CLINICAL LABORATORY IMPROVEMENT ADVISORY COMMITTEE (CLIAC)
CLIA REGULATIONS ASSESSMENT WORKGROUP

MEETING SUMMARY REPORT

April 1, 2022 Meeting

1. **At what point in the total testing process should CLIA regulations begin to apply, and where does CLIA coverage of the process end?**
   - How should the CLIA requirements be revised to clarify the laboratory's role and responsibilities for providing consultation for test selection, especially considering emerging technologies?
   - How should the CLIA requirements be revised to clarify the laboratory's role and responsibilities with respect to result interpretation and reporting, especially considering emerging technologies?

   Workgroup Discussion and Comments
   - Any new CLIA requirements should be crafted in such a way as to anticipate technology advancement and changing healthcare environments.
   - Comments on where CLIA should start in the total testing process (TTP):
     - The landscape is changing, laboratories are assisting clinicians in test selection, and algorithms are built to facilitate test selection, with artificial intelligence (AI) playing a role in the future.
     - Several workgroup members agreed that CLIA regulations should begin to apply at the time of request for a review or assistance with test selection. In contrast, others agreed that CLIA should start when a specimen arrives in the laboratory for testing.
     - Laboratories should be responsible for the stewardship of test selection, including the oversight of that laboratory's testing menu and the information regarding the test being performed. The regulations should ensure that the test menu reflects the specimen types that the laboratory has validated.
     - If a laboratory operates its own specimen collecting stations, those would be covered under the overseeing laboratory's CLIA certificate.
     - There may be some opportunity for expansion of CLIA around the pre-analytic assessment of specimen conditions and acceptability.
   - Comments on where CLIA should end in the TTP:
     - It would be difficult for CLIA regulations to cover clinical interpretation and follow-up.
     - The ability to conduct remote telepathology and control how data is handled once it leaves the laboratory makes it difficult to determine where CLIA regulations should end.
     - The testing process goes through reporting, including the data interpretation, even when performed remotely.
     - CLIA should regulate the interpretation of bioinformatics data and variant calling.

2. **Are there definitions included in the CLIA regulations that should be modified or added?**

   Workgroup Discussion and Comments
   - The CLIA Standards and Certification: Laboratory Requirements (42 CFR 493) regulations define a test system as "the instructions and all of the instrumentation, equipment, reagents, and supplies needed to perform an assay or examination and generate test results."
     - The definition should be modified to include the algorithm or software algorithm used to generate a test result.

- Definition of a test system will need to include components that will impact what the physician will use to make the clinical decision.
- When data leaves a laboratory to be analyzed and interpreted at another site, that process should be considered part of the test system.
- Consider adding the term "materials" to the definition of a test system and include a definition of materials in the CLIA regulations.

- The term "materials" is included in several sections of the CLIA Standards and Certification: Laboratory Requirements (42 CFR 493) law and regulations, but a definition is not provided.
  - Revisit the April 2019 CLIAC Nontraditional Testing Workflow Models Workgroup Recommendation that "HHS issue proposed regulations that reflect that the word "materials" in the CLIA-88 definition of a clinical laboratory shall include all data derived from a patient specimen, including images, genetic and protein sequence(s), –omics data, and other data."
  - Consider extending the definition of the term "materials" to be broad to encompass many things, even including a software company that processes, handles, analyzes, and interprets patient laboratory data.
- The term "specimen" is not defined in the CLIA Standards and Certification: Laboratory Requirements (42 CFR 493) regulations.
  - Data, sequencing, and image analysis are all integral parts of the laboratory process, and there may be a need to define these as specimens without impeding current workflows and efficiencies that have been built up over time
- The definition of a "laboratory" or "clinical laboratory" in the CLIA law: "As used in this section, the term ''laboratory'' or ''clinical laboratory'' means a facility for the biological, microbiological, serological, chemical, immuno-hematological, hematological, biophysical, cytological, pathological, or other examination of materials derived from the human body for the purpose of providing information for the diagnosis, prevention, or treatment of any disease or impairment of, or the assessment of the health of, human beings." The term is also included in other sections of the law without a definition provided. Clinical Laboratory Improvement Amendments (42 USC 263a).
  - The definition of a laboratory in the CLIA law includes the statement "materials derived from the human body." The term "derived" can be used to apply to images and data because they are derivations from the materials from the human body.

