COLLEGE of AMERICAN PATHOLOGISTS

Remote Sign-Out FAQs

SITUATION

Recognizing the urgency created by the current COVID-19 pandemic, the Centers for Medicare & Medicaid Services (CMS) has exercised enforcement discretion to ensure pathologists may review slides and sign out remotely. On March 26, 2020, CMS temporarily waived the requirement for remote locations to have separate CLIA licenses provided that the designated primary site or primary laboratory has a Clinical Laboratory Improvement Amendments (CLIA) certificate. Details on the CMS announcement can be found here.

Waiving this requirement allows remote sign out of pathology cases using digital pathology or glass slide review. It also includes review of clinical pathology images and data (e.g., electropherograms, gel images, fluorescence in situ hybridization, molecular results, flow cytometry dot plots, blood bank and HLA data). Other types of personnel, such as cytotechnologists, toxicologists and cytogeneticists may also review slides/data/images remotely at a temporary location during this time without obtaining a separate CLIA number. This waiver preserves the continuity of patient care, ensures ongoing quality by getting cases to the appropriate pathologists where subspecialty review is required. It optimizes the safety of pathologists by minimizing their exposure to busy hospitals with a concentration of patients, specimens and surfaces harboring SARS-CoV-2.

This positive outcome for pathologists is directly due to the grassroots advocacy efforts of the College of American Pathologists (CAP) along with other organizations such as the Alliance for Digital Pathology, Association of Pathology Informatics, Digital Pathology Association, American Hospital Association, American Clinical Laboratory Association, Association of Pathology Chairs, and American Society of Clinical Pathology. All were instrumental in making the case for more flexibility from CMS. A key advocacy driver was the white paper authored by the Digital and Computational Pathology Committee (DCPC) and the Informatics Committee (IC) of the CAP which explained the many benefits to the health system of remote work locations for pathologists. This paper was pivotal in persuading Congress to elevate this issue for swift action. The whitepaper can be found here.

In a follow-up to the CMS announcement, members of the DCPC and IC have been asked by the CAP Board of Governors to prepare a frequently asked questions (FAQ) document to guide CAP members who elect to engage in remote sign-out during the COVID-19 crisis. Given the charge of the DCPC and its role in advancing the adoption of digital pathology within the CAP, the use of properly validated whole slide imaging (WSI) systems for remote sign-out of anatomical pathology (AP) cases constitutes a primary focus of this document.

This is a critical time for pathology which is the cornerstone of quality patient care. The COVID-19 pandemic presents a tremendous challenge to laboratories, laboratory personnel, and the pathologists who are on the front lines, especially the labs that conduct SARS-CoV-2 testing. Using properly validated systems at non-CLIA licensed locations affiliated with a primary site that is licensed by CLIA will enable pathologists to continue to provide the most accurate diagnostic, prognostic and predictive information to guide quality patient care. What follows is a living document intended to provide guidance to CAP members on critical issues related to remote sign-out during this emergency. The document is not intended to be prescriptive nor is it all-inclusive. Additional questions will certainly arise as the pandemic continues to unfold. There is an absolute need for institutions implementing remote sign-out policies under emergency circumstances to exercise discretion and to ensure these policies are enacted in the best interest of all stakeholders. The DCPC and IC members thank the CAP members who asked important questions for us to address so far. We also urge readers of this document to provide feedback and raise additional questions. We are all in this together! Feedback can be sent to digpath@cap.org.

The FAQs and their responses are broken down into specific categories including:

1) CLIA '88 requirements concerning remote sign-out by digital pathology, glass slide review and/or review of clinical pathology images and data

2) HIPAA/privacy-related considerations

3) Role of hospital information technology and informatics

4) FDA regulations

5) Medicolegal considerations

6) Diagnostic procedures that could be reported remotely and implications for billing

7) Validation of digital pathology platforms prior to engaging in remote sign-out

8) Standard operating procedures (SOP's) for individual pathology departments.

THE FAQS:

1.CLIA '88:

a. What is "remote sign-out"?

Electronic verification of laboratory test results by qualified personnel under CLIA from a location that is NOT considered part of the main laboratory (e.g., pathologist's home or a hotel

room). In the context of AP, remote sign-out includes the review and diagnostic interpretation of cases by digital pathology (e.g. whole slide image or WSI) or by glass slides and a microscope.

b. What is a remote facility?

A remote facility is NOT within the main laboratory's CLIA address and includes offices where images or data files are reviewed and interpreted with frequency (i.e., recurrent or on a regular basis). These locations can include the pathologist's home or hotel room.

c. In summary, what is required in order to sign-out a case from a remote location under this temporary CMS waiver?

