



Proposal for Modernization of CLIA Regulations for Laboratory Developed Testing Procedures (LDPs)

Transparency. Quality. Innovation.

Desired Outcomes:

- Patients receive the most appropriate test(s) for their clinical condition.
- Laboratory tests are accurate, precise, clinically relevant, and monitored for continued quality performance.
- Health care professionals are able to provide professional services without undue restrictions.
- Preserve the ability of the laboratory community to provide surge capacity in public health emergencies including biological, chemical, radiological and nuclear threats, and infectious disease outbreaks.
 - Safeguard and strengthen the existing Laboratory Response Network, including public health laboratories, sentinel laboratories, national laboratories, commercial reference laboratories, clinical institutions, and hospital-based laboratories.
- Regulatory oversight does not slow innovation, constrain flexibility and adaptability, or limit a test's sustainability as a result of being unduly burdensome and beyond the fiscal capacity for the laboratory to reasonably perform or the healthcare system to financially support.
- Burdens on CMS are kept as minimal as possible; the use of Third Party Reviewers and Accreditors, *i.e.*, public-private partnerships, is strengthened.

Rationale for Modernizing Existing CLIA Regulations:

- The field of molecular diagnostics has grown and evolved significantly since the Clinical Laboratory Improvement Amendments (CLIA) of 1988 were enacted.
- Provision of molecular diagnostic services is a professional healthcare activity and healthcare services are under 42 CFR, the Public Health Law, as is CMS, which has responsibility for the CLIA program.
- Laboratory developed testing procedures are professional healthcare services. They are not medical devices; and as such, they are very different from test kits and systems that are manufactured and distributed throughout the country. A single set of regulations can never address both adequately.
- Separating the oversight of laboratory-related activities into two separate agencies would result in inefficient, burdensome, and duplicative regulations.
- It is the most streamlined, cost-effective approach to addressing clinical validity and other concerns expressed by stakeholders.
- Updating CLIA regulations preserves and strengthens the use of third party organizations to independently review validity and verify laboratory performance and procedures.

Key Features:

- Updates selected existing CLIA regulations
- Applied to laboratory developed testing procedures, which are considered high complexity under CLIA regulations
- Tiered; risk-based
- Provides assurance of quality, analytical validity and clinical validity without jeopardizing innovation or patient access to necessary care
- Provides for rapid response during public health emergencies
- Provides transparency so the ordering physician and patient can get essential information to inform selection of an appropriate LDP
- Provides for pre-introduction review of high and moderate risk LDPs
- Directs CMS to stipulate a minimum level of standards for LDP analytical and clinical validity
- Provides a distinct role for FDA: MAAAs with proprietary algorithms must be submitted to FDA unless the laboratory reveals its proprietary algorithm to Third Party Review and Inspection
- Requires laboratories to participate in proficiency testing or alternative assessment for all LDPs
- Does not change states' exempt status under CLIA
- Avoids duplication of activities within and between agencies
- Provides for shared LDP protocols
- Timeline: two years to final rule, another two years after final rule to take effect