3. Other Workgroup Discussions

- There is a need to redefine what a laboratory is and if there's an allowance for extensions of laboratories that would encompass those remote analysis sites. The analysis of laboratory data can be performed in almost any setting, so there is a need to determine when the CLIA certificate can be extended to remote data analysis. A suggestion would be that if an employee of a laboratory is working out of their home or at another remote location, then that data analysis and interpretation would be covered through an extension of the home laboratory's CLIA certificate. Under a distributive model where laboratory A does the wet lab work, and laboratory B interprets, those two sites should have separate and distinct CLIA certificates.
- The COVID-19 pandemic brought at-home specimen collection to the forefront. The workgroup agreed that laboratory testing quality begins at the time of specimen collection. Still, it would be very difficult to inspect the front-end process of specimen collection, including at-home or remote, packaging, transportation, patient information validation, etc. There should be more stringent requirements for stability studies both with the vendor and as a confirmation in the laboratory to address the specimen shipment issues.

    - Vendors should perform studies (stability, transportation, etc.) on at-home collected specimens and provide that information as part of the FDA approval process. These studies should include specimen stability.
    - FDA should consider requiring a human adequacy control for detection in a specimen and at-home collection devices and testing systems.
    - Specimen collection devices should have internal controls to ensure sufficient specimen was collected and monitor the specimen's integrity during transportation to the testing laboratory.
- Acceptable VPN and encryption standards based on current standards should be defined in regulatory standards.
    - HIPAA already requires any protected health information (PHI), including genetic information, defined as PHI under the HIPAA Omnibus Rule, to adhere to requirements under the HIPAA Final Security Rule.
- It is becoming rare for data from clinical testing only to be maintained in the laboratory. For instance, almost all high-throughput next generation sequencing (NGS) is processed in the cloud using tools provided by non-CLIA laboratories or companies. The current distributive testing model still does not accommodate software tools in the cloud.
    - Sites that perform informatic analysis on laboratory data should be certified under CLIA. This may require a new type of CLIA laboratory designation beyond Certificate of Compliance or Accreditation.
    - Sites that perform variant interpretation with "variant scientists" are not currently required to be CLIA-certified, resulting in a non-regulated practice by an external entity that may increase patient risk.
    - The process of generating a list of variants requires a significant degree of expertise and is a large component of the test analysis. Not only could a company hide variants from view so that the interpreter has no way of knowing that that variant existed, but they could also generate false positives with inaccurate variant allele fractions if they're not maintaining a list of their artifacts or their consistent false positives. So, even if they may not interpret the significance of those variants, it's still a part of that test.
    - The laboratory is responsible for validating the accuracy of the entire process, whether they outsource a piece to an independent bioinformatic entity or use a bioinformatic tool on site.
    - The vast majority of CLIA Laboratory Directors do not have sufficient knowledge, training, and experience to review laboratory reports involving variant interpretation using NGS technologies. Thus, there is a need for a distributive model to allow for interpretation at sites that should be regulated.
    - Professional certification may be needed for laboratory professionals who sign out reports that include clinical variant interpretations.
    - There is a need for a new class of personnel for the post-analytic analysis of laboratory data or results to accommodate other areas of practice such as NGS, drug screen toxicology, etc. There is no option to identify these types of laboratory personnel or companies performing these services to obtain a CLIA certificate.

May 6, 2022 Meeting

1. **Summary of the previous workgroup meeting (April 1, 2022)**
   Workgroup Discussion and Comments
   - A member commented that another possibility would be an additional specialty to accommodate the post-analytic analysis of laboratory data or results to accommodate other practice areas such as NGS, drug screen toxicology, etc. By adding an additional specialty, you can keep the existing CLIA certificate structure with oversight under a Certificate of Compliance or Certificate of Accreditation without creating a new certificate type.
   - Another member commented on the CLIA regulations' difficulty in covering clinical interpretation and follow-up and suggested additional discussion to define clinical interpretation properly. There is variant interpretation, and then there is result interpretation, and both should be considered separately.
   - Workgroup members noted that laboratory directors might not have sufficient knowledge, training, and experience to review laboratory reports involving variant interpretation using NGS technologies or other emerging technologies.
   - Sites performing informatics and data interpretation should be regulated under CLIA.