Under this temporary CMS waiver, all remote sign-out activities performed under the umbrella of the laboratory's CLIA license are eligible provided that:

1. The remote location has a designated primary site or primary laboratory with an active and valid CLIA certificate.
2. The specific process, assay and/or application have been validated to be performed remotely with appropriate validation documentation.
3. A procedure has been written and approved by the Medical Director of the designated primary site or primary laboratory with the active and valid CLIA certificate.
4. Personnel signing out remotely have access to all procedures and policies required to perform their remote sign-out duties.
5. The remote location is able to access systems securely under the HIPAA Final Security Rule and related HIPAA regulations. Additional information can be found here.
6. Personnel performing sign-out at such remote locations are able to securely view or store any protected health information (PHI) (e.g., slides, instrument printouts, documents) such that accidental or intentional unauthorized disclosure of PHI is extremely difficult or impossible.

d. During the COVID-19 crisis can I sign-out pathology and laboratory cases from home using digital pathology, glass slides and a microscope or by reviewing other clinical pathology images and data (e.g., electropherograms, gel images, fluorescence in situ hybridization, molecular results, flow cytometry dot plots, blood bank and HLA data)?

Prior to the CMS waiver and discretionary relaxation of CLIA rules, remote sign-out at a non-CLIA licensed location was not permitted. The home office of a pathologist is NOT automatically considered to be an extension of the CLIA-licensed laboratory in which they work. This requirement applies to digital and glass slide review as well as electropherograms, gel images, fluorescence in situ hybridization, molecular results, flow cytometry dot plots, blood bank and HLA data. The current CLIA regulation (pre-COVID-19 crisis), does have a small exception, allowing INFREQUENT sign-out of primary diagnoses or interpretations. The current waiver (COVID-19 era) has no such limit on the percentage or type of cases that can be signed out from a remote location. However, it is a temporary fix and will revert to the current statute when the public health emergency passes.

e. Under the temporary memorandum from CMS, do I need a CLIA-license to electronically sign my cases from a remote site?

CLIA '88 states that a CLIA-license is required at any site where testing is performed including where primary diagnoses and interpretations are rendered. The recent CMS memorandum temporarily waives that requirement during the pandemic provided that the designated primary site has a CLIA certificate. Therefore, it is important to know what the rules are prior to, and after the CMS waiver.

Here are 5 scenarios:

1. A case is dictated by a pathologist at a CLIA-licensed site, and a diagnosis rendered but not verified (i.e., not electronically signed-out). Later, from a remote site, the same pathologist securely logs into the AP lab information system (LIS), reviews the report, and electronically signs it out. Similarly, the pathologist may remotely correct typographical errors in the report and perhaps add results of special stains. In this scenario, the final diagnosis is not changed from what was originally transcribed at the primary site. This activity was permitted even prior to the COVID-19 crisis. The CMS waiver today therefore does not apply because these remote activities do not entail rendering a final diagnosis and thus do not require a CLIA license.
2. A pathologist reviews clinical pathology data from a remote location, renders an interpretation into the LIS via a secure portal/VPN and electronically verifies the interpretation. CMS rules usually require a CLIA license for this activity; however, this activity is now allowed under the temporary waiver.
3. The pathologist renders a primary diagnosis or interpretation of laboratory data from a remote site that already has its own CLIA license. The CMS waiver has no impact on pathologists who have already obtained CLIA certificates for their home or other sites separate from the primary testing site.
4. A pathologist with NO separate CLIA certificate for a home office sets up a microscope at home to allow remote review and sign-out of cases. The cases are delivered to their home as glass slides along with accompanying laboratory requisitions. The pathologist has secure (i.e., HIPAA-compliant) remote access to the APLIS and electronic patient records and can order and interpret any/all ancillary testing procedures required to generate complete diagnoses. The pathologist also has a mechanism for sharing cases with colleagues for purposes of quality assurance when deemed necessary. The review of cases and electronic sign-out all occur from the remote location. Prior to the CMS waiver, such activities could be performed on an INFREQUENT basis. Under the temporary waiver now in place, there is no limit on the number of cases that can be reviewed and signed out remotely.
5. A pathologist with NO separate CLIA certificate for a home office sets up a digital pathology workstation to allow remote review and reporting of cases. The cases will be accessed through an electronic worklist in the APLIS. The pathologist has secure (i.e., HIPAA-compliant) remote access to the APLIS and electronic patient records and can order and interpret any/all ancillary testing procedures required to generate complete diagnoses. The digital pathology system also facilitates sharing of cases with

colleagues for purposes of quality assurance when deemed necessary. The pathologist has a mechanism for deferring cases to glass slide review when deemed necessary. The review of cases and electronic sign-out all occur from the remote location. Prior to the CMS waiver, such activities could be performed on an INFREQUENT basis. Under the temporary waiver now in place, there is no limit on the number of cases that can be reviewed and signed out remotely by digital pathology. However, there is an absolute requirement to validate the digital pathology system prior to using it for remote sign-out (see validation FAQs for more information).