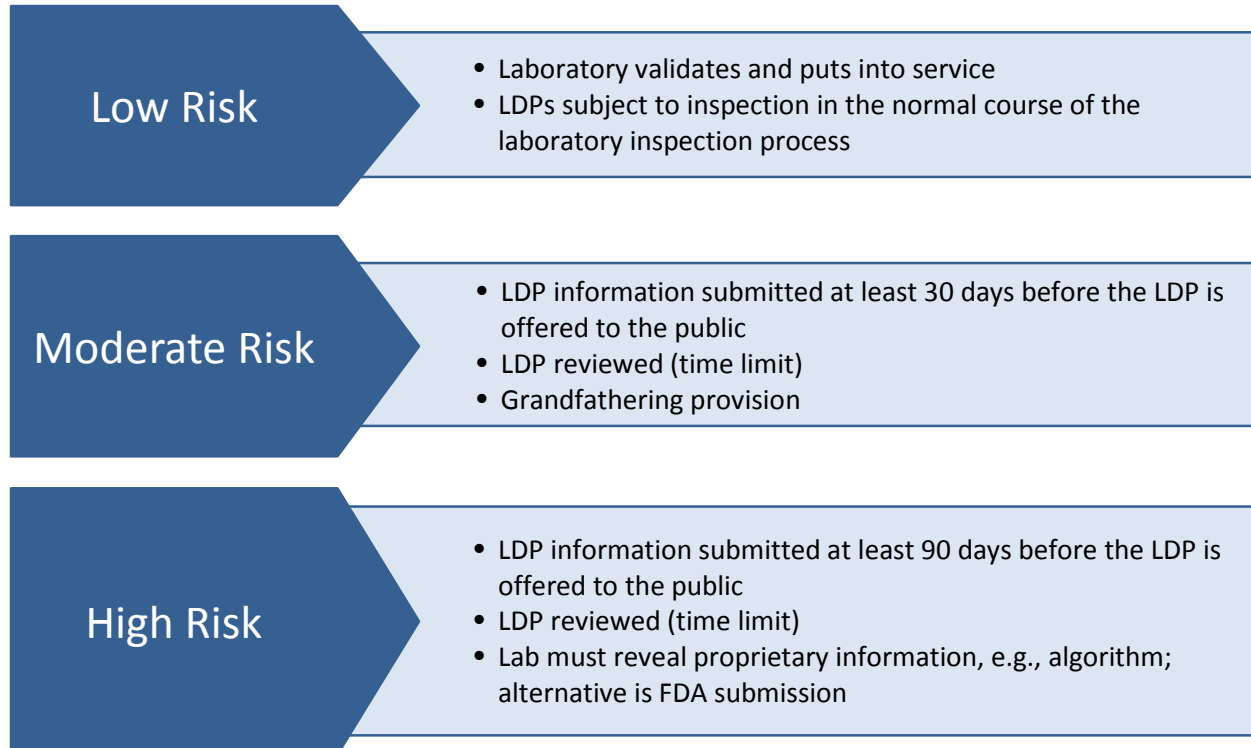
LDP Oversight Summary:

Table of Contents:

Section 1: Definitions

Section 2: Third Party Reviewer approval

Section 3: LDP risk classification

Section 4: LDP publication requirements

Section 3.1: Standardized format for information on LDPs

Section 3.2: Submission of information to CMS/Third Party Reviewer

Section 3.3: Require LDP information to be available publicly and electronically

Section 5: LDP review requirements

Section 4.1: Minimum level of standards

Section 4.2: Review of LDP information

Section 4.3: Evidence for clinical validity

Section 4.4: Third Party Reviewers not required to review High Risk LDPs

Section 6: Modifications

Section 5.1: When a new review is not required

Section 5.2: When a new review is required

Section 5.3: When FDA cleared or approved IVDs are modified

Section 7: Conditional approval

Section 8: Exemptions

Section 9: Minimum requirements for CMS-approved accrediting organizations' laboratory inspectors and the inspection process

Section 8.1: Inspector selection and training

Section 8.2: Inspection teams

Section 8.3: Feedback mechanism

Section 8.4: Records

Section 10: Update list of analytes for which proficiency testing is required

Section 9.1: Require regular list updates

Section 9.2: Utilization of advisory boards

Section 9.3: Proficiency testing or alternative assessment for all LDPs

Section 11: Mechanism for reporting laboratory and LDP errors

Section 10.1: Reporting errors

Section 10.2: Further investigation of errors

Section 12: Fees

Section 13: Ensure adequate scientific expertise

Section 14: Preemption

Section 15: Exempt status

Section 16: Protocol sharing

Section 17: Standardized reference materials

Section 18: Conforming amendment

Section 19: Timeline

Section 1: Definitions

Relevant code: 42 USC 263a(a)

- Clarify that an ‘examination’ or ‘procedure’ in 42 USC 263a includes laboratory developed testing procedures.
- Define laboratory developed testing procedures (LDPs) to mean “a testing procedure or service that encompasses and integrates, in a single CLIA-certified laboratory, the design, development, validation, verification, and quality systems used in laboratory testing and interpretative reporting in the context of clinical care or public health services.”