2. **Does using robotics in the laboratory impact the quality of testing?**
   - How does CLIA apply to the use of these technologies?
   - What requirements should be added or revised in CLIA to ensure testing quality when robotics is part of the total testing process?

   Workgroup Discussion and Comments
   - Robotics has been a part of the general chemistry laboratory for almost a decade. Using robotics has been shown to improve quality by standardizing repetitive operations.
   - The use of robotics should fall under CLIA because laboratory personnel ensures that the robotic equipment performs as expected through validation and establishment of performance characteristics.
   - Liquid handlers have become a regular part of laboratory operations for SARS-CoV-2 testing and should be covered under CLIA.
   - Robotics is an advanced way to perform specimen movement, handling, extraction, and processing, and all of those processes are currently regulated under CLIA.
   - Laboratories have different types of robotic equipment, from liquid handling to all-encompassing and producing results, such as the Clear Labs instrument that performs DNA extraction, library prep, sequencing, and analysis.

3. **How do technologies that utilize artificial intelligence play a role in the total testing process?**
   - How does CLIA apply to the use of these technologies?
   - What requirements should be added or revised in CLIA to ensure testing quality when artificial intelligence is part of the total testing process?

   Workgroup Discussion and Comments
   - A definition of artificial intelligence (AI) may be needed to determine CLIA applicability.
   - It is essential to understand some of the basics of artificial intelligence to help inform decisions. AI can be developed in different ways. One can develop and train a model, test it, validate it, and then test it, and that model stays static in its use. Another way is to develop a model that incorporates new data and trains itself again in an iterative process. One of those models is consistent with current CLIA regulations, and the other one is not unless you want to undergo continuous revalidation.

- Members agreed that a presentation on the basics of AI would be beneficial to set the stage for discussions. It is also essential to understand how AI differs from a bioinformatics pipeline and where the risks exist.
- Members also agreed that a presentation on the current practice of variant interpretation would be beneficial to continue the discussion on where CLIA regulations should end.

4. If analytical work or data analysis is performed by a contractor, a private company, or a different institution, how should the CLIA regulations apply to the contractor, private company, or other institution?

Workgroup Discussion and Comments

- In most cases, facilities that do not have a molecular pathologist, geneticist, or bioinformatician in-house will send out their bioinformatic pipelines to a different institution.
- Sites that perform informatic analysis on laboratory data should be certified under CLIA. This may require a new type of CLIA laboratory designation beyond Certificate of Compliance or Accreditation.
- The workgroup concurs with the following CLIAC recommendations:
  - November 2019: CLIAC recommends that the CLIA Program consider that when laboratory professionals are providing patient care through the selection, interpretation, and reporting of patient results by accessing data remotely in a secure environment, they shall be deemed as performing those services at the primary site that houses the CLIA Certificate.
  - April 2022: Laboratory practice over the last two years has demonstrated the success of remote analysis and interpretation of digital data securely. CLIAC augments its 2019 recommendation that CMS and the U.S. Department of Health and Human Services permanently codify that a laboratory's CLIA certificate covers employees of that laboratory who are performing data analysis and interpretation of digital information under the quality oversight from a primary site when working remotely under the home laboratory's CLIA certificate.

5. Data as a Specimen

- How does "data" fit into the total testing process as a specimen, especially when handed off to other entities for processing, analysis, or interpretation?
- If data were considered a specimen, what parts of CLIA would need to be updated, including additional terminology to be defined?
- If data were to be considered a specimen, which types of data analysis (or "activity involving such data" from the CLIAC recommendation) should be considered a "test system" or otherwise regulated under CLIA?
- Does the determination of whether data analysis is a separate "test system" depend on whether the entity conducting the analysis differs from the laboratory that performed the testing that generated the data?
- Which activity involving data (provided that the activity is related to the diagnosis, prevention, or treatment of disease or impairment of, or the assessment of, the health of human beings) would need to be performed under a CLIA certificate?

