



Summary of CAP's Legislative Proposal for the Regulatory Framework of Laboratory-Developed Tests (LDTs)

Overview of the CAP's Legislative Proposal

The College of American Pathologists (CAP) believes any regulatory framework for LDTs needs to enhance patient safety, maintain quality laboratory testing, and promote innovation without creating a significant new regulatory burden on laboratories. To effectively meet these goals, the CAP believes that any legislative proposal should rely on the existing Clinical Laboratory Improvement Amendments of 1988 (CLIA) framework as much as possible while also taking into account the unique roles of the Centers for Medicare & Medicaid Services (CMS) and the Food and Drug Administration (FDA). Since 2009, the CAP has maintained that enacting modifications to CLIA is the most effective and least burdensome approach to ensuring patient safety and sustaining continued innovation in diagnostic testing. However, the CAP continues to support a targeted role for the FDA to regulate high-risk LDTs to enhance patient safety.

The CAP's legislative proposal uses a stratified approach that effectively balances regulation by the FDA and CMS without stifling innovation or patient access to LDTs. The proposal also focuses FDA oversight on the tests that currently have the least transparency and highest potential patient risk. The CAP's proposal employs a three-tiered, stratified model that authorizes a role for third party accreditors and classifies tests based on their overall complexity and potential risk to patients based upon three categories: low, moderate, or high risk. In addition, analytic and clinical validation of LDTs should play a key role in any future LDT regulation.

Risk Based Model:

The CAP's legislative proposal is a three-tiered, stratified model that classifies tests based on their overall complexity and potential risk to patients based on different categories: low, moderate, or high risk.

Jurisdiction over LDTs:

The legislative proposal encourages coordination between the FDA and CMS to avoid duplicative or unduly burdensome requirements on laboratories.

- It provides statutory authority to the FDA to regulate high risk LDTs but not moderate or low risk LDTs, by amending the Federal Food, Drug, and Cosmetic Act (FD&C Act).
- It generally provides statutory authority to the CMS to regulate moderate and low risk LDTs, but not high-risk tests, by amending the CLIA provisions of the Public Health Service Act.



Definitions:

The legislative proposal includes the following definitions:

- **LDT:** is a laboratory examination or other procedure that is intended to be performed, and is designed and manufactured, by a single laboratory for which a CLIA certificate is in effect.
- **High Risk LDT:** is an LDT that produces a result that is not independently verifiable and the consequences of an incorrect result or incorrect interpretation include a high risk of serious morbidity/mortality. Examples include tests to predict risk of, progression of, or patient eligibility for a specific therapy to treat a disease associated with significant morbidity or mortality; and tests where the methodology uses proprietary algorithms or computations such that the test result cannot be tied to the methods used or inter-laboratory comparisons cannot be performed.
- **Moderate Risk LDT:** is an LDT that produces a result that is independently verifiable and the consequences of an incorrect result or incorrect interpretation include a moderate risk or high risk of serious morbidity/mortality. Examples include tests used for predicting disease progression or identifying whether a patient is eligible for a specific therapy, where the laboratory makes claims about clinical accuracy.
- **Low Risk LDT:** is an LDT that produces a result that is independently verifiable and the consequences of an incorrect result or incorrect interpretation include a low risk of serious morbidity/mortality. Examples include tests used in conjunction with other clinical findings to establish or confirm diagnosis, where there are no claims that the test alone determines prognosis or direction of therapy.
- **Meaningful Clinical Impact:** with respect to a modification of a LDT, the potential to result in a change to the patient's diagnosis or the therapy delivered to the patient.
- **LDT for an Unmet Need:** an LDT that is intended to be used to identify, measure, predict, monitor, or assist in selecting treatment for a serious or life-threatening disease or condition for which there is no existing FDA-approved or FDA-cleared diagnostic test with the same intended use and for which the LDT could lead to a meaningful improvement in treatment or therapy.



- **LDT for a Rare Disease or Condition:** an LDT that is intended to be used for a rare disease or condition, at the time the laboratory first solicits or accepts materials derived from the human body for examination using such LDT. For purposes of this definition, the term “rare disease or condition” has the meaning provided in section 526 of the FD&C Act. (relating to affecting fewer than 200,000 persons in the United States)

- **Traditional LDT:** is an LDT using techniques and components marketed for clinical use that are interpreted directly by qualified healthcare providers.

- **Low Volume LDT:** is an LDT that is intended only to detect a condition, and in which a total of less than 500 tests per year are performed by a laboratory entity (to include all laboratories that share a common ownership or control structure and perform that same test).

- **Public Health Laboratories:** are laboratories that perform core public health and environmental activities including the following:
 - Performance of public health reference tests
 - Disease prevention, control, and surveillance
 - Population-based interventions
 - Communication with healthcare providers on appropriate patient care
 - Coordination of emergency response efforts

LDT Regulatory Oversight:

The legislative proposal strengthens oversight through a partnership between the CMS, FDA and third party accreditors. The proposal relies on CLIA’s existing framework as much as possible, with the addition of a targeted role for the FDA with respect to high risk tests.

- **High Risk LDTs:** High Risk LDTs would be subject to existing FDA pre-market and post-market requirements. The laboratory would submit each test to the FDA for review prior to offering the test clinically. The CMS and third party accreditors would determine compliance.

- **Moderate Risk LDTs:** A laboratory would not be permitted to use a Moderate Risk LDT before either the Secretary or an accrediting body deemed by the Secretary has informed the laboratory that the LDT meets the moderate-risk standards established by the Secretary. If utilizing a CMS-deemed accrediting body, the laboratory must submit validation studies to the third party accreditor for review. The third party accreditor must make a determination that there is adequate evidence of analytical and clinical validity and that the



laboratory meets the standards established by the Secretary before the laboratory may offer the test clinically.