f. I understand that the address of the CLIA-licensed facility must appear on the pathology report. If I sign a case out from home, do I need to put my home address into the report?

The address of the primary CLIA-licensed facility and not the pathologist's remote non-CLIA licensed site needs to appear in the report. CMS requires that the final pathology report lists the physical address of the CLIA-licensed facility. If you have a CLIA license for your home, that home address must appear on the report. However, for sign-out at a remote location that does not have a CLIA license, under this temporary CMS waiver, the physical address of the designated primary site should be listed in order to comply with the requirements above.

g. What is the time frame of the CMS Waiver?

The waiver began on March 26 and will continue as long as CMS deems it appropriate. A specific date for lifting of the waiver has not been defined but most likely will follow shortly after the national emergency is over.

2. Privacy/HIPAA

a. Are there any HIPAA issues with remote sign-out?

While the Office of Civil Rights has extended some enforcement discretion regarding HIPAA for telehealth platforms and for notifying public health agencies about patients who test positive for COVID-19 (see reference at the end of this question), these enforcement discretions do **not** apply to the other aspects of HIPAA. Pathologists must ensure that any data taken or viewed outside of the CLIA-licensed facility for sign-out is protected from accidental or intentional unauthorized disclosure.

HIPAA issues are always a concern but even more so at a remote location that may not have as much security as a hospital office. Care must be taken that patient information on a computer screen, slide labels, paper requisitions, etc., cannot be easily accessed or viewed by unauthorized individuals. The CAP recommends that the remote sign-out location access laboratory information systems and other data with protected health information (PHI) using secure protocols already established by the healthcare organization. For any physical objects containing PHI, such as paper requisition forms, these items must be secured (e.g., under lock

and key) such that it would be extremely difficult or impossible for an unauthorized individual to view them.

Each site must provide reasonable and expected confidentiality and data security in both data storage and data transmission. For example, pathologists should not save patient information such as clinical data, files, or images on their personal computer which might be accessed by non-authorized individuals. The pathologist should also be sure that the network connection used to view data or access a desktop in the main health care facility uses a secure method such as a VPN. The IT support team can help with this implementation. Procedures might include message security, system and user authentication, activity logs, encryption, and access restrictions. With respect to patient identification--as is the case for any laboratory analysis--processes, procedures, and training must be in place to ensure that patient identification linked to glass and digital slides is accurate, maintained, and secure.

Similarly, if a pathology laboratory decides to send glass slides to remote locations for sign-out, the CAP recommends the Laboratory Medical Director work with courier services and pathologists to ensure secure and safe transportation of glass slides from the primary CLIA-licensed facility to the remote location for sign-out and vice versa.

In summary, for the practice of remote sign-out, the same security and privacy requirements of HIPAA apply to both remote and on-site locations. Best practices for security and privacy should be part of the standard operating procedures (SOP) established by the Medical Director of the primary CLIA site. Most organizations already have secure remote access protocols built into a hospital or lab infrastructure so extra steps and more vigilance may need to be taken when working with patient information at a remote site.

Reference:

- FAQs on 2013 Guidelines
- OCR Issues Bulletin on Civil Rights Laws and HIPAA Flexibilities That Apply During the COVID-19 Emergency

3. The Role of Hospital Information Technology (IT) and Informatics in helping Pathology Departments

a. Do you have suggestions for how to work with the hospital IT department when implementing remote sign-out?