Workgroup Discussion and Comments

- One member commented on outside data coming to a laboratory, such as at-home COVID-19 or glucometer results, and if that is regulated under CLIA and when it should be included in the medical record. It is hard to determine the authenticity and quality of these results for inclusion in the laboratory report.

- A member added that the Office of the National Coordinator for Health IT (ONC) is a venue to discuss at-home testing results and inclusion in the electronic health record (EHR). Including patient-generated results in an EHR is happening, but there is an appropriate way to label those results.
- A member noted that if data is considered a specimen, then sites that perform informatic analysis on laboratory data would fall under CLIA.
- Members agreed that the CLIA definition of a laboratory includes the terminology "materials derived from the human body" and that "derived" could apply to images and data because they are a derivation of material from the human body. It would be beneficial to have examples of the types of data currently transferred in laboratory testing.
- The workgroup members concurred with the April 2019 recommendations:
    - Any site that performs an activity that involves such data (provided that the activity is related to the diagnosis, prevention, or treatment of any disease or impairment of, or the assessment of, the health of human beings) shall be considered a "laboratory," if that site is not an extension of an existing CLIA-certified laboratory."
    - HHS issue proposed regulations that reflect that the word "materials" in the CLIA-88 definition of a clinical laboratory shall include all data derived from a patient specimen, including images, genetic and protein sequence(s), –omics data, and other data.
    - The CLIA Program considers that when laboratory professionals provide patient care through the selection, interpretation, and reporting of patient results by accessing data remotely in a secure environment, they shall be deemed as performing those services at the primary site that houses the CLIA Certificate.
- Several members commented on the need for proficiency testing (PT) to extend beyond the laboratory to assess the total testing process, especially with data transfer for analysis at another facility. The members agreed with the April 2019 CLIAC recommendation that HHS develop guidance to allow distributive PT models, including analytes currently subject to CLIA-required PT, to assure quality across the whole testing cycle.
- There is a need to redefine what a laboratory is and if there's an allowance for extensions of laboratories that would encompass those remote analysis sites. The analysis of laboratory data can be performed in almost any setting, so there is a need to determine when the CLIA certificate can be extended to remote data analysis.

June 3, 2022 Meeting

1. **Summary of the previous workgroup meeting (May 6, 2022)**
   Workgroup Discussion and Comments
   - The workgroup chairs provided an overview of the current workgroup agreements.
   - One member commented on the need to demonstrate testing proficiency before offering the test to the public.
   - The workgroup chairs provided an overview of the workgroup agreement process and presentation to CLIAC for deliberation.

2. **Testing Process Review – Artificial Intelligence (AI) Presentation and Discussion (Presentation provided by Dr. Alexis Carter)**
   - How do technologies that utilize artificial intelligence play a role in the total testing process?
     - How does CLIA apply to the use of these technologies?
     - What requirements should be added or revised in CLIA to ensure the quality of testing when artificial intelligence is part of the total testing process?

   Workgroup Discussion and Comments
   - There are certain principles on how to develop your AI model correctly and then verify performance. There may be a need for laboratories to have guidelines to assist in troubleshooting when the algorithm produces spurious data or when problems are detected with vendor-developed AI algorithms.
   - There is a need for CLIA to have definitions around personnel, such as a data scientist who looks at and helps mitigate issues with these algorithms.
   - AI performance algorithms can change over time due to shifts in population, shifts over time in the health of the general population or race, and ethnicity variations over time. In applying the current CLIA framework, there should be a verification process at the algorithm launch. There should also be a way to identify a shift and drift over time to determine when a reverification frequency on the patient population of that institution is needed.
   - For laboratory-developed machine learning algorithms, CLIA regulations should focus on how the algorithm was developed with defined criteria around how it was designed and the population used to create it. Also, proficiency testing (PT) is needed for that algorithm to prove that it achieves the correct answer.
   - Some checklists provide a list of requirements for developing a machine learning algorithm, but many focus on using accurate data at the onset. It is essential to clearly define the population and train the algorithm using good, quality data representative of the population.
   - Both laboratory-developed and FDA-cleared algorithms should be monitored, and discrepancies should be reported to the manufacturer and investigated in the laboratory. In some cases, the algorithm is retrained, and a new version is developed based on the provided updated training and data.
   - There is a need for guidance on validating algorithms to assure quality for static and adaptive algorithms.
   - Static algorithms should be used for laboratory testing. If the algorithm needs to be updated, re-verification and re-validation are required to ensure patient safety, similar to the practice used for bioinformatic pipelines.
   - CLIA could define QC and PT requirements for continuously improving algorithms.