Relevant code: 42 CFR 493 (referred to as “CLIA regulations” in the remainder of the proposal)

- Third Party Reviewer means a CMS-approved non-governmental organization that reviews LDP analytical and clinical validation data for a CLIA-certified laboratory and issues approval for that LDP to be offered to the public. These organizations may utilize the expertise of relevant government agencies.
- Rare disease means a disease or disorder with an incidence of fewer than 200,000 newly diagnosed individuals per year in the United States.
- Clinical validity, as it pertains to the CLIA regulations, means the association of a biomarker or analyte with the presence, absence, predisposition to, or risk of a specific clinical condition. Clinical validity is distinct from clinical utility.

Section 2: Third Party Reviewer approval

- 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 Reviewer for LDPs offered to residents of that state.
- CMS-approved accrediting organizations will also be eligible to be Third Party Reviewer organizations.

Section 3: LDP risk classification

- CMS will define risk classifications for LDPs as follows:
 - o High risk: Taking the medical context into consideration, an LDP that is 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, AND; uses methodologies that involve proprietary algorithms or computations such that the test results cannot be tied to the methods used or inter-laboratory comparisons cannot be performed.
 - Example: Multi-analyte Assay with Algorithmic Analysis (MAAA) that utilize proprietary algorithms
 - o Moderate risk: Taking the medical context into consideration, an LDP that is used to diagnose a disease, predict risk of disease, or risk of progression of a disease, or patient eligibility for a specific therapy to treat a disease, that is associated with significant morbidity or mortality, AND; the test methodology lends itself to inter-laboratory comparisons or proficiency testing.
 - Examples: Genomic sequencing procedures in oncology, *e.g.*, tumor profiling panels, or for inherited conditions; biomarker analysis as an aid to indicate potential responsiveness to therapy; Epstein-Barr Virus (EBV) detection for post-transplant lymphoproliferative

- disorders or disease (PTLD); human papilloma virus (HPV) genotyping; non-invasive prenatal testing
- o Low Risk: an LDP for which the laboratory makes no claim that the test result alone determines diagnosis, prognosis or direction of therapy, absent other clinical information or diagnostic procedures, OR; 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. LDPs used for rare diseases, for public health emergencies, and for infectious agents that are not serious threats to the public health are classified as low-risk.
 - Examples: Hereditary hemorrhagic telangiectasia (rare disease); Factor V Leiden; immunoglobulin clonality assessment; LDPs for emerging biothreats; human herpesvirus 6 (HHV-6) detection; EBV for diagnosis of infectious mononucleosis; CF carrier screening.

Section 4: LDP publication requirements

Relevant code: 42 CFR 493.1291; 42 USC 263a

Rationale: Healthcare professionals, patients, and regulatory agencies should be able to access information such as accuracy, precision, and known clinical significance of an LDP. Laboratories that offer high and moderate risk LDPs should submit information about that LDP, including summary data associated with analytical and clinical validity, to CMS in a CMS-provided/designated standardized format. It should be required that the information be publicly displayed in a searchable, standardized format to enable easy review and comparison between LDPs. This would ensure transparency of test information, enable treating physicians, laboratories, and patients to compare LDPs and enhance communication between them. Once clinical validity is established for an analyte/biomarker, laboratories should not be required to submit this information.

