The College of American Pathologists' Laboratory Accreditation Program (CAP-LAP) and Digital Pathology

Walter H. Henricks, MD, FCAP, Member, CAP Council on Accreditation

November 2, 2011
CAP Mission Statement

The College of American Pathologists, the leading organization of board-certified pathologists, serves patients, pathologists and the public by fostering and advocating excellence in the practice of pathology and laboratory medicine.
Objectives/Session Outline

• Describe the role of the College of American Pathologists Laboratory Accreditation Program and its role as a deemed laboratory accreditation organization under CLIA

• Describe digital pathology activities that may be subject to laboratory accreditation requirements

• Describe LAP accreditation requirements applicable to digital pathology activities.
CAP: Committed to laboratory improvement worldwide

- Pathologists launch CAP in 1946
- CAP advocates for high-quality, cost-effective patient care
- Community widely recognizes CAP as an international leader in quality assurance and management
  - Introduces first External Quality Assessment (EQA) in 1947 for glucose
  - Offers laboratory accreditation for 50 years, since 1961
  - Provides standards in quality lab and pathology practice
CAP: Extensive reach, impact on laboratory and pathology quality

- Integrates pathology and lab expertise from individuals in academic and community practice:
  - Laboratory Accreditation Program
  - EQA/Proficiency Testing (PT) and Interlaboratory Comparison Programs
  - Education Programs
  - Quality Management Tools
  - SNOMED Terminology Solutions
  - Standard Setting and Guidelines
  - Publications and Public Information
  - CAP Foundation
Today, the CAP’s presence spans the globe

- Works with distributors in select markets throughout the world
- Accredits laboratories in 45 countries
- Provides EQA/PT to laboratories in more than 90 countries
- Headquarters: Chicago, Illinois
- Employs ~600 people with two main offices (Chicago and Washington, DC)
The Laboratory Accreditation Program (LAP) of the College of American Pathologists (CAP) is a CMS-approved accreditation organization under CLIA.

Greater than 6000 laboratories in the U.S. and internationally rely on the CAP-LAP as their CLIA accreditation provider.

The CAP LAP assesses compliance with its Standards for Laboratory Accreditation largely through Checklists of requirements.
Whole Sliding Imaging (WSI)

- **Use of computer technology to convert analog microscopic images into digital images.**
- **Synonyms:** digital imaging, virtual slides, or virtual microscopy
- **Intended uses**
  - Consultation?
  - Education?
  - Primary diagnosis?
  - Quality control?
  - Other?
Agencies Potentially Involved in “Regulation” of WSI

• CMS
  o Enforces CLIA
  o Approves private accrediting organizations

• CAP Laboratory Accreditation Program
  o Functions as CMS-approved private accrediting organization

• FDA
  o Ensures device safety and effectiveness
CAP Entities Involved in Digital Pathology

- **CAP Laboratory Accreditation Program**
  - CMS-approved CLIA accreditation provider
  - Standards for Laboratory Accreditation based on CMS/CLIA requirements, other CAP-initiated requirements
  - Thorough vetting/approval process for new requirements

- **CAP Pathology and Laboratory Quality Center (CAP Center)**
  - Forum to author and maintain evidence-based guidelines and consensus statements
  - Best available evidence and majority expert agreement supported in practice; intended to assist in clinical decision-making and to identify targets for further research
  - Center Workgroup on recommendations for validating WSI
CAP Entities Involved in Digital Pathology (cont’d.)

• CAP Diagnostic Intelligence and Healthcare Information Technology Committee (DIHIT)
  o Development of/input into CAP Checklist requirements
  o Educational content related to digital pathology
CAP Center Recommendations for Validating WSI in Pathology

- Panel members with expertise in use of WSI in pathology
- Literature review and evidence assessment
- Development of 13 recommendation statements
- Public comment period; announcements to interested professional societies
- Evaluation of all comments received and revision of statements as necessary
- Manuscript preparation
CAP Center Recommendations for Validating WSI in Pathology (cont’d.)

• General principles
  o Validation should reflect intended use of WSI
    - Use cases (e.g. frozen section interpretation)
    - Specimen preparation type (e.g. frozen section slides)
  o Pathologist(s) must be involved in validation
  o Intra-observer variability is the key to assess
  o Washout period between WSI and glass review
  o Validation of specific diagnoses not required
CAP LAP Requirements vs. Center Recommendations

- Recommendations from CAP Center are not LAP accreditation requirements.
- LAP Checklists are currently silent on WSI validation.
- Some validation recommendations from the WG may become Checklist requirements, following a proposal and vetting process through the LAP as for all other Checklist requirements.
- Regulatory and other developments in the field will influence the process.
In Telepathology the pathologist:
- Views digitized or analog video or still image(s) AND
- Renders an interpretation that is included in a formal diagnostic report or documented in the patient record

Telepathology modes include:
- Static telepathology
- Dynamic telepathology
- Virtual slides/whole slide imaging
This checklist section applies to:
- Primary diagnoses made by telepathology
- Frozen section diagnoses
- Formal second-opinion consultations
- Ancillary techniques in which the pathologist participates in interpretation of images