3. **Total Testing Process Review and Data as a Specimen – The Practice of Variant Interpretation/Classification Presentation and Discussion (Presentation provided by Dr. Birgit Funke)**
   - How should the CLIA requirements be revised to clarify the laboratory's role and responsibilities with respect to result interpretation and reporting, especially considering emerging technologies?
   - Which activity involving data (provided that the activity is related to the diagnosis, prevention, or treatment of disease or impairment of, or the assessment of, the health of human beings) would need to be performed under a CLIA certificate?

Workgroup Discussion and Comments

- The personnel performing variant classification in laboratories include MD pathologists, PhD geneticists, and genetic counselors with additional training in laboratory genetics. The personnel performing variant classification should have documented expertise in human genetics and the ability to understand the published evidence.
- There are specific requirements needed for the variant scientists that work in the oncology setting, and there is a need for specific expertise depending on the genetics area. These requirements may not need to be as stringent for infectious disease testing, where personnel shortages are a challenge.
- New professional roles have emerged since the CLIA regulations were implemented, and there is a need to define these roles and their associated training and competency. The workgroup should define these roles and discuss educational, training, and competency requirements for testing personnel such as bioinformaticians and variant scientists.
- The CAP provides a molecular checklist with requirements beyond the CLIA requirements. These checklists could be helpful to use as a starting point for workgroup discussions.
- The current personnel requirements for high-complexity Technical Supervisors for transfusion medicine, histocompatibility, and anatomic pathology are more stringent. The workgroup could use those requirements as a guide to personnel discussions.
- The workgroup should look at the broad laboratory environment to determine the need to revise the current CLIA requirements.
- CLIA should regulate all steps of the testing process for variant classification that represent objective data gathering and application of rules. Laboratories must document their policies and procedures for the discipline of variant classification.

August 5, 2022 Meeting

1. **Summary of the previous workgroup meeting (June 3, 2022)**
   Workgroup Discussion and Comments
   - The workgroup chairs provided a summary from the June 3, 2022 meeting and an overview of the current workgroup agreements.
   - It is important to consider if the CLIA personnel requirements need to be modified to include data as a specimen as related to the transmittal and receiving of data. When a pathologist uses the data to make a clinical decision, that falls into the practice of medicine.

2. **Digital Pathology**
   - What changes should be made to current CLIA requirements to ensure the quality of digital pathology (e.g., microbiology, molecular, histopathology, cytology) or any testing process that involves a digital image when parts of the process may be performed in the same laboratory or in separate facilities or locations?
     - How should a laboratory validate a whole slide digital imaging system for diagnostic purposes before it is placed in clinical service? This includes the process, concordance rate, and the number of cases for review.
     - What should CLIA require for digital images to ensure proper specimen identification and integrity?
     - What should CLIA require for quality control of digital images and the digital pathology process?
     - Are current CLIA requirements for record retention applicable to digital images, or how should they be modified?
     - Should information retrieved during the conversion of the slide to a digital image be saved as data? Is it part of the total testing process?
     - What should CLIA require for personnel and competency assessments for staff performing digital pathology, including pathologist competency and staff (e.g., image technician, cytotechnologist, histotechnologist, physician assistants, information technology personnel, and/or consultants)?
     - Who should be responsible for each distinct part of the remote analysis process?
     - Does a laboratory's CLIA certificate cover the pathologist when using a VPN to review and report cases remotely?
   - How does a laboratory ensure patient confidentiality and the accurate electronic transfer and submission of patient data from one testing location to another protected under CLIA regulations?
   - How should the current CLIA requirements be revised to ensure information technology (IT) security and encryption, especially when test interpretation is performed off-site?
   - What are the advantages and disadvantages of allowing the remote review of histopathology slides, as permitted during the COVID-19 public health emergency?
     - How should CLIA be revised to ensure the quality, reliability, accuracy, and timeliness of test results if these CLIA flexibilities were permanently incorporated into the regulations?
     - What specialties and subspecialties, in addition to cytology have the potential for remote analysis and should be considered if this flexibility was made permanent?

