AMP/CAP LDT Legislative Proposal Side-By-Side

Issue	AMP	CAP
Statue(s) Modified	CLIA	CLIA (explicit authority to regulate low-and-moderate risk tests) and FDC Act (explicit authority over high-risk tests)
Definition of "High-Risk"	Must involve a proprietary computational method or algorithm AND be used "to diagnose a disease, predict risk of disease, or risk of progression of a disease, that is associated with significant morbidity or mortality, or threatens the public health."	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.
Definition of Moderate Risk	Used "to diagnose a disease, predict risk of disease, or risk of progression of a disease, that is associated with significant morbidity or	Produces a result that is independently verifiable and the consequences of an incorrect result or incorrect interpretation include a moderate risk or

	mortality, or threatens the public health." Unlike high-risk tests, moderate-risk tests would use a methodology that "lends itself to inter-laboratory comparisons or proficiency testing."	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.
Definition of low-risk	Would either be adjunctive in nature or protocols for which "the consequence of an incorrect result or interpretation is unlikely to lead to serious morbidity or mortality, either for the patient or the public health."	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.
Treatment of Low-Risk Tests	Low-risk tests would not undergo premarket review under the proposal. Rather, low-risk tests would be subject to inspection in the normal course of the laboratory inspection process.	Low-risk tests would not undergo premarket review under the proposal. 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.
Definition of Tests for Rare Disorders	Would modify the definition of rare disease to be a disease or disorder with an incidence of fewer than 200,000 newly diagnosed individuals per year in the United States	Has the meaning provided in section 526 of the FD&C Act. (disorder affecting fewer than 200,000 persons in the United States) (statutory definition does not mention "newly diagnosed")
Status of Tests for Rare Disorders	Tests used for rare diseases that are not serious threats to the public health are treated as low risk and thus exempt from premarket review.	Exempt from pre-market review (but not pre-market notification, which appears to be akin to listing, although it is to interpreted in future regulation), unless such review is deemed necessary by the Secretary, following consultation with the CMS and FDA.
Status of Tests for public health emergencies	Tests used for public health emergencies that are not serious threats to the public health are treated as low risk and thus exempt from premarket review.	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.
Status of tests for infectious diseases	Tests used for infectious diseases that are not serious threats to the	Secretary shall define a process that exempts LDTs from the above

	public health are treated as low risk and thus exempt from premarket review.	requirements during local, regional, or national infectious disease outbreaks, public health threats, bio-threats, or emergency health responses.
Treatment of Public Health Laboratories	Tests that are intended to be used solely for public health surveillance shall be exempt from all requirements. "Public health surveillance" means ongoing systematic activities, including collection, analysis, and interpretation of health-related data essential to planning, implementing, and evaluating public health practice closely integrated to the dissemination of data to those who need to know and linked to prevention and control.	Defined as laboratories that perform core public health and environmental activities including the following: o Performance of public health reference tests; o Disease prevention, control, and surveillance; o Population-based interventions; o Communication with healthcare providers on appropriate patient care; o Coordination of emergency response efforts; 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.
Definition and Treatment of Unmet Needs Tests	Not addressed	Defined as "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." 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.
Definition and Treatment of Traditional LDTs	Not addressed	Defined as "LDT using techniques and components marketed for clinical use that are interpreted directly by qualified healthcare providers." 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.
Definition and Treatment of Low-Volume Tests Performed by a Laboratory	Not addressed	Defined as "LDT that is intended only to detect a condition [sic—language appears to be missing], 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)." 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.
Instances when FDA Would Review Test	Laboratory voluntarily chooses to go through FDA PMA/510(k) process or if a protocol is high-risk and the laboratory does not want to give the proprietary information to the CMS or third-party reviewer.	All high-risk tests that do not meet one of the exemptions.
Time Limits for Review by CMS or Third-Party Reviewer	If a test is high-risk, the CMS or third-party reviewer has 90 days to review the submission. If a test is moderate risk, the CMS or third-party reviewer has 30 days to review the submission. If the CMS or third-party reviewer does not complete the review within the deadline the approval is automatically granted.	60 days after the laboratory submits the notification for moderate risk tests; FDA review times for high-risk tests.
Definition of Clinical	"The association of a	"The LDT consistently

