testing in Breast Cancer Samples Phase I

At least one tumor sample from all patients with invasive breast cancer (newly diagnosed, recurrent, or metastatic disease) is tested for estrogen receptors and HER2 (by IHC or ISH) if tissue is available.

REFERENCES
1) Wolff AC, Hammond EH, Allison KH, et al. Human Epidermal Growth Factor Receptor 2 Testing in Breast Cancer: American Society of Clinical Oncology/College of American Pathologists Clinical Practice Guideline Focused Update. *Arch Pathol Lab Med.* 2018; 142(11):1364-82.

*****NEW** 09/22/2021***

CYP.04550 Fixation - HER2 and ER Breast Cancer Predictive Marker Testing Phase I

If the laboratory assesses HER2 protein over-expression by immunocytochemistry, or estrogen receptor expression by immunocytochemistry for breast cancer predictive marker testing, the laboratory monitors cold ischemia time (one hour or less), if applicable, and appropriate specimen fixation time.

NOTE: The CAP strongly recommends that specimens subject to these tests be fixed in 10% neutral phosphate-buffered formalin for at least six hours and up to 72 hours at room temperature. Specimens must be fully submerged in the optimal volume of formalin to achieve a formalin to specimen volume of 10:1 or higher, or if not feasible (eg, large specimens) at least 4:1. For cases with negative HER2 results by immunocytochemistry that were fixed outside these limits, confirmatory analysis by in situ hybridization is strongly recommended.

Both the time of removal of the tissue and the time of immersion of the tissue in fixative must be recorded and communicated from the submitting service to the processing laboratory.

Communication to clinical services of the need for appropriate information on cold ischemia time, fixative, and fixation time may be through memoranda, website, phone, face-to-face meetings, or other means. Information about fixative, fixation time, and cold ischemia time (if applicable) for each specimen must be recorded as part of the permanent specimen record in the pathology report. The laboratory must monitor for compliance and take corrective action as needed.

If specimens are fixed in a solution other than 10% neutral phosphate-buffered formalin, the laboratory must perform a validation study showing that HER2 and ER 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 (if applicable) and time of fixation. Information on time of fixation may be obtained by appropriate questions on the laboratory's requisition form. If specimens have undergone any deviation from processing that may interfere with result interpretation, this must be annotated on the final report.

Evidence of Compliance:

- ✓ Records of communication of cold ischemia (if applicable) and fixation guidelines to clinical services **AND**
- ✓ Records of action taken when cold ischemia (if applicable) and fixation times are consistently outside of required parameters or are not available to the laboratory

REFERENCES
1) Wolff AC, Hammond EH, Allison KH, et al. Human Epidermal Growth Factor Receptor 2 Testing in Breast Cancer: American Society of Clinical Oncology/College of American Pathologists Clinical Practice Guideline Focused Update. *Arch Pathol Lab Med.* 2018; 142(11):1364-82.
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.
3) 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.

ON-SITE MICROSCOPIC REVIEW

On-site review of actual case (slide) material and corresponding reports is an important element of the inspection process. This is NOT a comprehensive rescreening of slides or evaluation of competency, but rather an action to facilitate the Inspector's evaluation of the laboratory's overall procedures.

Laboratories that do not file slides on-site (for example, some "read-only" laboratories) must retain a sample of 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 minimum, include all slides accessioned over a continuous two-week period within the previous two years. The laboratory must be able to produce any slide upon the request of an inspector during the required retention period for gynecologic and non-gynecologic slides (including fine needle aspiration slides).

Inspector Instructions:

DISCOVER

- Review a randomly selected representative sample of 10-15 cases using the table below to guide selection:

Gynecologic Cases	***Non-Gynecologic Cases (including FNA's)***
Unsatisfactory	*Negative for malignancy / Reactive*
Negative for intraepithelial lesion or malignancy (NILM) / Repair	*Atypical or suspicious with qualifiers / Suspicious for malignancy / Positive for malignancy*
Atypical squamous cells	
LSIL (encompassing HPV)	
HSIL / Carcinoma	

Cases should be selected by the laboratory pathologist and/or cytopathology supervisor in a random manner defined by the inspecting Team Leader (eg, the first 1-3 negative and abnormal cases in each specimen category from a certain date or week). The following are core elements of the on-site review:

- Evaluate slides for quality of technical preparation and specimen adequacy
- Determine if significant cells have been identified
- Compare slides with the diagnostic report for completeness and clarity of diagnostic terminology
- Determine if the information provided with the requisition and included in the diagnostic report is complete and appropriate

If, during the on-site review, there is believed to be a significant diagnostic discrepancy, this should be discussed by the pathologist team leader with the laboratory director. Interpretations may be considered discrepant if there is a significant diagnostic difference in interpretation. An example of this would be an interpretation of Negative for Intraepithelial Lesion/Malignancy, vs. an interpretation of LSIL or greater. Cases considered to be "ASC/AGC" (either by the Inspector or inspectee) should not be included in the analysis

to determine significant discrepancies, because of the current lack of interlaboratory reproducibility of these interpretations.

CYP.04900 Cellular/Nuclear Detail **Phase II**

Cellular and nuclear detail are sufficient for proper interpretation.

CYP.05000 On-Site Slide Review **Phase II**

The findings from the on-site slide review are free of any issues or any significant diagnostic discrepancies as defined in the Inspector Instructions.

INSTRUMENTS AND EQUIPMENT

The checklist requirements in this section should be used in conjunction with the requirements in the All Common Checklist relating to instruments and equipment.

Inspector Instructions:

- How does your laboratory perform ongoing monitoring of screening instrumentation? What corrective action is taken when tolerance limits are exceeded?
- How do you identify slides that have not successfully been processed by the automated screening instrument?

- Follow a slide through automated staining, cover-slipping and automated screening. Determine if practice matches procedure.

CYP.05292 Unsuccessful Slide Processing **Phase II**

The laboratory has a process to identify and handle slides that are not successfully processed by the automated screening instrument.

NOTE: Laboratories must clearly identify slides that fail screening by an automated instrument and ensure that these slides are completely rescreened by another method. In most instances, manual rescreening will be used.

Evidence of Compliance:

✓ Records of slide rescreening

RECORDS AND REPORTS

Inspector Instructions:

- Sampling of reporting policies and procedures
- Sampling of patient reports

- How are reports signed if the reviewing pathologist is not available?
- How do you record intra-departmental and extra-departmental consultations?
- If cases are resulted at different locations, how do you ensure that the testing laboratory name and address are correct on the final report?

CYP.05300 Cytopathology Report Elements **Phase II**

The cytopathology report includes all of the following elements:

1. **Name of patient and unique identifying number, if available**
2. **Age and/or birth date of patient**
3. **Date of collection**
4. **Accession number**
5. **Name of submitting physician and/or clinic**
6. **Name of the responsible reviewing pathologist, when applicable**
7. **Name and address of the laboratory location where the test was performed**
8. **Date of report**
9. **Test performed**
10. **Anatomic source and/or type of specimen**
11. **Basis for amendment (if applicable)**

NOTE: If slide screening is performed at one laboratory location and the interpreting pathologist is at a different location, the names and addresses of both laboratory locations must be on the report. If slide processing and staining are performed at one location and screening and interpretation at a second location, only the name/address of the second location need be on the report.

Refer to CYP.05316 below for additional details regarding the reviewing pathologist.

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):3711 [42CFR493.1274(e)(6)
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):3713 [42CFR493.1291(c)(1-6) and (k)(1,2)]

CYP.05316 Pathologist Identification on Report **Phase II**

The cytopathology report clearly indicates the name of the pathologist who has reviewed the slides, when applicable.

NOTE: The records must indicate those who have reviewed the cytology slides. Cytotechnologists should be identifiable by name, initials, or other identifier in laboratory records. When a pathologist has performed a diagnostic review of the slides, the report must indicate his/her name or signature (in written or electronic form). The reviewing pathologist's name must be distinct from any other pathologist names (eg, the laboratory director) on the report. Electronic signatures must be secure and traceable to the reviewing pathologist. A report may contain the signature/initials of a pathologist or cytotechnologist attesting to an activity other than review of the slides (for example, verification of results of automated screening instruments), but in such cases the report must clearly indicate that the signature/initials attest to the other activity, not review of the slides.

When slides are reviewed by a pathologist for quality control purposes only (eg, the 10% rescreen of gynecologic cytopathology cases), the name of the pathologist must be retained in laboratory records but need not be included on the report.

CYP.05332 Report Review **Phase II**

Cytopathology reports are reviewed and signed by the pathologist, when applicable.