It is important to have IT involved at the beginning of contingency planning. The COVID-19 virus has proven to be a fast spreading disease that can severely limit how care is provided, both from overburdening existing healthcare resources and from reducing the healthcare workforce when healthcare staff get sick. The Laboratory Medical Director should work with the IT department to develop HIPAA-compliant policies and procedures for signing out cases from home or other remote locations and should also include policies and procedures for

transcription, billing and other activities which may be performed from home without adversely impacting patient care. These plans would include developing or utilizing already existing secure remote access protocols which are in place in most organizations (e.g., VPN, two-factor authentication). IT can help determine if a pathologist's home computer is adequate to view WSIs (e.g., are the graphic cards good enough to handle these large image files). The Medical Director should gather a list of applications that would be needed for remote sign-out including access to the healthcare organization's electronic health record (EHR), barcode scanners, laboratory data files, laboratory images, digital pathology images, gross photographic images, laboratory policies/procedures and each applicable laboratory information system. IT should ensure all personnel working remotely have access and have successfully set up these applications and have been trained to use them. Proper documentation, user manuals and instructions should be provided. If not already in place, the CAP also recommends that Laboratory Medical Directors work with IT to develop or provide instructions for remote access for other aspects of laboratory activities that may be safely done from a remote location such as transcription, billing, quality reviews, etc.

4. FDA

a. What exactly is an FDA-cleared digital pathology system?

Currently, only two systems have been approved for primary diagnosis - one from Philips and the other from Leica. With respect to FDA terminology, the first of these systems was approved by the FDA based on a successful de novo application as a Class III medical device. Subsequent systems are considered Class II devices which are cleared by the 510(k) pathway.

The FDA considers WSI systems to be made up of basic two subsystems – (i) the image acquisition component, often referred to as the scanner, and (ii) the workstation, or the image viewing software, computer, and monitor/display. The FDA also considers this entire WSI system to be a closed unit. Details on the evolution of the FDA approval/clearance process for WSI can be found here.

b. What does "pixel pipeline" mean?

The pixel pipeline is a term used to illustrate which components comprise a digital pathology system: those that acquire the image, store the image, transform the image, present the image and display the image. As mentioned above, the components of a digital pathology system are the scanner, the server and image management software, the image viewer software, and the display. A digital pathology system must be validated as a whole. If the pixel pipeline is "disrupted" by using, for example, a different monitor than the one approved by the FDA, then the system is no longer in compliance. In other words, if the monitor that the pathologist has at a remote location such as the pathologist's home is different from the one approved by the FDA, then the overall system will not be FDA-cleared. This will not pose a problem as described in the response to the next FAQ.

c. Do I need an FDA-cleared scanner to sign-out cases remotely?

This is a common misconception. An FDA-cleared system is not needed to perform primary diagnosis using digital slides. The FDA oversees how manufacturers market their products, such as the specific intended use cases for the scanner (primary diagnosis, consultations, frozen sections, etc.). The FDA does not regulate the practice of medicine. A pathologist is free to use any microscope or validated digital pathology system to render a diagnosis. For digital pathology systems, the key is to ensure that the system has been validated for its intended use. In the United States, if you validate a non-FDA-cleared system, or validate an FDA-cleared system for a purpose other than its intended use, it would be considered a laboratory-developed test (LDT). It is recommended to validate the digital pathology system as it would be clinically used. The CAP has published validation guidelines for using digital pathology and the Digital Pathology Association has a white paper on the topic. Refer to the validation FAQ below.

d. Does the FDA have rules around remote sign-out?

No. The FDA regulates vendors and the marketing claims they make about their products. The FDA does not regulate health care professionals or medical practice (e.g. pathologists or the practice of pathology.)

5. Medicolegal Considerations:

a. Will I have malpractice insurance if I report cases remotely by digital pathology?

Many healthcare organizations allow secured remote access to the healthcare organization's clinical information systems. You may be covered by the healthcare organization's malpractice insurance when you are functioning in the capacity of the medical staff of your organization. Please follow your healthcare organization's guidance. It is important to emphasize the importance of having the Medical Director for the CLIA site establish a policy / SOP for remote sign-out to legitimize the remote sign out practice from a legal perspective.

Regarding incorrect diagnoses, such errors are always subject to malpractice suits, irrespective of how cases are reviewed. You should check with your malpractice carrier regarding coverage for remote sign-out and/or reading digital slides or data instead of glass slides or instrument printouts.

b. Am I required to save all digital slides and/or data used for remote primary diagnosis, interpretation or consultation during the COVID-19 pandemic?

