



# COLLEGE of AMERICAN PATHOLOGISTS

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**Response to Request for Information  
Senate Health, Education, Labor, and Pension Committee  
Ranking Member Cassidy**

**Possible Congressional Action for Clinical Diagnostics  
April 10, 2024**

The College of American Pathologists (CAP) appreciates the Senate Health, Education, Labor, and Pension (HELP) Committee and Ranking Member Cassidy's interest in oversight and reforms to clinical diagnostics. The CAP has been working on this issue for almost two decades and looks forward to continuing our work with the Committee and Congress moving forward. We currently oppose the proposed rule released by the United States Food and Drug Administration (FDA) and recommend an approach to oversight of laboratory developed tests (LDTs) that focuses on patient access and safety and includes a tiered-risk approach, with direct FDA regulatory oversight of only the highest-risk tests.

The CAP is the leading organization of board-certified pathologists, serving patients, pathologists, and the public by fostering and advocating excellence in the practice of pathology and laboratory medicine worldwide. Our members practice clinical and/or anatomic pathology in community hospitals, independent laboratories, academic medical centers, and federal and state health facilities. Pathologists are at the forefront of developing and utilizing new test methods and molecular analysis. This includes using molecular and genomic tests, many of which are LDTs, to predict risk of disease, diagnose disease, guide therapy selection, and assess a patient's response to a specific treatment. Utilizing teams of practicing laboratory professionals as inspectors, the CAP accreditation program helps laboratories maintain consistently high levels of quality and service throughout all levels of laboratory operations based on rigorous and continually updated standards and requirements.



### **CAP Priorities for Oversight of LDTs**

LDTs, by current definition, are tests developed and run by a single laboratory to meet specific diagnostic needs. Historically, LDTs were created manually by laboratory personnel utilizing standard and relatively simple laboratory methods. As such, they were viewed by the FDA as “lower risk” tests and therefore not subject to FDA enforcement. Just like medicine has evolved, LDTs have become more complex, often relying on high-tech instrumentation and complex laboratory methods to derive results. The CAP evaluates all LDTs through its deemed status accreditation program and proficiency testing (PT) processes under the Clinical Laboratory Improvement Amendments (CLIA). To date, the FDA has exercised enforcement discretion in the oversight of these tests. Congress has been working for over a decade to find a proper balance between LDT oversight and laboratory overburden. To that end, CAP believes a balanced, risk-based approach to potential new federal oversight of LDTs is needed to promote continued innovation, meet patient access needs, and ensure that each test is analytically and clinically valid, safe, and reliable. Through the years, the CAP has advocated for three main principles for LDT oversight:

- Protect patients,
- Ensure continued access to safe and innovative diagnostic tests, and
- Develop a framework that is the least burdensome for pathologists and their laboratories.

The CAP believes that a legislative and regulatory framework for LDTs should include a role for the FDA according to a test's risk level to a patient. This can be done by restricting direct FDA regulatory oversight to the highest-risk LDTs, providing flexibility in FDA oversight of



lower-risk LDTs and, where possible, leveraging the existing CLIA framework to avoid duplication in regulatory requirements. Oversight of LDTs must include a tiered risk-based structure that requires full FDA oversight of only the highest-risk LDTs and allows sufficient flexibility to ensure continued patient access to all LDTs and preservation of the quality of moderate- and low-risk LDTs. The highest-risk LDTs are those where there is little or no transparency in how the results are obtained, such as when proprietary test algorithms are used to produce results, no direct comparators to assess test performance, and no way to externally verify the accuracy of the results, such as through proficiency testing. We believe relatively few LDTs meet this definition of high risk. With the highest-risk LDTs, the chance of a misdiagnosis or otherwise inaccurate result and the subsequent impact on the patient's health are unacceptably high. Additionally, all LDTs should be required to meet analytical and clinical validity standards. Independent third-party accreditation organizations could assess the laboratories analytical and clinical validations for tests deemed low or moderate risk to prevent undue delays in test offerings.

We believe the development of LDTs does not constitute the practice of medicine. The CAP firmly supports that the practice of medicine should be determined at the state level and kept out of any future efforts of federal LDT oversight.