NOTE: For gynecologic cases reviewed by a pathologist, and for all non-gynecologic cases, the laboratory must ensure that records indicate that the reviewing pathologist has reviewed and approved the completed report before release. In the occasional situation when the diagnosing pathologist is not available for timely review and approval of the completed report, the laboratory may have a policy and procedure for review and approval of that report by another pathologist. In that circumstance, the names and responsibilities of both the pathologist who made the diagnosis and the pathologist who performs final verification must appear on the report.

This checklist requirement does not apply to cases reviewed by a pathologist for quality control purposes only (eg, the 10% rescreen of gynecologic cytopathology 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): [42CFR493.1274(e)(2)(3)]

CYP.05350 Cytopathology Report Elements **Phase I**

The cytopathology report includes all of the following elements:

1. **Date specimen received/accessioned by the laboratory**
2. **Description of specimen on receipt (eg, bloody fluid)**
3. **Description of fixative and pre-analytic variables that may affect ancillary testing (eg, type of fixative, time in fixative)**
4. **Designation of automated screening device, when applicable**

NOTE: For description of specimens on receipt, examples include the number of glass slides submitted and how fixed (eg, air-dried or alcohol-fixed); quantity of fluid and fixation (eg, 10 cc bloody fluid in alcohol); Thin Prep vial; SurePath vial; and brush in 10 cc clear yellow fluid.

Evidence of Compliance:

✓ Cytopathology reports including the required elements

CYP.06100 Report - Morphologic Findings **Phase II**

The cytopathology report includes an interpretation of the morphologic findings, and as appropriate, standard descriptive terminology.

NOTE: Cytopathology reports must clearly communicate whether disease is present, absent, or uncertain. When a definite diagnosis cannot be rendered (ie, terms such as “inconclusive,” “indeterminate” or “non-diagnostic” are used), the reason should be given.

Reports must include a concise descriptive diagnosis either in a format similar to a histopathology report, or standard descriptive terminology that includes a general categorization and descriptive diagnosis (as is recommended by the Bethesda System for gynecologic cytopathology reports). The use of diagnostic "classes" is not recommended, as it does not reflect current understanding of neoplasia, has no comparable equivalent in diagnostic histopathologic terminology, and does not provide for diagnosis of non-neoplastic conditions.

A simple diagnosis of "Negative" is not an adequate descriptive diagnosis. However, a diagnosis such as, "Negative for malignancy" or “No malignant cells identified" is acceptable for non-gynecologic exfoliative cytology specimens (ie, urine, fluids, washings and brushings). When appropriate (particularly for fine needle aspiration samples of mass lesions), a statement regarding the adequacy of the specimen should be included, with a description of the limitations of the specimen when a specific diagnosis cannot be made.

Evidence of Compliance:

✓ Cytopathology reports including morphologic findings

REFERENCES
1) Solomon D, *et al*. The 2001 Bethesda system. Terminology for reporting results of cervical cytology. *JAMA.* 2002:287:2114-2119

2) Solomon D, Nayar, R, *eds*. The Bethesda System for Reporting Cervical Cytology; Definitions, Criteria, and Explanatory Notes. 2nd ed., 2004
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): [42CFR493.1274(e)(5)]

***REVISED** 10/24/2022*

CYP.06450 Significant and Unexpected Findings **Phase II**

Significant and unexpected cytopathology findings are communicated to the responsible clinician and records of those communications are retained.

NOTE: Certain cytopathology diagnoses may be considered significant and unexpected, warranting special communication to the responsible clinician(s). The cytopathology department determines diagnoses to be defined as "significant and unexpected," in cooperation with local clinical medical staff. Examples include: invasive carcinoma found in a cervicovaginal specimen, amendments to reports that may significantly affect patient care, and malignancy in an effusion with no patient history of neoplasm.

There must be a reasonable effort to ensure that clinicians receive the communications. The records must include the following:

- *Date of communication*
- *Time of communication (if required by laboratory policy)*
- *Responsible individual communicating the result*
- *Person notified using identifiers traceable to that person (a first name alone is inadequate)*
- *Findings communicated.*

An appropriate notification includes a direct dialog with the responsible individual or an electronic communication (secure email or fax) with confirmation of receipt by the responsible individual.

The record of the communication may be included directly on the patient report or in a separate location. It is not necessary to separately summarize the findings communicated if the record of the communication is on the patient report. For communications recorded in a separate location, the findings communicated may be summarized or reference the case number.

This requirement takes the place of critical result notification in the All Common Checklist (COM.30000 and COM.30100) for cytopathology findings.

Evidence of Compliance:

✓ Records of communication of significant and unexpected findings

***REVISED** 10/24/2022*

CYP.06475 Amended Reports **Phase II**

The laboratory issues an amended report and promptly notifies the responsible clinician(s) when there are changes to reports that affect current patient care.

NOTE: The amended report must state the reason for the amendment. The format of amended reports is at the discretion of the laboratory.

Records of notification must include date, responsible laboratory individual, and person notified.

Evidence of Compliance:

✓ Patient reports containing reason for the amendment **AND**
✓ Records of notification

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):3713 [42CFR493.1274(e)(6)].

CYP.06600 Report Retention - Cytopathology **Phase II**

Cytopathology reports are retained for at least 10 years.

NOTE: Cytopathology reports must be retained in either paper or electronic format. If retained in electronic format alone, reports must include a secure pathologist electronic signature when applicable. Images of paper reports, such as microfiche, PDF files, including signature are acceptable.

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):7170 [42CFR493.1105(a)(7)(i)(A); 493.1274(f)(2) through (f)(4)]
2) College of American Pathologists. Retention of laboratory records and materials. Northfield, IL: CAP, current edition

CYP.06850 Correlation of Results - Non-gynecologic Cytopathology **Phase II**

The cytologic diagnoses for non-gynecologic cytopathology cases are correlated with the results of specialized studies (eg, molecular studies, immunocytochemistry).

NOTE: It is not in the best interests of the patient to have potentially conflicting diagnoses or interpretations rendered by different sections of the laboratory. The pathologist should issue a report reconciling potentially conflicting data, when appropriate.

RETENTION OF SLIDES

Inspector Instructions:

READ	• Sampling of slide handling policies and procedures
OBSERVE	• Slide storage area (organized, accessible, slides easily retrieved)
ASK	• For slides retained for different periods of time, how does your laboratory ensure that the slides are retained for the defined time period? • If using off-site storage, how do you ensure that slides are stored appropriately?

CYP.06900 Slide Retention - Cytopathology **Phase II**

All glass slides are retained for an appropriate period.

NOTE: Minimum requirements for laboratories rendering cytopathology services, providing these are not less stringent than national, federal, state (or provincial), or local laws and regulations, are:

1. *Gynecologic glass slides -five years*
2. *Non-gynecologic glass slides (including fine needle aspiration (FNA) slides)-10 years*

The retention period for non-gynecologic (non-FNA) glass slides changed from five years to 10 years in the 2019 Checklist edition. Cases diagnosed prior to December 31, 2014 are not subject to the 10-year retention requirement.

Laboratories may utilize archived slides for the benefit of the patient, even if that use destroys the slide. In such cases, the laboratory policy on material and record retention must authorize the destruction of a retained slide for such purposes (eg, molecular testing).

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):7170 [42CFR493.1105(a)(7)(i)(A); 493.1274(f)(2) through (f)(4)]
2) College of American Pathologists. Retention of laboratory records and materials. Northfield, IL: CAP, current edition

*****REVISED** 09/22/2021***

CYP.07100 Slide and Block Storage - Cytology — Phase II

Cytology slides and blocks are properly stored in a temperature controlled, pest-free, organized manner (ie, accessible for retrieval and properly identified).

NOTE: Slides and blocks must be stored in a manner to prevent contamination from blood or other fluids or tissues and be readily accessible for retrieval.

The storage area for blocks must be cool to prevent blocks from melting together. Storage temperature must be maintained between 18°C to 27°C.

For laboratories using off-site storage facilities, the laboratory director or designee must confirm that storage requirements are met.

Evidence of Compliance:

- ✓ Records of storage temperature monitoring (on-site and off-site locations), including deviations

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):7170 [42CFR493.1105(a)(7)(i)(A); 493.1274(f)(1) through (f)(4)]
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.

CYP.07200 Slide Handling — Phase II

The circulation, referral, transfer, and receipt of original slides follows a consistent process that includes records of the location of slides to ensure availability for consultation and legal proceedings.