The CAP recommends the conservative approach of following the existing accreditation guidelines for data retention as well as with applicable national, federal, state (or provincial),

and local laws and regulations. Where specific guidelines for retention of digital/electronic data are not specified, use the same retention strategy as would be used for the physical object. For example, the current CAP requirement is to keep glass slides for 10 years after diagnosis is rendered, so an equivalent approach would be to keep digital slides for the same period of time (10 years). But you do not need to keep both glass and digital images for 10 years. If a diagnosis is rendered with a digital image, it is acceptable to keep only the glass slide for 10 years and discard the digital images. There is only one scenario where a digital image must be retained, that being when the glass slide used to produce the digital image no longer exists (e.g. it was destroyed when tissue was scraped off for molecular analysis, including identity testing). Image retention policies should be developed in consultation with your institution's risk management department.

In another example, retention of clinical pathology data must include the original data to support primary results generated and re-analysis for a minimum of two years per CMS Clinical Laboratory Improvement Amendments (CLIA) Laboratory Guidance During COVID-19 Public Health Emergency Guidance, regulations at 42 CFR §493.1105(a)(7) Slides. Cytology slide preparations must be retained for at least 5 years from the date of examination; Histopathology slides must be retained for at least 10 years from the date of examination; Pathology specimen blocks must be retained for at least 2 years from the date of examination; and Remnants of tissue for pathology examination must be preserved until a diagnosis is made on the specimen.

6. Diagnostic Procedures Done Remotely

a. What constitutes a primary diagnosis in digital pathology?

Primary diagnosis in digital pathology is defined as reviewing digital slides in lieu of glass slides followed by electronic verification of a rendered pathology report (e.g., review of digital images without the use of a microscope and final reporting of the diagnoses). Primary diagnosis is the original diagnosis used for patient care. The FDA does not consider secondary consultations, rapid on-site evaluation (ROSE), or frozen sections read by telepathology under the purview of primary diagnosis. In addition, the analysis of special stains, immunohistochemical stains and other ancillary studies that aid in making a primary diagnosis are not considered primary diagnosis on their own.

b. Can rapid on-site evaluations (ROSE) procedures be done remotely?

Yes, as long as this process and application have been validated to be performed remotely and there is appropriate documentation.

c. Can I read out cytology slides remotely without a CLIA license?

Cytologic diagnoses are considered primary diagnoses by CLIA. This includes pap smears and non-GYN cases. A CLIA-license is needed at the site where the interpretation occurs. The CMS waiver applies and therefore these cases can temporarily be signed out remotely in

locations that do not have a CLIA license provided that the designated primary site or main laboratory does have a CLIA license.

It should be noted that interpretation of WSI scans of cytology cases can be challenging. Most scanners have a maximum magnification of 40x and there is no focusing capability unless z-stacking is performed. This can make interpretation of some cytology cases difficult. Pathologists should always exercise clinical judgment as to the quality of the scans and whether they are adequate for diagnosis. Validation studies must be performed in addition to the ones employed for routine H&E slides. The use of devices with live video microscopy capability may be more suitable for this purpose, provided proper validation has been performed.

Regarding cytotechnologists, they can screen slides at home during this period of waiver. If more than one cytotechnologist is screening cases in the same room, consider complying with social distancing requirements.

d. Can I sign-out intraoperative consultations (frozen sections) remotely?

Yes, as long as this process and application have been validated to be performed remotely (i.e., remote access to a workstation to view and render a diagnosis for an intraoperative frozen section consultation).

There are many different devices that can be used for telepathology for frozen sections, such as robotic microscopes, live video and WSI systems. Each case examined during validation should compare the diagnosis rendered at the time of frozen section using a traditional microscope against the diagnosis rendered when the same frozen section slide is reviewed digitally. The CAP has validation FAQs and published guidelines on the use of WSI for diagnosis. Special validation considerations may be required for using WSI for diagnosis from a remote non-CLIA licensed location.

Reference:

- FAQs on 2013 Guidelines
- Validation guidelines for WSI

e. Can I review immunohistochemistry (IHC) or other special stains using digital pathology from a non-CLIA licensed facility?

Yes, as long as the specific process, assay and/or application have been validated to be performed remotely with appropriate validation documentation (i.e., interpretation of immunohistochemistry). Because IHC and special stain review are not considered “primary diagnosis”, a CLIA license at the remote site is not needed. Validation guidelines for special stains and IHC used in WSI applications are located here.

A final diagnosis is often supported by special stains and IHC. The final diagnosis itself falls under the CLIA licensing requirement.

Image analysis and other IHC quantitative biomarkers that represent more complex testing can be remotely signed out under the temporary CMS waiver provided that the process for viewing and interpreting these cases has been validated.

Reference:

- FAQs on 2013 Guidelines
- CAP HER2 IHC QIA Guidelines

f. Can I review control slides for IHC and special stains remotely?