### **CAP Opposition to CLIA “Modernization”**

The CAP is strongly opposed to opening up CLIA for legislative changes to allow for oversight of LDTs. Congress and previous Administrations, as well as the current Administration, have firmly held that oversight of LDTs should remain with the FDA due to the agency's expertise in



approving diagnostic tests for patients. The CMS lacks the resources and expertise necessary to provide this oversight. Further, as recently as January 2024, the FDA and CMS clearly delineated each agency's authority and areas of expertise: the CMS regulates laboratory operations for patient testing, and the FDA oversees test development and production.

The CMS and the Centers for Disease Control and Prevention (CDC) have partnered to make targeted updates to CLIA, utilizing a regulatory approach, over the last several years. The agencies have finalized rules to update the following areas:

- Regulated Proficiency Testing (PT) Analytes,
- Revision of Personnel Regulations,
- Histocompatibility Regulations,
- Fees Under CLIA, and
- Proficiency Testing Referral Alternative Sanctions for Certificate of Waiver Laboratories.

Legislating changes to CLIA would severely disrupt the existing framework under which clinical laboratories in the U.S. have provided very high-quality laboratory testing for decades. Needed changes in CLIA have occurred and continue to occur through the existing iterative regulatory process. Much of this work is initiated through the Clinical Laboratory Improvement Advisory Committee (CLIAC) which performs a comprehensive review of CLIA and identifies topics for potential changes. Thus far, CLIAC identified the above areas for regulatory updates, in addition to retention of Next Generation Sequencing (NGS) Data in Clinical and Public Health Laboratories.



The CMS and CDC plan to focus future CLIA updates on topics of Histopathology, Cytology, Clinical Cytogenetics, NGS, and Biosafety. The agencies recently released an RFI last summer that included remote pathology and laboratory sign-out and histology laboratory regulations. The CMS and CDC have also formed CLIAC workgroups to develop recommendations for new CLIA requirements for NGS and biosafety. The CAP firmly supports this targeted regulatory approach to updating CLIA because it enables laboratories to continue providing services to patients without the major disruption CLIA-related congressional legislative intervention would cause.

Giving enhanced authority to CMS, through CLIA, over all LDTs is more than just hiring staff to assess clinical validity. It would require a structural change in the program. Currently, CMS uses a decentralized model, working with state health agencies to do its work of laboratory oversight through CLIA. If CMS is made responsible for providing enhanced oversight of LDTs, the agency would likely need to create an entirely new office to coordinate this work or set up 50 separate CLIA offices to provide this expanded level of oversight. We fail to see the advantages of upending CLIA and CMS' regulatory framework, while also implementing even more bureaucracy.

### **Alternative Proposals to FDA Rulemaking**

#### **CAP Support of the Verifying Accurate Leading-edge IVCT Development Act of 2023**

Should the FDA fail to modify the proposed rule to incorporate all the CAP's requested changes, Congress should pass legislation to regulate laboratory developed tests. Any legislation Congress passes should create a tiered risk-based structure for oversight of LDTs, include a targeted role for the FDA, introduce significant flexibility in LDT oversight, and utilize



whenever possible current laboratory reporting requirements. Legislation such as H.R. 2369, the VALID Act of 2023 (“VALID”) utilizes such a tier-based approach.

VALID reflects many of the policy priorities advocated by the CAP since 2009. It would establish a reasonable and balanced regulatory framework that would ensure quality laboratory testing for patients and minimize the regulatory burden on laboratories while allowing for continued innovation in laboratory testing. The CAP supports VALID’s: (1) three-tiered risk-based system, which would focus the FDA’s resources on the highest-risk LDTs, while leveraging existing structures to improve and promote patient safety; (2) “risk classification” framework, which is similar to one recommended by the CAP and other groups; (3) use of mitigating measures for the further down-classification of test risk; and (4) overall flexible regulatory framework.