Evidence of Compliance:

- ✓ Tracking sheet/log that includes identity of slides/blocks, identity of recipient and record of return of slides/blocks

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):7170 [42CFR493.1105(a)(7)(i)(A); 493.1274(f)(2) through (f)(4)]

CYP.07300 Acknowledgment of Receipt — Phase II

There are records, including acknowledgment of receipt, when original diagnostic material is loaned to special programs for the purpose of education and/or proficiency testing.

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):7170 [42CFR493.1105(a)(7)(i)(A); 493.1274(f)(3)
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):7170 [42CFR493.1105(a)(7)(i)(A); 493.1274(f)(2) through (f)(4)]

GYNECOLOGIC CYTOPATHOLOGY

Inspector Instructions:

	• Sampling of gynecologic cytopathology policies and procedures • Written criteria for unsatisfactory specimens • Sampling of patient reports for pathologist review and interpretation of specific screening diagnoses • Sampling of 10% rescreening records • Sampling of records of retrospective review and evidence of amended reports, if applicable • Statistical records including evidence of annual review and investigation when the laboratory falls outside the 5th or 95th percentiles • Records of employee performance monitoring including individual's discrepancies and corrective action
	• Use of Papanicolaou stain
	• What criteria are used to identify rejected or unsatisfactory specimens? • What is the laboratory's process for follow-up or investigation of significant results? • What is your course of action when you are unable to obtain histological reports or material when reporting gynecologic cases with HSIL? • What is your process for correlating gynecologic cytopathology findings with clinical information? • How do you educate providers that the Pap test is a screening test with false negative results? • What is the process for performance monitoring of cytotechnologists?
	• Follow a slide through automated staining, cover-slipping and automated screening. Determine if practice matches procedure. • Review records or specimen log for unsatisfactory specimens. Determine if the quality of the specimens follows defined criteria. • Review a sampling of rescreening records. Determine if the rescreening was performed by a qualified individual, results are not reported until the rescreen is complete and a minimum of 10% of cases for each screener are rescreened.

CYP.07439 Papanicolaou Stain **Phase II**

The Papanicolaou stain is used for gynecologic specimens.

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):7169 [42CFR493.1274(b)(1)]

***REVISED** 09/22/2021*

CYP.07452 Unsatisfactory Specimens - Gynecologic Cytopathology **Phase II**

The laboratory has written criteria for identification and reporting of unsatisfactory gynecologic specimens and slide preparations.

NOTE: Cytopathology reports must clearly specify when a specimen and/or slide preparation is unsatisfactory for evaluation and state the reason in the cytopathology report. The criteria for categorizing a specimen and/or slide preparation as unsatisfactory (eg, scant cellularity, obscuring blood, obscuring inflammation) must be defined by the laboratory. Unsatisfactory cases must not be reported as negative or normal. Gynecologic specimens with atypical cells are always "satisfactory," although the report may include comments on the quality of the preparation.

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):7169 [42CFR493.1274(e)(4)]
2) Davey DD, *et al.* Terminology and specimen adequacy in cervicovaginal cytology. *Arch Pathol Lab Med.* 1992;116:903-907
3) Ransdell JS, *et al.* Clinicopathologic correlation of the unsatisfactory Papanicolaou smear. *Cancer Cytopathol.* 1997;81:139-143
4) Renshaw AA, *et al.* Accuracy and reproducibility of estimating the adequacy of the squamous component of cervicovaginal smears. *Am J Clin Pathol.* 1999:11:38-42
5) Selvaggi SM. Is it time to revisit the classification system for cervicovaginal cytology? *Arch Pathol Lab Med.* 1999;123:993-994
6) Davey DD, *et al.* Atypical cells and specimen adequacy. Current laboratory practices of participants in the College of American Pathologists interlaboratory comparison program in cervicovaginal cytology. *Arch Pathol Lab Med.* 2000;124:203-211
7) Nakhleh RE, Fitzgibbons PL, *eds.* Quality management in anatomic pathology. Promoting patient safety through systems improvement and error reduction. Northfield, IL: College of American Pathologists, 2005
8) Solomon D, *et al*. The 2001 Bethesda system. Terminology for reporting results of cervical cytology. *JAMA*. 2002;287:2114-2119
9) Solomon D, Nayar, R, *eds*. The Bethesda system for reporting cervical/vaginal cytologic diagnoses: Definitions, criteria, and explanatory notes for terminology and specimen adequacy. New York, NY: Springer-Verlag; 2nd edition, 2004
10) Clinical and Laboratory Standards Institute. *Cervicovaginal Cytology Based on the Papanicolaou Technique; Approved Guideline*; 3rd ed. CLSI document GP15-A3. Clinical and Laboratory Standards Institute, Wayne, PA, 2008.

CYP.07465 Pathologist Interpretation — Phase II

All gynecologic slides in the following categories are interpreted by the pathologist.

1. **Malignant or suspicious for malignancy**
2. **Low and high-grade squamous intraepithelial lesions**
3. **Atypical squamous cells**
4. **Atypical glandular cells**
5. **Reactive or repair**

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):7169 [42CFR493. 1274(e)(1)(i) through (e)(1)(v), and (e)(2)]
2) Raab SS, *et al.* Interobserver variability of a Papanicolaou smear diagnosis of atypical glandular cells of undetermined significance. *Am J Clin Pathol.* 1998;110:653-659
3) Selvaggi SM. Is it time to revisit the classification system for cervicovaginal cytology? Arch Pathol Lab Med. 1999;123:993-994

CYP.07478 10% Rescreen — Phase II

At least 10% of each cytotechnologist's gynecologic cases that have been interpreted to be negative are rescreened.

NOTE: The 10% rescreening is a CLIA requirement, and only applicable to US laboratories and other laboratories subject to those regulations. An individual who qualifies as a cytotechnologist supervisor and who performs initial screening must also have a minimum of 10% of his or her cases that are initially interpreted as negative subjected to rescreening. This rescreening must include some cases from high-risk patients, based upon criteria established by the laboratory director, as well as random negative cases. Cases screened by MDs or DOs who are certified in Anatomic Pathology by the American Board of Pathology or the American Osteopathic Board of Pathology, or who possess qualifications that are equivalent to those required for the above certifications are not subject to this rescreening requirement. If FDA-approved automated instruments are used for quality control rescreening case selection, the laboratory must ensure that the methods used meet the requirements of CLIA, and that manufacturer and FDA recommendations for quality control are followed.

Slides must be rescreened in their entirety, including slides processed by imaging instruments that select a limited number of microscopic fields for examination by the cytotechnologist.

Evidence of Compliance:

- ✓ Defined qualifications of the individual to perform rescreening and the criteria for case selection **AND**
- ✓ Records of rescreened cases with comparison to original screening results

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):7169 [42CFR493.1274(c)(1)]
2) Krieger P, *et al.* Guest editorial: random rescreening of cytology smears: a practical and effective component of quality assurance programs in both large and small cytology laboratories. *Acta Cytol.* 1994;38:291-298
3) Krieger P, *et al.* A practical guide to Papanicolaou smear rescreens. How many slides must be reevaluated to make a statistically valid assessment of screening performance? *Cancer Cytopathol.* 1998;84:130-137
4) Renshaw AA, *et al.* Performance characteristics of rapid (30-second) prescreening. Implications for calculating the false-negative rate and comparison with other quality assurance techniques. *Am J Clin Pathol.* 1999;111:517-522
5) Intersociety Working Group for Cytology Technologies. Proposed method for evaluating secondary screening (rescreening) instruments for gynecologic cytology. *Am J Clin Pathol.* 1999;111:590-593
6) Raab SS, *et al.* Cost effectiveness of rescreening cervicovaginal smears. *Am J Clin Pathol.* 1999;111:601-609

CYP.07480 Rescreening or Prescreening Negative Cases — Phase II

For laboratories not subject to US regulations, the competency of each screener of gynecologic cytopathology specimens is assessed by either a pre-screening or rescreening process.

NOTE: Laboratories not subject to US regulations may follow the US requirement or may use an alternative procedure. Laboratories subject to US regulations are required to rescreen 10% of each cytotechnologist's gynecologic cases that have been interpreted to be negative, including some cases from high-risk patients, based upon criteria established by the laboratory director, as well as random negative cases. Alternative procedures for 10% rescreening could include, but are not limited to a rapid rescreening of all cases or rapid prescreening of all cases with targeted rescreening of discrepant cases. Slides must be rescreened or prescreened in their entirety, including slides processed by imaging instruments that select a limited number of microscopic fields for examination.