Yes, as long as the specific process, assay and/or application have been validated to be performed remotely with appropriate validation documentation.

g. Do the same CMS rules apply to clinical pathology activities? What are some examples of clinical pathology remote sign-outs?

Under this temporary CMS waiver, all remote sign-out activities performed under the umbrella of the laboratory's CLIA license are eligible provided that:

1. The remote location has a designated primary site or primary laboratory with an active and valid CLIA certificate.
2. The specific process, assay and/or application have been validated to be performed remotely with appropriate validation documentation.
3. A procedure has been written and approved by the Medical Director of the designated primary site or primary laboratory with the active and valid CLIA certificate.
4. Personnel signing out remotely have remote access to all procedures and policies required to perform their remote sign-out duties.
5. The remote location can access systems securely under the HIPAA Final Security Rule and related HIPAA regulations. Additional information can be found here.
6. Personnel performing sign-outs at such remote locations can securely store any objects containing PHI (e.g., slides, instrument printouts, documents) such that accidental or intentional unauthorized disclosure of PHI is extremely difficult or impossible.

Examples of Clinical Pathology activities which could be remotely signed out if the above criteria are met are shown below. These are only examples and are **not** intended to be a complete list.

- Serum and urine protein electrophoresis
- Hemoglobin electrophoresis
- Next-generation sequencing

- Genotyping assays
- Results of polymerase chain reaction, Sanger sequencing, and other molecular assays
- Karyotyping (banded chromosome analysis)
- Chromogenic in-situ hybridization (ISH) and Fluorescence in-situ hybridization (FISH)
- HLA results
- Blood bank interpretations (e.g., antibody reactions, transfusion reaction workups)
- Microbiology and coagulation assay interpretations.

h. Do I need a special CPT code for digital sign-out?

Currently, there are no specific billing codes for primary diagnosis using digital pathology or remote sign-out and such codes are not needed. The usual surgical pathology CPT codes for primary diagnosis or test interpretation (e.g., 88305, 88307, 81479, 88187, 88360 etc.) can be used. The only codes that are unique to digital pathology are if computer-assisted algorithms are applied when performing quantification of IHC stains: 88361. However, these codes would be the same for sign-out of these procedures whether or not they occurred at a CLIA-licensed facility or, under the temporary CMS waiver, at a remote location.

7. Validation in Advance of Remote Sign-Out

a. Do I need to perform validation for remote sign-out during an emergency situation such as the COVID-19 outbreak?

Validation is critical to ensure that the data, images and other materials that would be used by a pathologist are adequate to render a correct diagnosis or interpretation. With respect to WSI, it is important to note the following:

1. The requirement to validate a WSI system for diagnostic use is not removed for implementation during an emergency situation.
2. No guidelines have been developed to cover fast-tracked validation of WSI systems during emergency situations.

If laboratories have previously validated a digital pathology system for uses such as intraoperative consultations (frozen sections), consultations, or primary diagnosis, it is not necessary (or practical) to perform full validation studies on every single pathologist's home office. Alternately, these laboratories should carry out verification studies using a smaller number of cases prior to engaging in live remote sign-out. The number of cases can be determined at the discretion of the Laboratory Medical Director. It may be prudent for each pathologist intending to sign out remotely to participate in the verification process.

b. What should be considered when performing WSI validation for remote sign-out?

The CAP has previously published a validation guideline for use of WSI for diagnostic purposes (see reference below). As with any guideline, the WSI guideline must be considered in the

proper context. It is a guideline, not a standard of care. The Pathology and Laboratory Quality Center for Evidence-based Guidelines (the Center) of the CAP employs a standard disclaimer in each of its guidelines, including the guideline for WSI validation. Guidelines are intended to assist physicians and patients in clinical decision-making and to identify questions and settings for further research and are continually updated. They cannot account for individual variation and it is the responsibility of treating physicians, relying on independent experience and knowledge, to determine the best course of action according to individual circumstances.

It is also important to note for purposes of laboratory accreditation, the CAP Laboratory Accreditation Program (LAP) has only 2 requirements concerning validation of WSI systems:

1. validation has been performed and approved by the Laboratory Medical Director
2. users of the WSI system have been trained to use the system and the training has been documented.