The CAP appreciates the need for a premarket review process for the highest-risk LDTs defined in the legislation, and we support the streamlined pathway that the technology certification provision provides for the development of new tests on existing technological platforms. The exempted categories laid out in the legislation, especially the grandfathering provision, are also appropriate. Further, the CAP is supportive of provisions that clearly define test design and quality requirements, and the ability the legislation offers to modify existing LDTs to reduce burden and allow expedited patient care. Finally, the CAP continues to recommend that accreditors have the ability to submit documentation to the FDA on behalf of laboratories to further lessen the burden on laboratories.



### **Artificial Intelligence and Diagnostics**

Artificial intelligence and machine learning (AI/ML) are still in the very early stages of being considered for implementation in medicine and given the impact AI/ML will have on pathology and laboratory medicine the CAP urges a balance in the advancement in technology and innovation with patient safety and regulatory oversight. Regulations for AI will need to ensure the appropriate levels of safety can be reliably determined and maintained. The CAP has advocated for a risk-based approach to the FDA in ensuring safe and effective devices using any AI/ML technologies because of the myriad of uses in pathology and laboratory medicine, from digital pathology to next generation sequencing. Moreover, the robustness of the framework's requirements should depend on the risk classification of the AI/ML, thus allowing for innovation in any settings, especially the laboratory where initial development of these technologies may occur. Post-marketing (real world) quality control and performance monitoring requirements are needed to prove the efficacy and safety of modifications while differentiating local verification and data capture responsibilities between the developers and end-users (eg. laboratories and pathologists). In addition to the above-mentioned criteria for a regulatory structure, AI regulatory approaches need to consider the novel aspects of AI as a potentially autonomous system.

The CAP supports a legislative and regulatory framework for the oversight of LDTs that acknowledges the significant and important technological diagnostic advancements in medicine and the changing health care landscape. Legislative and regulatory activities in this space must ensure that patients continue to have access to high-quality, reliable, accurate, and innovative diagnostics.



FDA Regulatory Framework for Diagnostics

1. *How well is FDA's medical device framework working for the regulation of diagnostic products? Are there improvements that should be made?*

**CAP Response: The CAP believes that a legislative and regulatory framework for LDTs should include a role for the FDA according to a test's risk level to a patient.**

- A. *Of these specific changes, which would require Congressional action, and which can be effectuated by FDA alone?*

**CAP Response: This can be done by restricting direct FDA regulatory oversight to the highest-risk LDTs, providing flexibility in FDA oversight of lower-risk LDTs and, where possible, leveraging the existing CLIA framework to avoid duplication in regulatory requirements.**

2. *Does the current device regulatory framework support the review of diagnostics that are developed using AI or that incorporate AI?*

**CAP Response: Artificial intelligence and machine learning (AI/ML) are still in the very early stages of being considered for implementation in medicine and given the impact AI/ML will have on pathology and laboratory medicine the CAP urges a balance in the advancement in technology and innovation with patient safety and regulatory oversight.**

3. *What, if anything, makes diagnostics distinct among FDA-regulated medical products to warrant specific attention to how AI may be used in the review of product submissions?*

**CAP Response: The CAP has advocated for a risk-based approach to the FDA in ensuring safe and effective devices using any AI/ML technologies because of the myriad of uses in pathology and laboratory medicine, from digital pathology to next generation sequencing. Moreover, the robustness of the framework's requirements should depend on the risk classification of the AI/ML, thus allowing for innovation in any settings, especially the laboratory where initial development of these technologies may occur. Post-marketing (real world) quality control and performance monitoring requirements are needed to prove the efficacy and safety of modifications while differentiating local verification and data capture responsibilities between the developers and end-users (eg. laboratories and pathologists). In addition to the above-mentioned criteria for a**





***regulatory structure, AI regulatory approaches need to consider the novel aspects of AI as a potentially autonomous system.***

4. *Are the regulatory pathways intended to evaluate diagnostics for special populations (i.e. rare diseases or genetic disorders) working?*

***CAP Response: To date, the FDA has exercised enforcement discretion in the oversight of these tests. Congress has been working for over a decade to find a proper balance between LDT oversight and laboratory overburden. To that end, CAP believes a balanced, risk-based approach to potential new federal oversight of LDTs is needed to promote continued innovation, meet patient access needs, and ensure that each test is analytically and clinically valid, safe, and reliable.***