Evidence of Compliance:

- ✓ Defined method to be used for rescreening or prescreening and the criteria for case selection **AND**
- ✓ Records of rescreened or prescreened cases with comparison to final comprehensive screening results

CYP.07491 Result Reporting — Phase II

The results of gynecologic cases selected for rescreening are not reported until the rescreen is complete.

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): [42CFR493.1274(c)(1)]

CYP.07504 Rescreener Qualifications — Phase II

The rescreening of negative gynecologic cases is performed by an individual qualified as a cytopathology supervisor (see CYP.08100).

Evidence of Compliance:

- ✓ Records of section director/technical supervisor or supervisor/general supervisor qualifications including degree or transcript, certification/registration, current license (if required) and work history in related field for each individual performing rescreening

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):7169 [42CFR493.1274(c)(1)]

CYP.07517 Retrospective Review **Phase II**

All available (either on-site or in storage) previously negative slides received within the past five years are reviewed whenever a new high-grade squamous intraepithelial lesion (moderate or severe dysplasia, carcinoma in situ, CIN II or III) or malignant cervical/vaginal cytology is reported.

NOTE: Previously negative slides (read manually or automated) from the index patient must be rescreened or reviewed by an individual qualified as a cytology supervisor (see CYP.08100). Laboratory policy should specify which cases require pathologist review.

REFERENCES

1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Medicare, Medicaid and CLIA programs; CLIA fee collection; correction and final rule. *Fed Register.* 2003(Jan 24):5232 [42CFR493.1274(c)(3)]
2) Jones BA. Rescreening in gynecologic cytology. Rescreening of 3762 previous cases for current high-grade squamous intraepithelial lesions and carcinoma - a College of American Pathologists Q-Probes study of 312 institutions. *Arch Pathol Lab Med.* 1995;119:1097-1103
3) Jones BA. Rescreening in gynecologic cytology. Rescreening of 8096 previous cases for current low-grade and indeterminate-grade squamous intraepithelial lesion diagnoses - a College of American Pathologists Q-Probes study of 323 laboratories. *Arch Pathol Lab Med.* 1996;120:519-522
4) Davey DD. Papanicolaou smear five year retrospective review: what's required by the Clinical Laboratory Improvement Amendments of 1988? *Arch Pathol Lab Med.* 1997;121:296-298
5) Clary KM, *et al*. Cytohistologic discrepancies. A means to improve pathology practice and patient outcomes. *Am J Clin Pathol.* 2002;117:567-573

CYP.07530 Retrospective Review Requiring Amendment **Phase II**

If a significant discrepancy, which would affect current patient care, is found during the retrospective review, an amended report is issued.

Evidence of Compliance:

✓ Records of retrospective reviews and amended reports, as necessary

REFERENCES

1) Davey DD. Papanicolaou 5-year retrospective review. *Arch Pathol Lab Med.* 1997;121:296-298
2) Freedman LF. Implications of mandating amended reports following retrospective review of Papanicolaou smears. *Arch Pathol Lab Med.* 1997;121:299-300
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): [42CFR493.1274(c)(3)]

*****REVISED** 10/24/2022***

CYP.07543 Correlation of Results **Phase II**

Records of attempts to obtain and review follow-up histological reports or material are available within the laboratory when gynecologic cases with high-grade squamous intraepithelial lesion (HSIL) or malignant cytological findings are reported.

NOTE: When the histologic diagnosis is available, correlation to the cytologic findings must be recorded and these records must be readily accessible. The number of cases that have histologic correlation must be recorded.

Evidence of Compliance:

✓ Records of the attempts made to obtain and review histological reports or materials

REFERENCES

1) Joste NE, *et al.* Cytologic/histologic correlation for quality control in cervicovaginal cytology: experience with 1,582 paired cases. *Am J Clin Pathol.* 1995:103:32-34
2) Tritz DM, *et al.* Etiologies for non-correlating cervical cytologies and biopsies. *Am J Clin Pathol.* 1995;103:594-597
3) Jones BA, *et al.* Q-Probes - cervical biopsy-cytology correlation: a College of American Pathologists Q-Probes study of 22439 correlations in 348 laboratories. *Arch Pathol Lab Med.* 1996;120:523-531
4) Nakhleh RE, Fitzgibbons PL, *eds.* Quality management in anatomic pathology. Promoting patient safety through systems improvement and error reduction. Northfield, IL: College of American Pathologists, 2005
5) Wright, DC, *et al.* 2001 Consensus guidelines for the management of women with cervical cytological abnormalities. *JAMA.* 2002;287:2120-2129

6) Clary KM, *et al*. Cytohistologic discrepancies. A means to improve pathology practice and patient outcomes. *Am J Clin Pathol.* 2002;117:567-573
7) Renshaw A, Granter SR. Appropriate follow-up interval for biopsy confirmation of squamous intraepithelial lesions diagnosed on cervical smear cytology. *Am J Clin Pathol.* 1997;108:275-279
8) 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): [42CFR493.1274(c)(2)]

CYP.07556 Additional Reports — Phase II

When a follow-up histological report or material is not available within the laboratory, there are records of attempts to obtain follow-up histological information for correlative review when gynecologic cases with significantly abnormal (high-grade SIL) or malignant cytological findings are reported.

Evidence of Compliance:

✓ Records of attempts to obtain the information (eg, follow-up correspondence, telephone calls, or requests included in the report)

REFERENCES

1) Jones BA, *et al.* Q-Probes - cervical biopsy-cytology correlation: a College of American Pathologists Q-Probes study of 22439 correlations in 348 laboratories. *Arch Pathol Lab Med.* 1996;120:523-531
2) Clary KM, *et al*. Cytohistologic discrepancies. A means to improve pathology practice and patient outcomes. *Am J Clin Pathol.* 2002;117:567-573
3) Wright, DC, *et al*. 2001 Consensus guidelines for the management of women with cervical cytological abnormalities. *JAMA.* 2002;287:2120-2129

CYP.07569 Correlation of Results - Gynecologic Cytopathology — Phase II

Gynecologic cytopathology findings are correlated with clinical information, when available.

NOTE: Methods of clinical correlation must be defined. Examples of clinical correlation methods include: focused rescreening of cases based on clinical history, history of bleeding, or previous abnormality; correlation of glandular cells with hysterectomy status, age of patient, and last menstrual period; review of previous or current biopsy material.

Evidence of Compliance:

✓ Records of clinical correlation (eg, policies, problem logs with resolution, or notes in reports)

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):7169 [42CFR493.1274(c)(2)]
2) Joste NE, *et al.* Cytologic/histologic correlation for quality control in cervicovaginal cytology. Experience with 1,582 paired cases. *Am J Clin Pathol.* 1995;103:32-34
3) Jones BA, Novis DA. Follow-up of abnormal gynecologic cytology. A College of American Pathologists Q-Probes study of 16 132 cases from 306 laboratories. *Arch Pathol Lab Med.* 2000;124:665-671
4) Wright, DC, *et al.* 2001 Consensus guidelines for the management of women with cervical cytological abnormalities. *JAMA.* 2002;287:2120-2129
5) Clary KM, *et al*. Cytohistologic discrepancies. A means to improve pathology practice and patient outcomes. *Am J Clin Pathol.* 2002;117:567-573

CYP.07582 Pap Test - False Negative Notification — Phase I

There is a mechanism to educate providers of cervicovaginal specimens that the Pap test is a screening test for cervical cancer with inherent false negative results.

NOTE: The preferred mechanism is an educational note on all negative Pap test reports. Other mechanisms include sending periodic educational information to providers, conference presentations, specimen collection manual, etc.

REFERENCES

1) Robb JA. The Pap smear is a cancer screening test: why not put the screening error rate in the report? *Diagn Cytopathol.* 1993;9:485-486
2) Mitchell, H. Report disclaimers and informed expectations about Papanicolaou smears; an Australian view. *Arch Pathol Lab Med.* 1997;121:327-330

***REVISED** 10/24/2022*

CYP.07600 Statistical Records - Gynecologic Cytopathology **Phase II**

For gynecologic cytopathology cases, statistical records are maintained and evaluated at least annually, and include the following:

- **Total number of gynecologic cytology cases examined**
- **Number of cases reported by diagnosis for each specimen type (including the number reported as unsatisfactory for diagnostic interpretation)**
- **Number of cases with a diagnosis of HSIL, adenocarcinoma, or other malignant neoplasm for which histology results were available for comparison**
- **Number of cases where cytology and histology are discrepant**
- **Number of cases where any rescreen of a normal or negative specimen results in reclassification as low-grade squamous intraepithelial (LSIL), HSIL, adenocarcinoma, or other malignant neoplasms**
- **Number of negative cases rescreened before sign-out.**

NOTE: The data must be evaluated by the laboratory and included in the annual cytopathology statistical report. Inclusion of AGC data is optional. Separate statistics for conventional and each type of liquid-based preparations are required.