LAP criteria do not dictate how validation is performed and do not require laboratories to follow the CAP guidelines to the letter. As such, laboratories can use discretion when designing a WSI validation protocol with the aim being to demonstrate a WSI system will perform as expected (i.e., equivalent to glass slides and a microscope) for a specific intended use. The following core elements should be considered:

1. Validation should assess diagnostic concordance between WSI and glass slide review for the same observer, whether the intended use is intraoperative consultation (frozen sections), consultation/second opinion or primary diagnosis.
2. Validation should be based on cases which reasonably represent the spectrum of diagnoses to be encountered during the intended use of WSI for patient care.
3. The number of cases being evaluated should be sufficient to allow pathologists to establish trust in diagnoses made using WSI as well to identify and rectify risks associated with the technology. It must also strike a balance with respect to time required to complete the process. The 60 cases recommended in the CAP guideline is based on systematic review of available peer-reviewed literature and is a suggested minimum number. There is no evidence that adding more cases influences the validation results. The 2018 Royal College of Pathologists Best Practice Recommendations for Implementing Digital Pathology does not mention a specific number of cases, instead stating the sample size and duration of the validation process can vary according to specific circumstances (see reference below).
4. Whether an individual validation case includes all slides and parts associated with a specific accession number or representative parts and slides is left to the discretion of pathologists completing the validation
5. The use of a washout period between WSI and glass slide review is intended to control for the impact of recall bias on validation data. The 2-week washout period in the CAP guideline may be impractical during the urgency of the COVID-19 outbreak. Laboratories should be able to consider washout periods of any duration they might

deem more practical while attempting to control for recall bias. One approach to validate WSI systems on an urgent basis is to use cases that were signed out in the past 2-6 months. Pathologists who originally reported these cases based on glass slides can review the same cases by WSI, removing the need for validation-specific glass slide review and its associated washout period.

6. All discordant diagnoses during validation should be reviewed and reconciled, with a particular emphasis on major discordances affecting patient management. Where major discordances attributable to WSI cannot be rectified, it follows that the use of WSI to review similar cases should be carefully re-considered or deferred to glass slide review.
7. It is important to make sure that all the tissue on a glass slide is present (i.e., ensure it was scanned) on the corresponding WSI. One of the best ways to do this is to check the macro image (not just the thumbnail) of each WSI.

For other assays and activities which do not have specific published guidelines, the Medical Director for the designated primary CLIA-licensed facility must determine (or Medical Director's designee qualified to make such determination) the appropriate level of validation to ensure that the activity can be performed safely and accurately from a remote non-CLIA licensed location.

References:

- "Validating Whole Slide Imaging (WSI) for Diagnostic Purposes in Pathology Guideline"
- FAQs on 2013 Guidelines
- 2018 Best Practice Recommendations for Implementing Digital Pathology
- Visual Memory Effects on Intraoperator Study Design | American Journal of Clinical Pathology
- http://www.jpathinformatics.org/temp/JPatholInform9146-6484336_180043.pdf

c. Do I need to validate the monitor or laptop that I use at the remote location if the digital pathology system is already validated?

The validation study should encompass the entire clinical and reporting pipeline using all components of the digital pathology system as would be used clinically. It is not necessary to validate separately each individual component (e.g., computer hardware, monitor, network, scanner) of the system nor the individual steps of the digital imaging process, but a validated system in the hospital may not be exactly the same as the remote site. For example, the viewing screen may be a laptop display rather than a medical-grade monitor. The bandwidth at the remote site may be different. To account for the variabilities, it would be prudent to verify and document that the system's performance at the remote site is acceptable or document minimum required specifications for use. As mentioned above, pathologists should engage their IT personnel to verify that their home computer is adequate for reviewing WSIs (e.g., the graphic cards are sufficient to handle these large image files). The Laboratory Medical Director must establish criteria for that verification. Individuals performing the remote sign-out must

have been properly trained in the workings of the system. Such validation and training also should be documented.

Reference:

- "Validating Whole Slide Imaging (WSI) for Diagnostic Purposes in Pathology Guideline"

8. Standard Operating Procedures (SOPs) to Enable Remote Sign-Out for primary diagnosis or interpretation in Emergency Situations Such as the COVID-19 Pandemic

a. What basic elements should be present in the SOP?

The basic elements for laboratory procedures and policies are the same as they are for any other laboratory procedure or policy. This would apply to light microscopic as well as digital sign-out. Please refer to the requirements of your laboratory accreditation organization and/or applicable local, state and federal laws.

For all procedures in which the remote sign-out procedure is an adjunct to the usual procedure followed when at the primary CLIA-licensed facility, the most important things to address are any **differences** in process or policy that occur when a case is signed-out at the remote location. If this approach to procedure writing is taken, then the adjunct remote sign-out procedure must reference the procedure for sign-out that occurs at the primary CLIA-licensed facility.