- **Low Risk LDTs:** The laboratory would internally perform analytical validation and determine adequacy of clinical validation prior to offering any Low Risk LDT for clinical testing. The third party accreditor, during normally scheduled inspections, would verify that the laboratory performed appropriate validation studies.
- **LDTs for Rare Diseases or Conditions, LDTs for Unmet Needs, Low Volume LDTs and Traditional LDTs:** LDTs for Rare Diseases or Conditions, LDTs for Unmet Needs, Low Volume LDTs and Traditional LDTs would be exempt from pre-market review (but not pre-market notification), unless such review is deemed necessary by the Secretary, following consultation with the CMS and FDA.
- **LDTs Developed by Public Health Laboratories:** LDTs developed by public health laboratories would be exempt from pre-market review (but not pre-market notification), unless such review is deemed necessary by the Secretary, following consultation with the CMS and FDA.
- **Modified LDTs:** Reporting would be required for any modification to a Moderate Risk LDT or Low Risk LDT that results in a change to the intended use and has a Meaningful Clinical Impact. The laboratory would notify the Secretary or third party accreditor of any such modification. The Secretary or third party accreditor would then determine if the change would be subject to the pre-market review process set forth above for Moderate Risk LDTs.

CLIA Enhanced Standards:

The legislative proposal calls for the Secretary to develop standards, and a process for determining how laboratories meet these standards for Moderate Risk and Low Risk LDTs. The Secretary may directly determine if laboratories are meeting the standards for Moderate Risk and Low Risk LDTs, or develop a program that allows accrediting bodies to make that determination.

When determining standards, the Secretary would include requirements for the laboratory to meet analytical and clinical validity for Moderate Risk and Low Risk LDTs. The Secretary would establish evidence-based standards for analytical and clinical validity.

- **Accreditation Bodies:**

The Secretary would have authority to develop a program under which accreditation bodies will determine if laboratories offering Moderate Risk or Low Risk LDTs are meeting established standards by the Secretary.



- **Definition of Analytical and Clinical Validity:**

- Analytical Validity: The LDT is a valid and reliable method of identifying or measuring the analyte or substance with respect to which the LDT was designed to identify or measure.
- Clinical Validity: The LDT consistently and accurately identifies, measures or predicts: 1) a disease or condition in an individual; or 2) characteristics related to the clinical status of the individual.

- **Adverse Reporting / Complaint Investigations:**

The CAP's legislative proposal requires adverse event reporting by laboratories to the Secretary or deemed accrediting bodies. If a laboratory markets, offers or performs a Moderate Risk LDT or Low Risk LDT and has reason to believe the test may have caused or contributed to a death or serious bodily injury, then the laboratory shall investigate the incident. If the laboratory determines that the LDT may have caused or contributed to a death or serious bodily injury, the laboratory shall report the incident to the Secretary within ten days of making such a determination. The laboratory will maintain records of each incident investigated and each report to the Secretary of the incident.

- **Public Reporting:**

The CAP's legislative proposal promotes transparency by making validation summaries for Moderate Risk LDTs publicly available. It would require a laboratory's proprietary test information to remain confidential.

Regulations and Transitional Provisions:

- **Classification and Reclassification:**

The legislative proposal provides that there be a public and transparent process for classification of LDTs into risk categories and for reclassification of LDTs from one risk category to another when necessary. The classification process will include both initial classification by the Secretary with respect to certain LDTs, as well as self-classification of LDTs by laboratories, subject to notification to and ultimate approval by the Secretary, in each case based on standards established by the Secretary. In the case of self-classification, the Secretary must make a determination regarding a laboratory's notification within 60 days for every LDT. Under the legislative proposal the Secretary is authorized to utilize an expert panel to determine appropriate risk classification.

- **Notification:**

The legislative proposal directs the Secretary to issue regulations defining a process and criteria for submission of a notification for each LDT no later than one year after enactment of the legislation. No later than two years after the date



of enactment of the legislation, each laboratory would submit a notification to the Secretary for each LDT in use after April 23, 2003 and would continue soliciting and accepting materials derived from the human body for examination using the LDT unless the Secretary requires otherwise. The Secretary may use third party accreditors to administer the notification process and shall provide a standardized format for laboratories to use in the notification process.

A laboratory would self-classify and notify the Secretary or third party accreditor if an LDT is offered on or after the enactment of final regulations.

- **Exceptions:**

The legislative proposal also recognizes the need for exceptions to the regulatory scheme described above for:

(i) *Public Health Emergencies.* The legislative proposal provides that the Secretary shall define a process that exempts LDTs from the above requirements during local, regional, or national infectious disease outbreaks, public health threats, bio-threats, or emergency health responses.

(ii) *LDTs approved by states that hold exempt status under CLIA.* The legislative proposal provides that laboratories not be subject to duplicative regulation. Laboratories may be subject to LDT oversight by either the CLIA-exempt state or the federal CLIA program, but CLIA-exempt states must follow the new federal requirements discussed in this legislative proposal (e.g., CLIA-exempt states may not impose more onerous or burdensome requirements on laboratories).

- **Grandfather Clause:**

The legislative proposal provides that LDTs in use prior to April 23, 2003, are exempt from the requirements above.

- **Transition Provision:**

In addition, under the legislative proposal laboratories may continue to use all LDTs prior to promulgation of final regulations required by the legislative proposal, and may continue to use LDTs thereafter in accordance with such regulations.