# Statement to the
# Clinical Laboratory Improvements Advisory Committee
# on the
# CLIA Regulations Assessment Workgroup

The College of American Pathologists (CAP) appreciates the opportunity to provide written comments to the Clinical Laboratory Improvement Advisory Committee (CLIAC) on the **Clinical Laboratory Improvements Amendments of 1988 (CLIA) Regulations Assessment Workgroup Report.** As the world's largest organization of board-certified pathologists and leading provider of laboratory accreditation and proficiency testing programs, the CAP serves patients, pathologists, and the public by fostering and advocating excellence in the practice of pathology and laboratory medicine worldwide.

With the rapid changes in technology and integration of the health care delivery system, clinical laboratories are no longer just stand-alone sites but are an integral part of the health systems, which includes at least one hospital and at least one group of physicians providing comprehensive care (including primary and specialty care) that connect with one another and the hospital through common ownership or joint management. Moreover, these health care systems are using advances in technology to perform clinical laboratory testing in a myriad of settings that are closer to the patients. **CLIA provides an adequate baseline to ensure the accuracy and reliability of clinical laboratory results, but we recognize that specific updates to CLIA are needed to address and accommodate the changes in practice and technology.** Hence, the CAP offers the following comments on developing policies and/or guidance for bioinformatic and emerging technologies.

**Total testing process**

Distributive testing occurs when clinical laboratory testing is performed on a specimen, or an aliquot thereof, and requires sharing it between two or more laboratories to obtain the necessary data in order to complete an interpretation or calculation necessary and provide a final test result. When such testing occurs at multiple locations with different CLIA certificates, it is considered distributive.[1] The CAP supports distributive testing models being regulated under CLIA. Specifically, clinical laboratories should perform proficiency testing (PT) by observing the same process that they do for patient samples, including moving samples among multiple sites to complete all aspects of testing. Doing so should not constitute intent to commit proficiency testing referral.

PT is an important quality metric in determining clinical laboratory testing accuracy and reliability. As we have testified previously, the CAP launched in 2015 PT for NGS where laboratories can test up to 200 variants in a method-based challenge using either gene panels, exome, and/or whole genome sequencing. The initial NGS PT program, designed to assess the ability of laboratories to detect germline variants, was followed by NGS PT for the detection of somatic variants and other NGS clinical testing applications. The programs can test "wet" and "dry" bench components of NGS testing. Under the current regulatory paradigm, clinical laboratories are unable to test the entire system if portion of the test is performed in a "distributive testing model"

[1] (https://www.lawinsider.com/dictionary/distributive-testing)

such as bioinformatics and cloud-based software computing. This makes it difficult to assess the complete process (pre-analytic, analytic, and post-analytic) and is an insufficient quality indicator.

**Data as a specimen**

The CAP supports data being defined as a specimen under CLIA. With the increasing penetration of high-throughput data generating techniques such as next-generation sequencing and personalized medicine and emergence of new technology such as whole slide imaging, clinical laboratory data are common tools to support laboratory medicine practice. These data can be generated outside of the clinical laboratory but contribute to the laboratory results reported to the patient. Inclusion of regulatory requirements within CLIA will ensure data generation activities ensure accurate and reliable results are reported to patients. As a minimum requirement, proprietary or complex algorithms (including bioinformatics) used in the generation of a test result are analytical components of high complexity clinical laboratory testing and should be subject to the requirements of CLIA. In addition, there should be personnel requirements for those responsible for data generation activities, record retention requirements for data files, and software maintenance requirements. As previously mentioned, PT should be required and handled with the same good laboratory practices as performed for other patient samples, including moving samples among multiple sites to complete all aspects of testing.

**Analytical Testing Specifications**

The CAP supports the inclusion of analytical performance specification requirements to accommodate next generation sequencing (NGS). Since publishing our first NGS specific checklist for laboratory accreditation in 2012, we have continuously worked to improve and update the checklist to reflect advances in NGS technology and the ever-growing diversity of clinical applications to which NGS is being applied. The CAP continually revises the NGS checklist items to add recommended metrics and quality control parameters for this dynamic field including the stand-alone bioinformatics facilities. It is important that a proprietary or complex algorithm (including bioinformatics) used in the generation of a test result has oversight since it is an analytical component of high complexity influencing clinical laboratory testing results. **As such, CLIA certification should be required of any organization performing portions of the testing process, including application of proprietary or complex algorithmic interpretations of a clinical laboratory test that generates an individual result, whether that organization receives or processes physical specimens.**

**Histopathology**

The CAP recommends that the current practice be maintained: that histology labs remain outside of the scope of CLIA regulations. Currently, the CAP provides oversight for over 100 laboratories that conduct histopathology preparation and processing in addition to higher-complexity testing which is in scope of regulatory oversight. Although these high-complexity labs may not necessarily be representative of the wider laboratory community, the CAP through our oversight of these laboratories has not identified issues with quality originating in slide staining and preparation. Instituting CLIA oversight of histopathology would mean both increased regulatory burden for laboratories while reducing the flexibilities available to laboratory directors, who must make decisions on laboratory workflow based on the best interest of the patient balanced with the realities of constricting financial resources. In addition to adapting to workforce challenges, technology is rapidly changing the field of histology, and it may be premature to develop regulations as practices remain in flux and issues with quality have yet to be identified.

In addition, changing or formalizing current interpretative guidelines on the timeframe for review and confirmation of the tissue findings by the technical supervisor after the gross tissue examination is performed (currently "should" do in 24 hours) may be infeasible for some laboratories.

**Digital pathology**

The primary site certification was required by CLIA to ensure quality testing and safety of patients by providing greater oversight for gynecologic cytology laboratories. In recent years, we have similar quality concerns regarding specialty physician groups using the in-office ancillary services (IOAS) exception for anatomic pathology (AP) services. Removal of the primary site CLIA certification allows for slides to be read at various locations other than the physician's practice, potentially increasing the volume of slides read and decreasing oversight. While the CAP recognizes the benefits in continuing to allow remote work, **we strongly recommend closely monitoring the following: remote sign-out usage to determine the settings, personnel qualifications, and documentation of compliance with primary site policies and procedures to ensure CLIA maintains quality practices for all testing settings and to prevent potential fraud and abuse by "Pap mills" and "pod laboratories". This information should be collected for at least one survey cycle after the PHE declaration ends. According to the CAP's 2023 Practice Leader Survey Report, pathologists took advantage of PHE, in which 30% adopted remote sign out. Moving forward, an additional 11% plan on doing this via digital means. Therefore, the CAP supports adoption and use of standards for pathologists to remotely examine histopathology and cytology slides and images, with controls that utilize or adapt existing CAP accreditation requirements. The CMS, prior to any rulemaking, should collect and report the on the above to CLIAC.**

**The CAP continues to advocate for a clear distinction between remote diagnosis by pathologist (aka remote sign out) vs remote collection of samples (aka remote testing). A remote testing location should be defined as one not physically connected with the testing facility at the address listed on the CLIA certificate but under the same Laboratory Director listed on the CLIA certificate and connected to the hospital system of the same via secure internet connection (i.e., VPN). This will allow for remote testing while ensuring responsibility for clinical accuracy and patient safety sits with a licensed provider and under CLIA regulatory oversight. The CAP suggests that remote sign-out should be defined by the pathologist review and signing out on the materials while physically in a location other than the address listed on the CLIA certificate and connected to that location's system via a secure internet connection.**

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The CAP welcomes the opportunity to discuss our concerns and recommendations for implementation at your earliest. Please contact Helena Duncan at hduncan@cap.org or 202.354.7131.

Closing,

***The College of American Pathologists***