Section 4.1: Standardized format for information on LDPs

- Require that CMS develop (itself or through one or more contractors) a standardized format, *e.g.*, electronic form(s), through a public process that involves input from relevant clinical laboratory professionals. The purpose shall be to provide information necessary for pre-introduction review according to the requirements in Section 5; and, to provide validity summary information such that it is available publicly, *i.e.*, to the ordering physician and patient before it is ordered. Such information should include:
 - o LDP description (*i.e.*, information associated with claims, intended use, and/or indication for use);
 - o Analytical validity summary data; (for Publication)
 - o Analytical validity full data (for Review)
 - o Clinical validity summary data; (see “Three of a Kind” exception below) (for Publication)
 - o Clinical validity full data (see “Three of a Kind” exception below) (for Review)
 - o LDP methodology/technology;
 - o The date the LDP was put into service;
 - o Risk classification of the LDP as determined by the laboratory;
 - o Contact information for the laboratory;
 - o Certification / licensure number for the laboratory;
- Require that laboratories:
 - o Adopt the standardized format;

- o Provide the required information in the CMS-provided/designated, standardized format to CMS/Third Party Reviewer for any LDP that is not an FDA cleared or approved IVD;
- o Provide the required information in the CMS-provided/designated, standardized format to CMS/Third Party Reviewer for any FDA cleared or approved IVD that the laboratory modifies in accordance with Section 6;
- o Certify the information contained in each form as truthful and accurate;
- o Make this information readily available, *e.g.*, upon request, and provide instructions on how to access the information in any marketing materials, (as already required by 42 CFR 493.1291), for any LDP that is not an FDA cleared or approved IVD; and
- o Ensure that this information and any marketing materials about the LDP do not contain any unsupported claims of performance or validity.
- o “Three of a Kind” clinical validity exception: If the CMS database described in Section 4.3 contains clinical validity summary data for the analyte/biomarker involved in the LDP being submitted, the laboratory is not required to submit clinical validity data, but may reference the database entry.

Section 4.2: Submission of information to CMS/Third Party Reviewer

- Require laboratories to submit the information described in Section 4.1 to CMS/Third Party Reviewer before the LDP is introduced into clinical service as follows:
 - o High risk: 90 days
 - o Moderate risk: 30 days
 - o Low risk: Exempt
- Require CMS/Third Party Accreditor to develop a mechanism to receive and review this information electronically. This mechanism should allow laboratories to be able to track the status of the submission/review electronically.

Section 4.3: Require LDP information to be available publicly and electronically

- Require CMS develop and continuously update a searchable electronic database containing entries for all high and moderate risk LDPs using the LDP information submitted to CMS/Third Party Reviewer (as required in Section 4.1 and 4.2).
- Require CMS to display the information about the LDP publicly and electronically.
 - o Only summary data for analytical and clinical validity will be made public.
- Require new and updated information be published within 30 days of either finalizing a review of an LDP or receiving information about an LDP from the laboratory or Third Party Reviewer.
- Once three (3) laboratories have LDP information in the database, CMS will aggregate the clinical validity summary data and place it in a designated section of the database.
 - o CMS will place an electronic reference, *e.g.*, hyperlink, in the clinical validity field for any LDP that is permitted to reference the database under the “Three of a Kind” exception.

Section 4.4: Clarification provision

- Nothing in this proposal is to be construed to prohibit a laboratory from seeking FDA clearance or approval for any of its LDPs.

Section 5. LDP review requirements

Relevant code: 42 CFR 493.1253(b)(2); 42 USC 263a

Rationale: CMS should require a stipulated minimum level of standards for reviewing LDP information to reduce variability in oversight among the various Third Party Reviewers. Standards for analytical and clinical validity should be standardized in all categories of LDPs. CMS should use relevant specialty subject matter experts and a public process for developing these standards. Clinical validity is a vital characteristic that should be considered when designing, ordering, performing, and interpreting an LDP. Clinical validity is typically not established by the laboratory itself but by the scientific or medical community, *e.g.*, in peer-reviewed scientific literature before an LDP is developed. However, when it is not, then data should be collected and/or documented to clinically validate an LDP. Information on clinical validation should be made available to health care professionals and patients as noted in Section 4.

Section 5.1: Minimum level of standards

- CMS will develop and periodically review a minimum level of standards for analytical and clinical validity.
 - Require that the mechanism use separate specialty public advisory boards made up of the following:
 - No fewer than four subject matter experts familiar with relevant LDPs each, and includes representatives from medical center, public health and commercial reference laboratories, and;
 - Third Party Reviewers and CMS-approved accreditation organizations.
 - Require CMS to appoint subject matter expert members of the advisory boards using a nomination process that includes professional associations.
 - Require that members of advisory boards have term limits.
- Standards for analytical and clinical validity should be standardized in all categories of LDPs.