The benchmarking data listed in the table below are based on 2019 case volumes. These benchmarking data may not be applicable for laboratories that utilize primary HPV screening for a significant portion of cervical cancer screening. In evaluating its statistics, the laboratory's patient population should be taken into consideration. Percentile-reporting rates refer to the distribution of individual laboratory responses from reporting rates in various categories. Responses are ranked from lowest to highest, and the 50th percentile-reporting rate refers to the median response. A 25th percentile-reporting rate (which corresponds to 1.7% in the table) for the ThinPrep LSIL category means that a quarter of laboratories have LSIL rates of 1.7% or less. A 90th percentile-reporting rate (which corresponds to 15.2% in the table) for ASC-US in ThinPrep preparations means that 9 of 10 laboratories have an ASC-US rate of 15.2% or less.

The reporting rates for ASC-US, ASC-H, AGC, LSIL, HSIL, and UNSATISFACTORY are given as percentages of total case volume. An ASC-US rate of 2.0% means 2/100 cases in the lab are designated ASC-US. The ASC/SIL figure is a calculated ratio: the percentage or number of a laboratory's ASC-US and ASC-H cases divided by the percentage or number of LSIL, HSIL, and malignant cases. A laboratory with 4% ASC cases and 3% SIL cases has an ASC/SIL ratio of 1.3, as compared to the median ASC/SIL ratio of 1.6 for conventional Paps, 1.9 for ThinPrep® and 2.0 for SurePath.

CONVENTIONAL* ***Laboratory Percentile-Reporting Rate***							
CATEGORY	*5th*	*10th*	*25th*	*Median*	*75th*	*90th*	*95th*
Unsatisfactory (%)	*0.0*	*0.1*	*0.2*	*1.1*	*2.9*	*4.4*	*5.0*
LSIL (%)	*0.0*	*0.0*	*0.2*	*0.8*	*1.5*	*2.4*	*3.7*
HSIL (%)	*0.0*	*0.0*	*0.0*	*0.2*	*0.5*	*1.0*	*1.2*
ASC-US (%)	*0.2*	*0.4*	*1.0*	*1.7*	*3.7*	*6.7*	*8.2*
ASC-H (%)	*0.0*	*0.0*	*0.0*	*0.1*	*0.4*	*1.0*	*1.5*
AGC (%)	*0.0*	*0.0*	*0.0*	*0.1*	*0.2*	*0.3*	*0.9*
ASC/SIL	*0.5*	*0.9*	*1.2*	*1.6*	*2.9*	*3.5*	*4.8*

ThinPrep** ***Laboratory Percentile-Reporting Rate***							
CATEGORY	*5th*	*10th*	*25th*	Median	*75th*	*90th*	*95th*
Unsatisfactory (%)	*0.3*	*0.4*	*0.9*	*1.6*	*2.7*	*4.7*	*6.3*
LSIL (%)	*0.5*	*0.9*	*1.7*	*2.4*	*3.4*	*4.5*	*6.0*
HSIL (%)	*0.1*	*0.1*	*0.2*	*0.4*	*0.7*	*1.1*	*1.5*
ASC-US (%)	*1.0*	*2.1*	*3.6*	*5.4*	*7.7*	*10.7*	*15.2*
ASC-H (%)	*0.0*	*0.1*	*0.2*	*0.4*	*0.6*	*1.0*	*1.4*
AGC (%)	*0.0*	*0.0*	*0.1*	*0.2*	*0.4*	*0.7*	*1.0*
ASC/SIL	*0.8*	1.1	*1.4*	*1.9*	*2.6*	*3.4*	*4.5*

SurePath** ***Laboratory Percentile-Reporting Rate***							
CATEGORY	*5th*	*10th*	*25th*	*Median*	*75th*	*90th*	*95th*
Unsatisfactory (%)	*0.0*	*0.0*	*0.1*	*0.3*	*0.7*	*1.2*	*1.6*
LSIL (%)	*0.5*	*0.7*	*1.4*	*2.2*	*3.4*	*5.0*	*6.9*
HSIL (%)	*0.0*	*0.1*	*0.2*	*0.3*	*0.5*	*0.8*	*1.3*
ASC-US (%)	*0.8*	*1.5*	*3.2*	*4.7*	*7.1*	*10.6*	*15.2*
ASC-H (%)	*0.0*	*0.0*	*0.1*	*0.3*	*0.5*	*0.9*	*1.4*
AGC (%)	*0.0*	*0.1*	*0.1*	*0.2*	*0.4*	*0.8*	*1.6*
ASC/SIL	*0.5*	*1.0*	*1.3*	*2.0*	*2.6*	*3.5*	*4.5*

**Includes conventional annual test volume of >60.*

***Includes SurePath and ThinPrep annual test volume of >300.*

Evidence of Compliance:

- ✓ Records of statistical data for defined categories **AND**
- ✓ Records of data review and evaluation against benchmark data by the laboratory director or designee

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):7169 [42CFR493.1274(c)(5)(i) through (c)(5)(vi)]
2) Davey DD, Souers RJ, Goodrich K, Mody DR, Tabbara SO, Booth CN. Bethesda 2014 implementation and human papillomavirus primary screening: practices of laboratories participating in the College of American Pathologists PAP Education Program. *Arch Pathol Lab Med.* 2019;143:1196-1202
3) Genest DR, *et al.* Qualifying the cytologic diagnosis of "atypical squamous cells of undetermined significance" affects the predictive value of a squamous intraepithelial lesion on subsequent biopsy. *Arch Pathol Lab Med.* 1998;122:338-341
4) Raab SS, *et al.* Interobserver variability of a Papanicolaou smear diagnosis of atypical glandular cells of undetermined significance. *Am J Clin Pathol.* 1998;110:653-659
5) Schiffman M, *et al*. HPV DNA testing in cervical cancer screening results for women in a high risk province in Costa Rica. *JAMA*. 2000;283:87-93
6) Solomon D, *et al*. Comparison of three management strategies for patients with ASCUS. *J Natl Cancer Inst.* 2000;93:293-299
7) Juskevicius R, *et al*. An analysis of factors that influence the ASCUS/SIL ratio of pathologists. *Am J Clin Pathol.* 2001;116:331-335

*****REVISED** 10/24/2022***

CYP.07650 Statistical Records - Outliers **Phase I**

If the laboratory's annual ASC/SIL ratio for gynecologic cases falls outside of the 5th or 95th percentiles, the laboratory determines and records the reason(s).

NOTE: The ASC/SIL ratio is useful for interlaboratory comparisons, because the number of ASC and SIL cases varies greatly between laboratories (eg, a private practice with very few HPV

infections, a sexually transmitted disease clinic, and a dysplasia clinic). This ratio is one good indicator for the under- or over-interpretation of ASC.

For example, a laboratory with 9% ASC cases might appear to be over diagnosing ASC, since this is higher than the 75% percentile-reporting rate. However, if this same laboratory also has a SIL rate of 6.0%, the ASC/SIL ratio of 1.5 is close to the national median, and it can be concluded that this laboratory serves a high-risk population. A laboratory with 3.0% ASC cases and 0.75% SIL appears to show average ASC rates, but the ASC/SIL ratio of 4.0 is higher than the average laboratory.

The benchmarking data provided in CYP.07600 may not be applicable for laboratories that utilize primary HPV screening for a significant portion of cervical cancer screening.

CYP.07653 HR-HPV Records **Phase I**

If available, records are maintained for high-risk human papillomavirus (HR-HPV) tests performed on ASC-US including:

1. **Total number of HR-HPV tests performed on ASC-US cases**
2. **Total number of positive HR-HPV ASC-US cases**

NOTE: The percentage of ASC-US cases with a positive HR-HPV result may be a helpful quality metric for both overall laboratory performance and individual performance of pathologists, especially when combined with an individual's ASC-SIL ratio. Data for other HR-HPV testing results (eg, co-testing with a Pap test in women > 30 years of age) may also be helpful quality metrics but should be kept separately.