- A. *How could they be enhanced to accelerate and authorize products for special populations, for example, certain companion diagnostics for rare biomarkers?*

***CAP Response: Through the years, the CAP has advocated for three main principles for LDT oversight:***

- 1. Protect patients,***
- 2. Ensure continued access to safe and innovative diagnostic tests, and***
- 3. Develop a framework that is the least burdensome for pathologists and their laboratories.***

5. *Are there regulatory hurdles to expanding the settings in which diagnostics are performed, i.e. point-of-care (POC) tests performed in patients' homes?*

***CAP Response: The CAP would welcome the opportunity to discuss this issue in detail.***

- A. *In what ways could/should FDA leverage regulatory flexibilities to reduce testing barriers?*

6. *What are your views on FDA's implementation of predetermined change control plans; is FDA's approach in its recent guidance readily applicable to IVDs and other diagnostic products?*

***CAP Response: The CAP would welcome the opportunity to discuss this issue in detail.***

7. *Does FDA's current risk classification framework properly measure risk versus regulatory controls for diagnostics products?*



**CAP Response: The CAP would welcome the opportunity to discuss this issue in detail.**

A. *If not, how can FDA's risk-based regulatory approach to diagnostics be improved to better align the degree of regulatory oversight with patient risk and benefit?*

8. *In considering reforms to FDA's risk classification framework for diagnostics, what types of IVDs should be exempt from premarket review?*

**CAP Response: The CAP appreciates the need for a premarket review process for the highest-risk LDTs defined in the legislation, and we support the streamlined pathway that the technology certification provision provides for the development of new tests on existing technological platforms. The exempted categories laid out in the legislation, especially the grandfathering provision, are also appropriate.**

A. *What factors related to risk management should be applied to risk classification of IVDs?*

**CAP Response: The CAP is supportive of provisions that clearly define test design and quality requirements, and the ability the legislation offers to modify existing LDTs to reduce burden and allow expedited patient care. Finally, the CAP continues to recommend that accreditors have the ability to submit documentation to the FDA on behalf of laboratories to further lessen the burden on laboratories.**

9. *Is the "safety and effectiveness" standard against which diagnostics are reviewed the most appropriate review standard to assign risk management for clinical tests?*

**CAP Response: The CAP currently opposes the proposed rule released by the United States Food and Drug Administration (FDA) and recommend an approach to oversight of laboratory developed tests (LDTs) that focuses on patient access and safety and includes a tiered-risk approach, with direct FDA regulatory oversight of only the highest-risk tests.**

10. *Do the proposed reforms to FDA's device framework warrant the establishment of a new regulatory pathway specific to diagnostics? If yes, what are the principles that should guide such a new framework, as it would be applied to diagnostics currently subject to FDA premarket review?*

**CAP Response: The CAP welcomes the opportunity to discuss this issue in detail.**



CLIA Regulatory Framework for LDTs

1. *What updates to the clinical laboratory regulatory structure under CLIA should Congress consider to reflect the latest scientific practices and safety standards?*

**CAP Response: The CAP is strongly opposed to opening up CLIA for legislative changes to allow for oversight of LDTs. Congress and previous Administrations, as well as the current Administration, have firmly held that oversight of LDTs should remain with the FDA due to the agency's expertise in approving diagnostic tests for patients. The CMS lacks the resources and expertise necessary to provide this oversight. Further, as recently as January 2024, the FDA and CMS clearly delineated each agency's authority and areas of expertise: the CMS regulates laboratory operations for patient testing, and the FDA oversees test development and production.**

2. *What are your views on the effectiveness and use of the Clinical Laboratory Improvement Advisory Committee (CLIAC) in providing scientific and technical guidance to inform potential updates to CLIA standards?*

**CAP Response: The CMS and the Centers for Disease Control and Prevention (CDC) have partnered to make targeted updates to CLIA, utilizing a regulatory approach, over the last several years. The agencies have finalized rules to update the following areas:**

1. **Regulated Proficiency Testing (PT) Analytes,**
2. **Revision of Personnel Regulations,**
3. **Histocompatibility Regulations,**
4. **Fees Under CLIA, and**
5. **Proficiency Testing Referral Alternative Sanctions for Certificate of Waiver Laboratories.**