Section 5.2: Review of LDP information

- Require that CMS/Third Party Reviewer review this information using appropriately trained staff within the time limits noted below after receiving a new submission for information on an LDP (See Section 6 for information on modifications):
 - High risk LDPs: 90 days
 - Moderate risk LDPs: 30 days
 - Low risk LDPs: Exempt
- The LDP is presumptively approved if CMS/Third Party Reviewer does not issue a decision within the time limit.
- Require Third Party Reviewers to notify CMS and the laboratory of the review decision electronically within three (3) days of review completion.
- Require Third Party Reviewer to forward any necessary LDP information to CMS within seven (7) days after completing the review for which an approval decision is reached.
- Permit CMS/Third Party Reviewer to request and review proprietary information, *e.g.*, algorithm.
 - Require CMS to protect such proprietary information. Validation summary data will not be considered proprietary and, as noted in Section 4.3, will be made available to the public.
 - Laboratories may choose to submit their LDPs to FDA rather than provide proprietary information to CMS/Third Party Reviewers.

- Grant CMS the authority to reclassify the risk during this review time period and CMS must provide the scientific basis for the reclassification in writing to the laboratory.
- Instruct CMS to develop a mechanism for laboratories to appeal a change in risk classification or an approval decision.

Section 5.3: Evidence for clinical validity

- Establish that valid scientific evidence used to determine a test's clinical validity, for the purposes of review by CMS/Third Party Reviewer. Acceptable sources of evidence, may include, but shall not be limited to:
 - o peer reviewed literature;
 - o clinical practice guidelines;
 - o subject matter expert opinion;
 - o bench studies, including use of archived specimens;
 - o past experience with similar products;
 - o case studies;
 - o clinical data;
 - o consensus standards;
 - o reference standards;
 - o data registries, *e.g.*, ClinGen, ClinVar, CancerLinQ, or other curated relevant database;
 - o post-market data; or
 - o clinical trials, including those conducted outside of the U.S.
- Specify that CMS/Third Party Reviewer may require that a laboratory conduct a clinical trial only if CMS/Third Party Reviewer determines that no other approach can provide the necessary information to support the laboratory's claims, may only make such a requirement for High Risk LDPs (as defined in Section 3), and provides a written explanation to the laboratory that describes the scientific and clinical basis for that decision.

Section 5.4: Third Party Reviewers not required to review High Risk LDPs

- Third Party Reviewers shall not be required to agree to review High Risk LDPs as a condition for CMS approval.
- Third Party Reviewers may choose to not review any High Risk LDP.