Validity	biomarker or analyte with the presence, absence, predisposition to, or risk of a specific clinical condition." The proposal notes that clinical validity is distinct from clinical utility.	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."
When Clinical Studies Required	A third-party reviewer could require a laboratory to conduct a clinical trial only for a high-risk protocol and only if the CMS or the third-party reviewer determines that no other approach can provide the necessary information to support the laboratory's claims, and provides written justification for that decision.	For moderate-risk tests, if utilizing a CMS-deemed accrediting body, the laboratory must submit validation studies to the third-party accreditor for review. High-risk tests will be subject to FDA requirements for clinical studies.
Establishment of Standards by CMS	CMS to stipulate a minimum level of standards for analytical and clinical validity.	Secretary must 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

		(through CMS) 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.
Establishment of third-party review program by CMS	CMS will establish a transparent process whereby non-federal-governmental organizations may be approved as a third-party reviewer organization. State agencies may be a CMS-approved third party for tests offered in that state. CMS-approved accrediting organizations will also be eligible to be third-party reviewer organizations.	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.
Classification or Reclassification of Tests	The test review information must be sent to CMS within three days after completion of review of the test. CMS can reclassify the risk of the test.	Establishment of 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. Under the legislative proposal the Secretary is authorized to utilize an expert panel to determine appropriate risk classification
Conditional Approval	Laboratories with demonstrated success with approved tests in the same or higher-risk classification will be conditionally approved to begin testing with tests that use similar technologies or methodologies while review of the submission is pending.	No such provision in publicly available summary
CMS Posting of Summaries about Tests	Laboratories must prepare summaries about the test that could be posted by CMS except that: low-risk tests would not have to provide these summaries. Moderate-risk tests on the market as of April 24, 2003, would not have to provide these summaries. (The significance of this particular date is unclear to us). Once there have been three tests of the same kind the laboratory seeking to market a new test does not need to	Requires laboratories to make validation summaries for moderate-risk LDTs publicly available. It would require a laboratory's proprietary test information to remain confidential.

	prepare a summary of the clinical validity for the test but can instead reference the database.	
Notification of Tests	Not addressed	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 (the significance of this date is unclear to us) 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.
Modifications of Tests	If a laboratory modifies a test after going through the review process, that modified test would have to undergo new review if the change elevates the test to a higher risk classification or if the modification significantly changes the performance characteristics. Moreover, if a laboratory modifies an FDA-approved or cleared test in a way that significantly changes the performance characteristics, and the modified test is high risk or moderate risk, the modified test would need to undergo premarket review as described above. If the modification to the approved or cleared device does not change the performance characteristics, the laboratory would need to provide summary information.	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. Meaningful Clinical Impact means "the potential for modification to result in a change to the patient's diagnosis or the therapy delivered to the patient."
Grandfathering of Tests from Premarket Review	There is no grandfathering for high-risk tests. There would be grandfathering for moderate-risk tests on the market prior to enactment of the law.	LDTs in use prior to April 23, 2003, are exempt from the requirements regardless of risk.

Rulemaking	CMS must issue final updated CLIA regulations within two years after the legislation is enacted.	No later than one year after enactment of the legislation; only explicitly mentioned in context of notification.
Effective Date	Two years after the regulations are finalized.	Two years after final regulations issued for notification provisions. Appears to be date final regulations issued for rest of the proposal.
User Fees	Would authorize CMS to collect an annual user fee, limited to cost recovery, from laboratories determined by the number of tests the laboratory offers.	Not addressed
Modifications to Other CLIA Provisions	Modifies CLIA requirements related to proficiency testing, inspections, recordkeeping, and reporting of laboratory errors.	Provisions related to adverse event reporting and complaint investigations