REFERENCES

1) Wright TC, Massad LS, Dunton CJ, *et al* for the 2006 American Society for Colposcopy and Cervical Pathology-sponsored Consensus Conference. *Am J Ob Gyn* 2007; 346-355
2) Moriarty AT, Schwartz MR, Eversole G, *et a*l. Human Papillomavirus (HPV) Testing and Reporting Rates: Practices of Participants in the College of American Pathologists' Interlaboratory Comparison Program in Gynecologic Cytology in 2006. *Arch Pathol Lab Med.* 2008 132: 12901294
3) Ko V, Shabin N, Tambouret RH, *et al*. Testing for HPV as an Objective Measure for Quality Assurance in Gynecologic Cytology: Positive rates in equivocal and abnormal specimens and comparison with the ASCUS to SIL ratio. *Cancer (Cancer Cytopathol)* 2007;111:67-73
4) Khan MJ, Castle PE, Lorincz AT, *et a*l. The elevated 10 year risk of cervical precancer and cancer in women with human papillomavirus (HPV) type 16 or 18 and the possible utility of type specific HPV testing in clinical practice. *J Natl Cancer Inst* 2005;97:1072-9
5) Cibas ES, Zou KH, Crum CP, *et al*. Using the rate of positive high-risk HPV test results for ASC-US together with the ASC-US/SIL ratio in evaluating the performance of cytopathologists. *Am J Clin Pathol*. 2008;129:97-101

CYP.07655 Screening Performance **Phase II**

The laboratory evaluates and records the ongoing performance of individuals who do cervicovaginal cytology screening against the overall statistics for the laboratory as a whole.

NOTE: Mechanisms can include evaluation of rescreening and interpretive discrepancies and detection rates for abnormalities.

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):7169 [42CFR493.1274(d)(1)(i)(B)]
2) Jones BA, Davey DD. Quality management in gynecologic cytology using interlaboratory comparison. *Arch Pathol Lab Med.* 2000;124:672-681
3) Cibas, ES, *et al*. Quality assurance in gynecologic cytology: the value of cytotechnologist-cytopathologist discrepancy logs. *Am J Clin Pathol.* 2001;115:512-516
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): [42CFR493.1274(c)(6)]
5) Nakhleh RE, Fitzgibbons PL, *eds.* College of American Pathologists. Quality improvement manual in anatomic pathology, second edition. Northfield, IL: CAP, 2002

CYP.07660 Diagnostic Discrepancies/Corrective Action **Phase II**

There are records of each individual's diagnostic discrepancies, and corrective action taken.

REFERENCES

1) Cibas, ES, *et al*. Quality assurance in gynecologic cytology: the value of cytotechnologist-cytopathologist discrepancy logs. *Am J Clin Pathol.* 2001;115:512-516
2) Nakhleh RE, Fitzgibbons PL, *eds.* College of American Pathologists. Quality improvement manual in anatomic pathology, second edition. Northfield, IL: CAP, 2002

NON-GYNECOLOGIC CYTOPATHOLOGY

Inspector Instructions:

READ	• Sampling of non-gynecologic cytopathology policies and procedures • Sampling of patient reports for pathologist review and signature • Statistical reporting policy • Statistical records and annual summary
ASK	• What procedures are in place to prevent cross-contamination during staining? • What is your process for correlating non-gynecologic cytopathology findings with histological and clinical information?

*****NEW** 09/22/2021***

CYP.07666 Unsatisfactory Specimens - Non-gynecologic Cytopathology Phase II

The laboratory follows defined criteria for identification and reporting of unsatisfactory non-gynecologic specimens, as applicable.

NOTE: The cytopathology report must state the reason for an unsatisfactory specimen.

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):7169 [42CFR493.1274(e)(4)]

*****REVISED** 09/22/2021***

CYP.07670 Pathologist Slide and Report Review - Non-gynecologic Cytopathology Phase II

All non-gynecologic slides are reviewed and the reports are signed by a qualified pathologist.

REFERENCES

1) Nakhleh RE, Fitzgibbons PL, *eds.* College of American Pathologists. Quality improvement manual in anatomic pathology, second edition. Northfield, IL: CAP, 2002
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): [42CFR493.1274(e)(3)]

CYP.07675 Correlation of Results - Non-Gynecologic Cytopathology Phase II

Non-gynecologic cytopathology findings are correlated with histological and clinical findings, when appropriate.

NOTE: Correlation of all, or a subset of, non-gynecologic cytology specimens should be performed. Methods of correlation should be recorded in the laboratory procedure manual and selected reports can be reviewed to confirm practice. Possible mechanisms for correlation of histology include correlation of current specimens, focused review of specific specimen/ organ types, and/or follow-up of suspicious/positive specimens. Possible clinical correlation

mechanisms include additional review or testing based on clinical history or physical findings, review of radiologic findings, microbiology, flow cytometry, or other test results. Clinical correlation may be recorded in quality management records, problem logs, or in patient reports. There is a way to easily reference other material results for correlation and/or diagnosis.

Evidence of Compliance:

✓ Records of clinical correlation (eg, quality management records, problem logs, or in patient reports)

REFERENCES

1) Nakhleh RE, Fitzgibbons PL, *eds.* College of American Pathologists. Quality improvement manual in anatomic pathology, second edition. Northfield, IL: CAP, 2002

CYP.07685 Stains - Non-gynecologic Cytopathology **Phase II**

The Papanicolaou stain or another appropriate permanent stain is used for non-gynecologic specimens.

REFERENCES

1) Clinical and Laboratory Standards Institute. *Nongynecological Cytology Specimens; Preexamination, Examination, and Postexamination Processes; Approved Guideline.* 2nd ed. CLSI document GP23-A2. Clinical and Laboratory Standards Institute, Wayne, PA; 2014.

*****REVISED** 09/22/2021***

CYP.07692 Statistical Records - Non-gynecologic Cytopathology **Phase II**

For non-gynecologic cytopathology cases, statistical records are maintained and evaluated at least annually, and include the following:

- **Total number of non-gynecologic cases examined**
- **Number of cases by diagnostic category**
- **Number of unsatisfactory/nondiagnostic cases, as applicable**

NOTE: Sub-categorization of non-gynecologic specimen types (eg, urine, pleural fluid, peritoneal fluid, FNA) is at the discretion of the laboratory.

The definition of "unsatisfactory/nondiagnostic" for non-gynecologic cases must be defined by the laboratory. The specific diagnostic categories (eg, benign, atypical, malignant) are at the discretion of the laboratory. The CAP recommends following established guidelines, where available (eg, The Bethesda System for Reporting Thyroid Cytopathology).

Evidence of Compliance:

✓ Annual statistical records

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):3710 [42CFR493.1274(c)(5)]

PERSONNEL

For laboratories not subject to US regulations, national, state or provincial, and local personnel laws and regulations apply.

Inspector Instructions:

READ

- Section director's/technical supervisor's qualifications and job description
- General supervisor's qualifications and job description
- Cytotechnologist's qualifications and job description

***REVISED** 10/24/2022*

CYP.07700 Section Director/Technical Supervisor **Phase II**

The cytopathology laboratory has a qualified pathologist as the section director/technical supervisor.

NOTE: The section director/technical supervisor of the cytopathology laboratory must be a doctor of medicine or a doctor of osteopathy licensed to practice medicine in the jurisdiction in which the laboratory is located.

For laboratories subject to US regulations, the section director must also be certified in anatomic pathology by the American Board of Pathology or the American Osteopathic Board of Pathology or possess qualifications equivalent to those required for board certification.

If more stringent state or local regulations are in place for supervisory qualifications, including requirements for state licensure, they must be followed.

For laboratories not subject to US regulations, education, experience, and/or certification qualifications must meet or be equivalent to US qualifications or meet, national, state or provincial, or local laws and regulations.

Evidence of Compliance:

✓ Records of section director/technical supervisor qualifications including degree or transcript, certification/registration, 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.* 1992(Feb 28):7179 [42CFR493.1449(k)(1)]

CYP.07800 Non-Supervisory Personnel **Phase II**

All non-supervisory cytotechnologists meet at least one of the following qualifications.

1. **Graduated from a school of cytotechnology accredited by the Commission on Accreditation of Allied Health Education Programs or other organization approved by Health and Human Services (HHS); or**
2. **Certified in cytotechnology by a certification agency approved by HHS (eg, American Society of Clinical Pathology); or**
3. **Before September 1, 1992, have successfully completed two years in an accredited institution (12 semester hours in science, eight of which are in biology) and have 12 months training in an approved school of cytotechnology; or have received six months formal training in an approved school and six months full-time experience; or**
4. **Before September 1, 1992, have achieved a satisfactory grade in an HHS proficiency test for cytotechnologists**
5. **Before September 1, 1994, have two years full-time experience or equivalent within the preceding five years examining slides under the supervision of a physician certified in pathology and before January 1, 1969, be a high school graduate with six months cytotechnology training in a laboratory directed by a physician and completed two years fulltime supervised experience in cytotechnology before 1/1/69; or**

6. **On or before September 1, 1994, have two years full-time experience or equivalent within preceding five years in the US and on or before September 1, 1995, have either graduated from a CAHEA-approved school or be certified as a cytotechnologist**

NOTE: If more stringent state or local regulations are in place for cytotechnologist qualifications, including requirements for state licensure, they must be followed.