**Much of this work is initiated through the Clinical Laboratory Improvement Advisory Committee (CLIAC) which performed a comprehensive review of CLIA and identifies topics for potential changes. Thus far, CLIAC identified the above areas for regulatory updates, in addition to retention of Next Generation Sequencing (NGS) Data in Clinical and Public Health Laboratories.**

3. *Do the proficiency testing programs currently approved by the Department of Health and Human Services (HHS) reflect the latest clinical standards of laboratory medicine?*



*Are there specialties, subspecialties, or analytes that should receive greater consideration for HHS approval?*

***CAP Response: The CMS and the Centers for Disease Control and Prevention (CDC) have partnered to finalize rules making needed changes to Regulated Proficiency Testing (PT) Analytes and Proficiency Testing Referral Alternative Sanctions for Certificate of Waiver Laboratories. In addition, the current structure allows for PT programs provide the challenges that reflect the latest clinical standards of laboratory medicine while balancing the cost and availability of materials to develop these challenges.***

4. *How well does the existing enforcement structure under CLIA work in ensuring compliance with regulatory requirements and taking action against noncompliance? What should be improved, if anything at all?*

***CAP Response: The existing enforcement process works adequately as intended to ensure quality testing is available for patients especially in rural and underserved areas.***

5. *Should legislative reforms address CLIA's quality system requirements? If yes, which of those changes would require Congressional action, and which could be effectuated by CMS alone?*

***CAP Response: Legislating changes to CLIA would severely disrupt the existing framework under which clinical laboratories in the U.S. have provided very high-quality laboratory testing for decades. Needed changes in CLIA have occurred and continue to occur through the existing iterative regulatory process.***

***The CMS and CDC plan to focus future CLIA updates on topics of Histopathology, Cytology, Clinical Cytogenetics, NGS, and Biosafety. The agencies recently released an RFI last summer that included remote pathology and laboratory sign-out and histology laboratory regulations. The CMS and CDC have also formed CLIAC workgroups to develop recommendations for new CLIA requirements for NGS and biosafety. The CAP firmly supports this targeted regulatory approach to updating CLIA because it enables laboratories to continue providing services to patients without the major disruption CLIA-related congressional legislative intervention would cause.***



6. *Where does redundancy exist, if at all, within the current CLIA regulatory structure with respect to accreditation standards under federal and state licensure programs, as well as through CMS-approved accreditation organizations?*

**CAP Response:** *CMS-approved accreditors are deemed to perform compliance activities in lieu of CMS; therefore, if a clinical laboratory decides to be accredited the laboratory agrees to meet the accreditation organizations requirements. These requirements by statute must be equivalent or more stringent than the CLIA regulations. Therefore, there is no duplication amongst CLIA and Accreditation program standards.*

7. *In considering legislative reforms to CLIA, should LDTs be defined in statute? What aspects of test development would characterize such a definition?*

**CAP Response:** *Again, the CAP is strongly opposed to opening up CLIA for legislative changes to allow for oversight of LDTs. Therefore, LDTs should not be defined in the CLIA statute.*

8. *How should Congress consider issues relating to the practice of medicine and its relationship with labeling for LDTs? Should there be additional oversight of the information conveyed to patients serviced by LDTs?*

**CAP Response:** *The CAP believes the development of LDTs does not constitute the practice of medicine. The CAP firmly supports that the practice of medicine should be determined at the state level and kept out of any future efforts of federal LDT oversight.*

9. *Should certain CLIA regulations be updated, would it necessitate a reevaluation of the CLIA fee schedule?*

**CAP Response:** *The CAP believes that changes to CLIA, including the fee schedule, are best handled through rulemaking, which has recently been updated in a final rule.*

10. *What compliance challenges would legislative reforms to CLIA create? How should new regulatory requirements apply to tests currently available to patients?*

**CAP Response:** *Legislating changes to CLIA would severely disrupt the existing framework under which clinical laboratories in the U.S. have provided very high-quality laboratory testing for decades.*