Suggestions for elements to cover in a remote sign-out procedure:

1. Procedure to access necessary laboratory information systems, EHRs, images and other data from the remote location
2. Procedures to transport items with PHI (e.g., slides, documents) between the primary CLIA-licensed laboratory and the remote location
3. Procedures to contacting the laboratory to place orders for additional stains, request repeat testing or request ancillary testing if different from the usual process.
4. Procedures to request intradepartmental consultation along with transport of objects or case images to a different pathologist for review
5. Procedure to sign-out cases, if different from the usual on-site process
6. Ways to issue an addendum or correct the report, if different from the usual on-site process.
7. Reporting of critical values, if different from the usual on-site process
8. Mechanisms for compliance with HIPAA to protect patient confidentiality and privacy should be considered in a setting where family members may be present
9. Recognition that COVID19 can exist on hard surfaces for several hours and may be present on slide tray folders and glass surfaces

10. The importance of chain of custody for all patient materials, establishing a tracking mechanism for slides sent out of the primary CLIA site to a remote site and received back in with appropriate procedures for timely reconciliation of missing patient materials (A barcode system may be of help here)
11. Recognition that the risk for logistic errors is higher during implementation of a new SOP for remote sign out; special care to ensure the correct diagnosis is being reported for the correct patient, that all glass slides have been received and reviewed, and that communication channel between the pathologist and clinical providers is maintained in the remote setting
12. Consideration of documentation somewhere on how and where the primary diagnosis was rendered for auditing purposes; this does not have to be specifically stated on the final report but could be part of the laboratory or anatomic pathology information system.
13. A quality management plan with periodic data analytics to be reviewed by the Medical Director to ensure that remote sign out is not compromising patient care.

b. Does a Laboratory Medical Director need to approve this SOP?

Yes. The individual approving the SOP must be a qualified Laboratory Medical Director for the designated CLIA-licensed primary site or primary laboratory associated with the remote location.

c. If my state has a separate Department of Health, or my laboratory is not CAP accredited, will my validation need their approval?

The laboratory should follow guidance from the respective accreditation body for the primary CLIA-licensed facility. For laboratories accredited by the CAP, the guidance in this FAQ dictates guidance on validation for remote reporting of patient's pathology reports.

d. Are there minimal required specifications for hardware and software for use in remote sign-out?

While there are no definitive established minimum required specifications for hardware or software, remote workstations may have lower specifications (e.g., monitor resolution, contrast, brightness; CPU, network bandwidth, graphic cards) than department configured workstations (may use medical grade monitors, high network bandwidth). Adequate validation of the entire digital pathology system is needed to evaluate performance. Pathologists should use discretion as to whether they have sufficient resources to perform remote sign-out. Pathologists should refer to vendor provided minimum specifications to be used as guidelines for remote hardware and software specifications.

The Department of Pathology in Leeds, UK have developed a point of use quality assurance (POUQA) tool for pathologists to quickly evaluate if their home digital pathology display is good enough. It is freely available here.

e. What are the risks of using digital pathology for remote sign-out

With any technology there exists risks that users should be aware of:

1. Pre-analytical variables of glass slide production affect downstream scanning of the tissue present (e.g., air bubbles, obstructed slide label information, tissue present under coverslips or overhanging the glass slide edge). These may present delays in successful scanning or complete rendering of a patient diagnosis.
2. Depending on the resolution of the WSI, certain diagnoses may be found to be challenging compared to a glass slide (e.g. identification of certain microorganisms such as helicobacter, quantification of mitotic figures, and evaluation of polarized tissue).
3. Users should also be aware of WSI artifacts (e.g. out of focus, tiling/striping, tissue obstruction due to ink, etc.) and should communicate per standard operating procedures to the CLIA-licensed laboratory for remediation. The laboratory should ensure appropriate measures to minimize these artifacts.
4. Tracking is especially important during remote sign-out. It is imperative that all assets (slides/WSIs) leaving the CLIA lab to go to a non-CLIA site are tracking-enabled using barcodes or other logistical systems.

It is important to try and prevent and/or troubleshoot these risks. For example, in the pre-analytical part of the workflow, re-coverslipping a slide may be needed, or a new histology section taken in which the tissue is properly centered. Regarding resolution of the image, scanning at 40x may be better. Artifacts may require rescanning. In all instances, the pathologist should have a very low threshold for re-scans. Finally, it is important to remember that if the digital scan is not adequate, pathologists can always defer to the glass slide.