For laboratories not subject to US regulations, education, experience, and/or certification qualifications must meet or be equivalent to US qualifications or meet national, state or provincial, or local laws and regulations.

Evidence of Compliance:

✓ Records of qualifications including degree or transcript, certification/registration, 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.* 1992(Feb 28):7182 [42CFR493.1483]
2) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Extension of certain effective dates for clinical laboratory requirements and personnel requirements for cytologists. *Fed Register.* 1994(Dec 6):62608

CYP.07900 Screening Personnel — Phase II

All screening personnel satisfy one or more of the following three criteria.

1. **Pathologist or physician qualified as section director or technical supervisor**
2. **Supervisory level cytotechnologist**
3. **Qualified cytotechnologist**

Evidence of Compliance:

✓ Records of qualifications including degree or transcript, certification/registration, 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.* 1992(Feb 28):7179 [42 CFR493.1449(k)(1)], 7182 [42CFR493.1469, 1483]

CYP.08100 General Supervisor — Phase II

The cytopathology laboratory has a general supervisor who meets the qualifications defined by CLIA (for laboratories subject to US regulations) and other applicable national, federal, state (or provincial), or local laws and regulations.

NOTE: The supervisor can be a pathologist boarded in anatomic pathology. Alternatively, the supervisor can be qualified as a cytotechnologist, with at least three years of full-time experience as a cytotechnologist within the preceding 10 years. The section director/technical supervisor may also serve as the general supervisor

For laboratories not subject to US regulations, appropriate national, state or provincial, or local laws and regulations also apply.

Evidence of Compliance:

✓ Records of qualifications including degree or transcript, certification/registration, 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.* 1992(Feb 28):7182 [42CFR493.1469], [42CFR493.1467]

CYP.08200 General Supervisor Responsibilities — Phase II

The cytopathology general supervisor fulfills defined responsibilities.

NOTE: The general supervisor, as designated by the laboratory/section director, is responsible for day-to-day supervision or oversight of the laboratory operation and personnel performing testing and reporting test results. This individual must also:

1. *Be accessible to provide consultation to resolve technical problems*
2. *Record the slide interpretation results of each case he or she examined or reviewed*
3. *For each 24-hour period, record the total number of slides he/she examined (screened/rescreened) or reviewed, as well as ensuring the recording of the total number of slides evaluated by others*
4. *Record the number of hours he/she spent examining slides in each 24-hour period*

For laboratories not subject to US regulations, appropriate national, state or provincial, or local laws and regulations also apply.

Evidence of Compliance:

✓ Written job description stating the duties of the general supervisor

REFERENCES

1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register.* 1992(Feb 28):7182 [42CFR493.1471]

CYP.08300 Cytotechnologist Responsibilities — Phase II

The cytotechnologist fulfills defined responsibilities.

NOTE: The cytotechnologist is responsible for recording:

1. *The slide interpretation results of each case examined or reviewed*
2. *For each 24-hour period, the total number of slides examined or reviewed in all laboratories*
3. *The number of hours spent examining slides in each 24-hour period*

For laboratories not subject to US regulations, appropriate national, state or provincial, or local laws and regulations also apply.

Evidence of Compliance:

✓ Written job description stating the duties of the cytotechnologist

REFERENCES

1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register.* 1992(Feb 28):7182 [42CFR493.1485]

CYTOLOGY WORKLOAD

Inspector Instructions:

	• Workload reporting policies and procedures • Policy for setting individual workload limits • Sampling of workload recording records for all individuals (cytotechnologists and pathologists) performing primary screening and for automated screening instruments • Sampling of personnel assessments for the setting of workload limits
	• Workload recording practices in screening area, including computerized and manual recording systems
	• What criteria does your laboratory use when evaluating individual cytology workload limits? • Describe your workload recording process • How often are workload recording limits exceeded? • If employees screen slides at other laboratories on days when screening is performed, how is it captured in the laboratory's workload recording? • What type of action is taken when there is a workload violation?
	Select random examples of workload recording logs for each primary screener (pathologists and cytotechnologists) over the previous two-year period • Determine if the records include the number of slides screened and the amount of time spent screening, including slides screened at other laboratories • Confirm that daily workload is counted and calculated correctly • Identify if workload is within the established workload limits for each screener (not to exceed 100 slides/day • For cytotechnologists, confirm that gynecologic (including 10% rescreen and five year look-back cases) and non-gynecologic slides are included If problems are identified with workload violations, further evaluate the laboratory's records to determine if actions taken were effective and consistent with laboratory policy. Select a sampling of automated screening records over the previous two-year period and follow examples requiring a full manual review to evaluate the workload recording.

CYP.08400 Screening Workload - Laboratories Subject to US Regulations **Phase II**

There are sufficient qualified personnel available to handle the volume and variety of cytopathology cases submitted to the laboratory.

NOTE: While federal and state regulations on slide workload limits must never be exceeded, the CAP does not rely solely upon those specific workload limits because: a) the type of case material varies among laboratories; b) the number of cases that may be accurately reviewed by individual screening personnel differs; and c) such personnel may perform other duties. The

Inspector should carefully evaluate these factors together with applicable quality control and quality management data when judging the adequacy of cytopathology laboratory staffing.

Evidence of Compliance:

✓ Records of workload screening for each individual

REFERENCES

1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Medicare, Medicaid and CLIA programs; CLIA fee collection; correction and final rule. *Fed Register.* 2003(Jan 24):5232 [42CFR493.1274(d)]
2) Kline TS. The challenge of quality improvement with the Papanicolaou smear. *Arch Pathol Lab Med.* 1997;121:253-255
3) Mody DR, *et al.* Guest editorial - "workload limits" and CLIA '88 in the 1990's: how much is too much? Or too little? *Diagn Cytopathol.* 1997;16:VII-VIII
4) Cibas, ES, *et al*. Quality assurance in gynecologic cytology: the value of cytotechnologist-cytopathologist discrepancy logs. *Am J Clin Pathol.* 2001;115:512-516
5) Moriarty AT. Cytology workload calculation—Has anything really changed? *Cancer Cytopath.* 2001;119(2):77-79.

CYP.08450 Screening Workload - Laboratories Not Subject to US Regulations Phase II

Each individual screening cytology slides by manual microscopic technique examines no more than 100 gynecologic slides per 24 hours.

NOTE: This checklist requirement applies only to laboratories NOT subject to US regulations. The laboratory must comply with local regulations or laws if more stringent than this requirement.

This maximum workload may be completed in no less than eight hours.

When automated screening instruments are used, laboratories should follow manufacturer's instructions to establish the maximum daily workload. In any case, the total daily workload may not exceed the equivalent of 100 slides undergoing full manual review (or the daily workload limit in the jurisdiction where the laboratory is located, if such limit is fewer than 100 slides).

For purposes of workload limits, gynecologic liquid-based slides must be counted as one slide.

*****REVISED** 09/22/2021***

CYP.08500 Manual Screening - Laboratories Subject to US Regulations Phase II

Workload data are recorded for cytotechnologists and pathologists who manually screen previously unscreened gynecologic and non-gynecologic (including FNA) slides.

NOTE: This checklist requirement applies only to laboratories subject to US regulations. The final rule implementing CLIA requires that each individual evaluating cytology preparations by manual microscopic technique must examine no more than 100 slides (gynecologic and non-gynecologic or both) in 24-hours. In addition, if there are different state regulations for cytology workload, the most stringent regulation must be followed (eg, workload for cytotechnologists manually screening gynecologic smears under a California state laboratory license is limited to 80 gynecologic slides in a 24-hour period, and reduced proportionately based on other duties performed).

Gynecologic slides include new routine slides, 10% rescreen slides, and five-year look-back negative slides. Records must be maintained showing the total number of slides examined by each individual during each 24-hours.

For primary manual screening of non-gynecologic liquid-based slide preparations, each slide may be counted as one-half slide for the purpose of workload recording, provided that cells are dispersed over one-half or less of the total available slide area.

For primary manual screening of all other slide types (including gynecologic liquid-based preparations), each slide must be counted as a single slide for the purpose of workload recording.