   Workgroup Discussion and Comments
   - CAP published the following:
     - Validating whole slide imaging for diagnostic purposes in pathology: guideline from the College of American Pathologists Pathology and Laboratory Quality Center in 2013.
     - Validating Whole Slide Imaging Systems for Diagnostic Purposes in Pathology: Guideline Update From the College of American Pathologists in Collaboration With the American Society for Clinical Pathology and the Association for Pathology Informatics in 2022.

- There should be clear, separate verification, validation, and training requirements. Many times, laboratories will group these three together when working with a vendor to onboard a test system.
- Laboratories should have a quality assurance (QA) program to monitor the entire workflow.
- Quality control (QC) applies to some areas of digital pathology. For example, in quantitative image analysis using algorithms, there is an assumption that the algorithm is always correct. By requiring QC steps, the laboratory can identify problem areas. The overall QA program would dictate which QC is required for each application.
- Part of a QC check also ensures that the images are scanned with appropriate resolution, quality, and color. Vendors do not offer tools for this QC step when using a whole slide scanner.
- One challenge with whole slide imaging is when there is a small piece of detached cancer on a slide outside of the image detection algorithm, and it does not get scanned. The vendors do not offer technology to identify those areas with an alert or for the laboratories to know the right image to look at, the macro image, thumbnail, etc.
- When developing requirements for digital pathology, there needs to be an understanding that laboratories will have difficulty meeting the requirements if there are no processes or the technology is unavailable from vendors.
- Pathology assistants should be included in the personnel and competency discussions.
- CLIA cytology control regulations at §493.1274(c)(3) state that for each patient with a current HSIL, adenocarcinoma, or other malignant neoplasms, a laboratory review of all normal or negative gynecologic specimens received within the previous five years, if available in the laboratory (either on-site or in storage). If significant discrepancies are found that will affect current patient care, the laboratory must notify the patient's physician and issue an amended report. Digital imaging with AI complicates this requirement. For instance, are the slides scanned again, and is the AI algorithm re-run? What if it analyzes completely different cells? Or do you leave the original AI scan of the case and utilize a different cytologist to look at the results of the previous AI algorithm? Is the control for the cytologist or the AI system?
- Possible solutions to ensure quality include modular proficiency testing to monitor the AI pathway.
- Many digital pathology systems, including FDA-approved systems, are not compliant with HIPAA Final Security regulations, putting laboratories in a difficult position if the system is not compliant with federal regulations.
- Laboratories should have a policy/procedure to ensure specimen integrity throughout the analytical process.
- The bioinformatics pipeline validation guideline for patient identification requires four different identifiers for the specimen, the run, and the patient. More prescriptive CLIA requirements would force vendors to comply with the requirements from the laboratories. Any time a device is going to be storing data on a specimen, whether that's the pipeline, digital image, etc., the device needs to be able to store some unique identifier about the scan or the run, in the case of NGS or the assay. Because a single sample could be analyzed multiple times. There should be an identifier for the actual specimen and then something for the patient.
- CAP specifies that digital images for diagnosis must be retained for ten years if original glass slides are unavailable. There is no retention requirement for images of glass slide preparations when the source slides remain readable for the required retention period. See CAP's Anatomic Pathology Checklist, ANP.12500-Record, and Material Retention - Surgical Pathology.
- Storing digital images is an extensive part of the laboratory process and may require a large portion of the budget devoted to data storage.
- One member added that frozen slides must be retained when storing images for telepathology. Another member noted that many frozen sections are being done using robotic microscopy, and

nothing is saved. There may need to be different requirements for whole slide imaging versus live images and the specimen type.