This checklist section is NOT applicable to:
- Informal reviews without formal reporting
- Image analysis, in which the image is not interpreted by a pathologist
- Educational or research use of these systems
GEN - Telepathology

• GEN.50057
  o Slide/Image ID Phase II
    - There is a method for the telepathologist to ensure that correct patient identification and slides/images are submitted for review.
    - Can be verbal

• GEN.50614
  o Clinical Information Access Phase I
    - The telepathologist has access to pertinent clinical information at the time of slide/image(s) review.
    - Typically at least requisition-type information
• **GEN.51171**  
  ○ Telepathology Appropriate Use Phase I  
    - The methods and systems in place ensure that the system used for telepathology is appropriate for its intended clinical use.

• **NOTE:** There should be a policy statement in the procedure manual that identifies appropriate and inappropriate use cases

• For instance, for frozen sections only
• GEN.51728
  o Telepathology Training  Phase I
    - The lab has a procedure addressing training requirements for all users of the telepathology system.

• GEN.52842
  o Telepathology and HIPAA  Phase II
    - There are procedures in place to ensure that sites engaging in telepathology provide reasonable confidentiality, security and conformance to HIPAA requirements.
Glass slides that are used for primary diagnosis must be retained for 10 years.

Retention of WSI images is left to the discretion of the Laboratory Director.
CAP Accreditation

• Full Anatomic Pathology checklist (ANP)
  o Includes a Digital Image Analysis section
    − Validation and Calibration
    − Quality Control
    − Specimen Analysis
    − DNA staining
    − Reports
    − Personnel
Checklist Definition:

- Digital image analysis is the computer-assisted detection or quantification of specific features in an image following enhancement and processing of that image, including IHC, DNA analysis, morphometric analysis, and FISH.
- It is not regulation of the imaging of the glass slide.
ANP - Validation and Calibration

- **ANP.23004**
  - **Preanalytic Documentation Phase II**
    - There is documentation that the preanalytic phase of the test system has been validated for each assay, including definition of acceptable specimen preservation, fixation and processing, and definition of how microscopic fields are selected for analysis.

- **NOTE:** Test results may be affected by fixation parameters including time of fixation and the type of fixative used, and by hemorrhage, necrosis, and autolysis of tissue.
ANP - Validation and Calibration

- **ANP.23006**
  - Test System Validation Phase II
    - There is documentation that the analytic phase of each test system has been validated.
  - **NOTE:** Validation must include evaluation of antigen retrieval, antibody sensitivity and specificity, the detection system, and the counter-stain, as applicable to each assay.

- For commercial "closed" systems, the vendor-provided validation information must be verified by the laboratory.
ANP - Validation and Calibration

- **ANP.23009**
  - Calibration Phase II
    - Appropriate slides are used for calibration.
  - Pixel-based systems
  - Object-based systems (e.g. nucleus)
- This requirement does not apply to systems that feature “internal calibration.”
Checklist Definition: Controls are samples that act as surrogates for patient/client specimens. They are periodically processed like a patient/client sample to monitor the ongoing performance of the analytic process.
ANP - Quality Control

- **ANP.23018**
  - Daily QC Phase II
    - Control materials at more than one expression (level) are run at least daily.
  - Controls should verify test performance at relevant decision points. For many tests, a positive and a negative control are sufficient.

- **ANP.23020**
  - QC Handling Phase II
    - Control specimens are tested in the same manner and by the same personnel as patient/client samples.
ANP - Quality Control

• **ANP.23021**
  - **Positive Threshold Level Phase II**
    - A negative control is used to ensure that non-staining areas are scored as negative.

• **ANP.23022**
  - **QC Verification Phase II**
    - The results of controls are verified for acceptability before reporting results.
ANP - Specimen Analysis

- **ANP.23027**
  - Area of Analysis Phase II
    - A qualified pathologist selects the appropriate areas for analysis.

- **ANP.23028**
  - Analysis Guidelines Phase II
    - There are documented guidelines for identification of appropriate areas and cells for analysis.

- **NOTE:** Evaluation of heterogeneous cell populations requires use of specific guidelines and procedures, particularly if there is background or nonspecific staining, or if there is cell debris, endogenous pigment, and/or artifacts of aging, sectioning or preparation.
The final report includes an interpretation by the responsible pathologist.

The final report includes a reference to either the reference (normal) range appropriate for the age and/or clinical status of the patient, or a comment regarding the expected result for the patient and site of the specimen, if applicable.

The final report includes the specimen source, name of the vendor and system used, the antibody clone and source, and the antigen retrieval method, as well as any limitations of the test result.
ANP - Digital Image Analysis - Personnel

- **ANP.23041 Imaging Operator Qualifications Phase II**
  - Personnel who operate the imaging system are qualified as high-complexity testing personnel under CLIA.

- **ANP.23042 Personnel - Technical Operations Phase II**
  - The person in charge of technical operations is qualified to perform high-complexity testing under CLIA, with at least one year's experience in image analysis under a qualified laboratory director.