The maximum workload can be completed in no less than an eight-hour workday. These total limits apply regardless of the number of laboratories in which an individual works on a given

day. For employees screening less than eight hours at an individual laboratory, this workload maximum must be prorated according to the formula: number of hours spent screening X 100/8.

Pathologists who screen previously unscreened gynecologic slides and previously unscreened non-gynecologic slides (including FNA slides) must adhere to the above workload limit and retain records of compliance.

For all screening personnel, adequacy assessment of fine needle aspiration (FNA) smears or rapid on-site evaluation (ROSE) is not considered primary cytology screening; however, the time spent performing adequacy assessments must be used to prorate the maximum number of slides the individual can screen in a 24-hour period.

The following are not subject to the workload limit for pathologists:

1. *Previously screened reactive/repair, atypical, premalignant and malignant gynecologic slides*
2. *Rescreened five-year look-back slides*
3. *10% rescreen of negative gynecologic slides*
4. *Previously screened non-gynecologic slides*
5. *Previously screened FNA slides*

Evidence of Compliance:

✓ Records of workload recording for each individual

REFERENCES

1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Medicare, Medicaid and CLIA programs; CLIA fee collection; correction and final rule. *Fed Register.* 2003(Jan 24):5232 [42CFR493.1274(d)]
2) Kline TS. The challenge of quality improvement with the Papanicolaou smear. *Arch Pathol Lab Med.* 1997;121:253-255
3) Nakhleh RE, Fitzgibbons PL, *eds.* College of American Pathologists. Quality improvement manual in anatomic pathology, second edition. Northfield, IL: CAP, 2002
4) Moriarty AT. Cytology workload calculation—Has anything really changed? *Cancer Cytopath.* 2001;119(2):77-79.
5) Centers for Medicare and Medicaid Services. *Clarification Regarding Fine Needle Aspiration (FNA) Specimen Adequacy Assessment, Rapid On-Site Evaluation (ROSE) and Workload Limits.* March 16, 2018. Baltimore, M: Department of Health and Human Services; Ref: QSO18-14-CLIA.

CYP.08550 Automated Screening - Laboratories Subject to US Regulations Phase II

If applicable, workload data are recorded for the automated screening of cytology slides.

NOTE: This checklist requirement applies only to laboratories subject to US regulations. Workload calculations may vary with the use of automated screening instruments. Laboratories must assure that CLIA requirements are fulfilled. The following includes information on calculating workload using semi-automated gynecologic cytology screening devices:

- *All slides with full manual review (FMR) count as one slide equivalent (as mandated by CLIA for manual screening)*
- *All slides with field of view (FOV) only review count as 0.5 or 1/2 slide equivalents*
- *Slides with **both** FOV and FMR count as 1.5 or 1-1/2 slide equivalents*
- *These values should be used to count workload, not exceeding the CLIA maximum limit of 100 slides in no less than an eight-hour day*

In addition, if there are different state regulations for cytology workload, the most stringent regulation must be followed (eg, workload for cytotechnologists performing automated and semi-automated gynecologic smears under a California state laboratory license is limited to 100 gynecologic slides in a 24-hour period).

REFERENCES

1) 07/27/10 FDA Alert - How Laboratorians Can Safely Calculate Workload for FDA-Approved Semi-Automated Gynecologic Cytology Screening Devices
2) Crothers BA, Darragh TM, Tambouret RH, et al. Trends in Cervical Cytology Screening and Reporting Practices: Results from the College of American Pathologists 2011 PAP Educational Supplemental Questionnaire. *Arch Pathol Lab Med.* 2016; 140(1):13-21.
3) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Medicare, Medicaid and CLIA programs; CLIA fee collection; correction and final rule. *Fed Register.* 2003(Jan 24):5232 [42CFR493.1274(d),(g)].

***REVISED** 09/22/2021*

CYP.08575 Individual Maximum Workload - Laboratories Subject to US Regulations **Phase II**

Individual maximum workloads are established for cytology slide screening, including processes for reassessment at least every six months and adjustment when necessary.

NOTE: This checklist requirement applies only to laboratories subject to US regulations. The section director (technical supervisor) must establish the maximum workload limit (based on capability/recorded performance evaluation) for each individual who screens slides (including pathologists who screen slides); this maximum workload limit must conform to applicable federal and state regulations.

Performance must be reassessed using the following:

- *Re-evaluation of 10 percent of the cases interpreted to be negative by cytotechnologists*
- *Comparing the cytotechnologist's interpretation in gynecologic specimens with the final cytologic diagnosis*
- *Comparing, in a manner determined by the laboratory, the cytotechnologist's interpretation in non-gynecologic specimens with the final cytologic diagnosis.*

These are minimal requirements and the laboratory may use additional methods of evaluating performance such as retrospective reviews, comparison of individual statistic with overall lab statistics, and competency assessment.

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): [42CFR493.1274(d)(1)]

CYP.08900 Screening Facility **Phase II**

All cytopathology screening is performed within the laboratory facility or an approved referral laboratory.

NOTE: Cytopathology screening must be performed within the laboratory facility or an approved referral laboratory to provide proper access to technical and professional supervision, pathologist consultation and a controlled working environment. For laboratories subject to US regulations, all cytopathology screening must be performed within a CLIA certified facility or equivalent.

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): [42CFR493.1274(a)]

PHYSICAL FACILITIES

Inspector Instructions:

OBSERVE

- Space and utilities are sufficient

CYP.09000 Adequate Space and Utilities **Phase I**

Space and utilities (water, electrical) are sufficient for processing cytologic material and for microscopic screening of slides.

LABORATORY SAFETY

The inspector should review relevant requirements from the Safety section of the Laboratory General Checklist to assure that the Cytopathology laboratory is in compliance. Please elaborate upon the location and the details of each deficiency in the Inspector's Summation Report.

Inspector Instructions:

	• Hazardous waste disposal policy • Sampling of microwave reproducibility and ventilation checks
	• How does your laboratory dispose of infectious specimens and contaminated material?

***REVISED** 10/24/2022*

CYP.09700 Infectious Tissue and Material Disposal **Phase II**

Infectious tissues and other potentially contaminated materials are safely stored and disposed of in compliance with all national, federal, state (or provincial), and local laws and regulations.

REFERENCES
1) Clinical and Laboratory Standards Institute (CLSI). *Clinical Laboratory Waste Management; Approved Guideline—Third Edition*. CLSI document GP05-A3 (ISBN 1-56238-744-8). Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898, USA 2011.

***REVISED** 10/24/2022*

CYP.09910 Microwave Usage **Phase I**

Microwave devices are used in accordance with manufacturer's instructions.

***REVISED** 10/24/2022*

CYP.09920 Microwave Monitoring **Phase I**

Microwave devices are monitored for reproducibility at least annually.

NOTE: Reproducibility is defined as consistency in diagnostic quality obtained from microwave equipment and procedures. For some devices, reproducibility may be evaluated by monitoring the temperatures of identical samples after microwave processing. For those microwave devices (particularly those incorporated into histology processing equipment) that use temperature-independent methods to evaluate reproducibility, the reproducibility must be assessed following instrument manufacturer's instructions.

The microwave device must be tested for radiation leakage if there is visible damage to the device. A description of the specific damage along with the result of the test must be recorded.

Evidence of Compliance:

✓ Records of monitoring the diagnostic quality of specimens processed using microwaves

***REVISED** 10/24/2022*

CYP.09930 Microwave Container Venting **Phase I**

All containers used in microwave devices are vented or are used in compliance with manufacturer's instructions for the microwave instrumentation used.

NOTE: Venting of containers is necessary so that processing occurs at atmospheric pressure, to prevent explosion. For procedures using pressure above that of the atmosphere, specialized containers must be used with strict adherence to manufacturer's instructions.

***REVISED** 10/24/2022*

CYP.09940 Microwave Venting **Phase I**

Microwave devices are properly vented and the effectiveness of ventilation is monitored at least annually.

NOTE: Some types of microwave devices need to be operated in an appropriate ventilation hood to contain airborne chemical contaminants and potentially infectious agents. Before operation of the microwave device, flammable and corrosive reagents must be removed from the hood, to prevent fire or chemical damage to the electronic components of the device. Microwave devices used outside a fume hood must have an integral fume extractor certified by the manufacturer for use in a clinical laboratory.

This checklist item does not apply to microwave devices that are designed by the manufacturer to operate without venting. It also does not apply if only non-hazardous reagents (as defined in the safety data sheets) and non-infectious specimens (eg, paraffin specimens) are used in the device.

Evidence of Compliance:

- ✓ Records of annual evaluation of ventilation effectiveness