- Some retention factors were addressed in the American Telemedicine Association clinical guidelines for telepathology publication.
- A suggestion was made that a laboratory should have a retention policy that defines the length of time and what they store. This allows CLIA to be broad and enables the laboratories to have the flexibility to design their retention policy.
- There may be a need to address image technicians as a CLIA personnel category.
- The National Society for Histotechnology, in collaboration with the Digital Pathology Association, developed the Digital Pathology Certificate Program. It is an online, self-paced certificate program to increase competency and improve knowledge in whole slide imaging and digital pathology to meet the educational needs of the growing community of individuals involved with and utilizing this technology.
- CLIA should have personnel and competency assessment requirements for staff performing digital pathology. Competency assessment needs to cover familiarity with the technology and the use of the new technology. CAP's Anatomic Pathology Checklist, ANP.10010-Professional Competency, states that the laboratory director ensures the professional competency of pathologists who provide interpretive services to the anatomic pathology laboratory. The mechanism for competency assessment must be pertinent to the type of interpretive services provided (e.g., general anatomic, neuropathology, renal pathology, forensic pathology). There must be a written policy for assessing professional competency at defined intervals, criteria for the assessment, and records of the assessment must demonstrate review by the laboratory director.
- If a laboratory uses a VPN to a site, the main laboratory's CLIA certificate is responsible for the quality, analysis, and QA/QC of the entire remote analytical process.
- The CLIA regulations should include references to the HIPAA final security rule or the HIPAA regulations. This requirement could go a long way to helping laboratories tell vendors that their systems need to be compliant. There are issues with digital imaging systems that are outdated and no longer supported by Microsoft. The vendors are not responsible for being data entry points for ransomware or malware. Also, the internal security team will turn off systems without notice if they are determined to pose a risk. This could be critical if the system is being used for patient testing.
- The HIPAA Security Rule establishes national standards to protect individuals' electronic personal health information that is created, received, used, or maintained by a covered entity. The Security Rule requires appropriate administrative, physical and technical safeguards to ensure the confidentiality, integrity, and security of electronically protected health information. Any data transfer must adhere to the HIPAA Security Rule, and bioinformatic companies must have a CLIA certificate and adhere to the HIPAA Security Rule.
- A list of references for HIPAA:
    - Privacy and security of patient data in the pathology laboratory
    - Considerations for Genomic Data Privacy and Security when Working in the Cloud
    - Guidance on HIPAA & Cloud Computing
- The medical director is responsible for ensuring that pathologists are privileged to practice at the site where you send tests. The Medical Director of the site you practice under is ultimately responsible even when referring the specimen.

October 7, 2022 Meeting

The workgroup reviewed the current list of workgroup agreements and refined them in preparation for the November 9-10, 2022 workgroup report and CLIAC discussion.

Workgroup Agreements (Ongoing List)

- Sites performing informatics and data interpretation should be regulated under CLIA.
- Sites that perform informatic analysis on laboratory data should be certified under CLIA. This may require a new type of CLIA laboratory designation beyond Certificate of Compliance or Accreditation.
- The CLIA definition of a laboratory includes the terminology "materials derived from the human body," and that "derived" could apply to images and data because they are a derivation of material from the human body. It would be beneficial to have examples of the types of data currently transferred in laboratory testing.
- If a laboratory employee works out of their home or at another remote location performing duties such as data analysis and interpretation associated with that laboratory, then that would be covered through an extension of that laboratory's CLIA certificate.
- Under a distributive model where a laboratory performs the wet laboratory work, and another separate entity performs the data analysis and/or interpretation, those two sites should have separate and distinct CLIA certificates, and proficiency testing should be required for both locations.
- The COVID-19 pandemic brought at-home specimen collection to the forefront. The workgroup agreed that laboratory testing quality begins during specimen collection. Still, it would be very difficult to inspect the front-end process of specimen collection, including at-home or remote, packaging, transportation, patient information validation, etc. There should be more stringent requirements for stability studies both with the vendor and as a confirmation in the laboratory to address the specimen shipment issues.
    - Vendors should perform studies (stability, transportation, etc.) on at-home collected specimens and provide that information as part of the FDA approval process. These studies should include specimen stability.
    - FDA should consider requiring a human adequacy control for detection in a specimen and at-home collection and testing.
    - Specimen collection devices should have internal controls to ensure sufficient specimen was collected and monitor the specimen's integrity during transportation to the testing laboratory.
    - Laboratories that choose to use a home collection device that has not been cleared for use by the FDA will need to submit that device for FDA review and approval.
    - Laboratories must have policies in place to accept and reject specimens collected outside of their laboratory, including home-collected specimens. If the laboratory chooses to test a specimen that falls outside of the collection device's manufacturer's instructions, then the laboratory will need to provide performance studies to validate that modification.
- Workgroup members agree that CLIA should broadly define new personnel roles, such as the personnel performing activities such as bioinformatic data analysis, variant classification, variant analysis for patient care, etc. (variant scientists).
- There is a need to consider an additional specialty to accommodate the post-analytic analysis of laboratory data or results to accommodate other practice areas such as NGS, drug screen toxicology, etc. By adding an additional specialty, you can keep the existing CLIA certificate structure with oversight under a Certificate of Compliance or Certificate of Accreditation without creating a new certificate type.
- The use of robotics should fall under CLIA because laboratory personnel must ensure that the robotic equipment performs as expected through validation and establishment of performance characteristics.

- The workgroup concurs with the following CLIAC recommendations:
  - April 2019: Any site that performs an activity that involves such data (provided that the activity is related to the diagnosis, prevention, or treatment of any disease or impairment of, or the assessment of, the health of human beings) shall be considered a "laboratory," if that site is not an extension of an existing CLIA-certified laboratory."
  - April 2019: HHS issue proposed regulations that reflect that the word "materials" in the CLIA-88 definition of a clinical laboratory shall include all data derived from a patient specimen, including images, genetic and protein sequence(s), –omics data, and other data.
  - April 2019: HHS develop guidance to allow distributive proficiency testing (PT) models, including analytes that are currently subject to CLIA-required PT, to assure quality across the whole testing cycle.
  - November 2019: CLIAC recommends that the CLIA Program consider that when laboratory professionals are providing patient care through the selection, interpretation, and reporting of patient results by accessing data remotely in a secure environment, they shall be deemed as performing those services at the primary site that houses the CLIA Certificate.
  - April 2022: Laboratory practice over the last two years has demonstrated the success of remote analysis and interpretation of digital data securely. CLIAC augments its 2019 recommendation that CMS and the U.S. Department of Health and Human Services permanently codify that a laboratory's CLIA certificate covers employees of that laboratory who are performing data analysis and interpretation of digital information under the quality oversight from a primary site when working remotely under the home laboratory's CLIA certificate.
- For any digital data, laboratories should have a policy/procedure to ensure specimen integrity throughout the analytical process.
- Any device storing data should require an identification number for the image, a patient identifier, and an institutional identifier.
- Laboratories must implement software and devices compliant with the applicable components of the HIPAA Final Security Rule. In addition, laboratories must ensure that implemented devices do not pose a significant risk to the safety and security of the patient data that the laboratory stores, manages, creates, or analyzes.
- CLIA should require training and competency assessments for staff such as pathology assistants, image technicians, cytotechnologists, and histotechnologists performing digital pathology.
- A laboratory's CLIA certificate covers the qualified laboratory personnel when using a VPN to review and report cases remotely.
- If an entity is manipulating information, performing data analysis, etc., received from a clinical laboratory and returning it to the laboratory for inclusion in the patient report or for patient care, that entity needs to have the appropriate CLIA certificate. Under that CLIA certificate, they are subject to the same patient confidentiality and requirements as the referring laboratory.
- The CLIA regulations should be revised to allow remote analysis for any CLIA specialty or subspecialty.