Section 6: Modifications

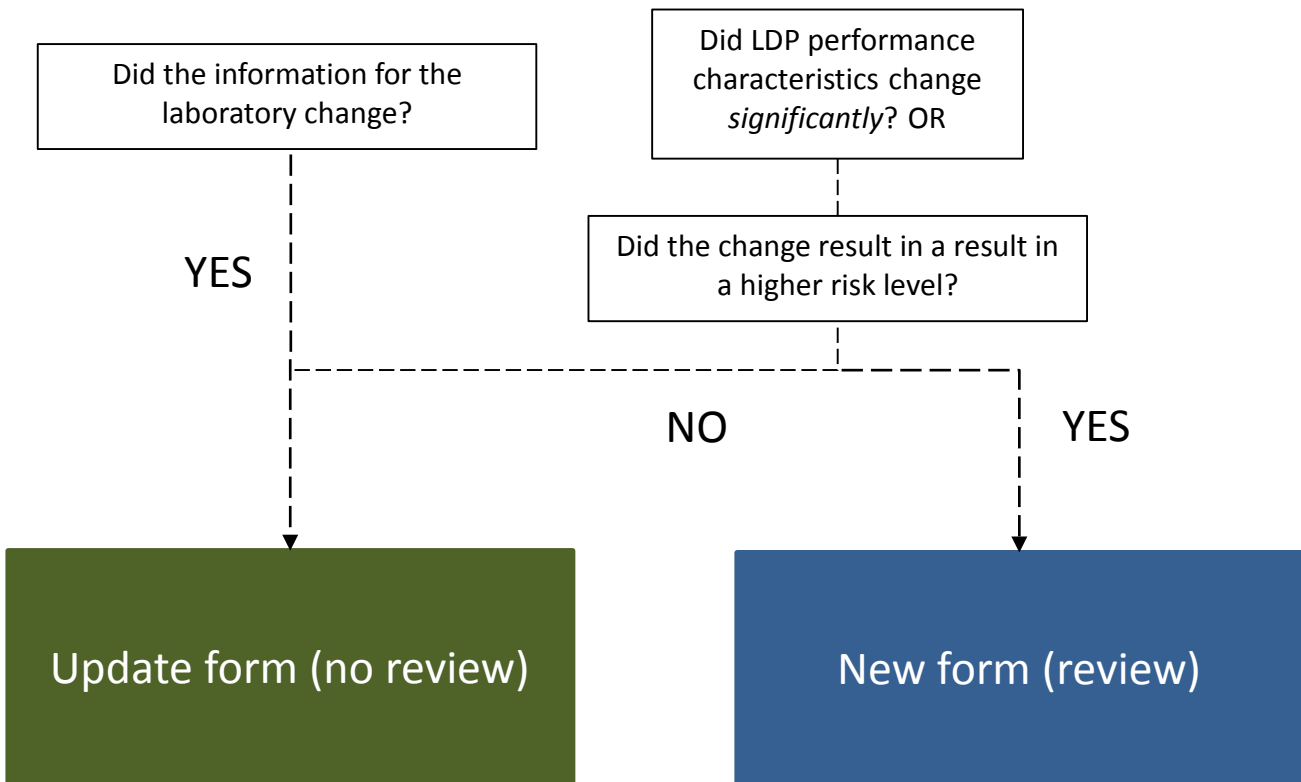
Section 6.1: Updated Information only required

- Require that laboratories provide updated information, *e.g.*, electronic update, but a new review will not be required, about an LDP whenever:
 - o Contact information changes for the laboratory.
 - o Certification or licensure information for the laboratory changes.
 - An LDP is modified but the changes do not significantly alter the performance characteristics (as currently defined by CLIA).

Section 6.2: New review required

- Require that laboratories provide updated and/or new information and a new review is required whenever the modification(s):
 - Changes the LDP such that it meets the definition of a higher risk classification level.
 - Significantly changes the performance characteristics (as currently defined by CLIA) of the LDP.

Modifications Schematic



Section 6.3: Modification of an FDA cleared or approved IVD

- When an FDA cleared or approved IVD is modified such that it alters the performance characteristics established by the manufacturer, it will be considered an LDP and subject to the CLIA regulations, and the laboratory will be required to:
 - Establish for each test system the performance specifications for the performance characteristics required by 42 CFR 493.1253 (b)(2).
 - If the performance characteristics have not been changed significantly: submit the information according to the LDP Publication requirements of Section 4.
 - If the performance characteristics have been changed significantly: submit the information according to the LDP Publication and Review requirements of Section 4 and Section 5.
- The laboratory is also subject to the requirements in this section if the LDP created from the FDA cleared or approved IVD is further modified in the future.

Section 7: Conditional approval

Rationale: Similar to the requirements of the NY State Clinical Laboratory Evaluation Program (CLEP) (<http://www.wadsworth.org/labcert/clep/clep.html>), laboratories that demonstrate a satisfactory aptitude with a specific technology or methodology, should be permitted to begin testing while the LDP is under review.

- Laboratories with demonstrated success with approved LDPs in the same or higher risk classification, will be conditionally approved to begin testing with LDPs that use similar technologies or methodologies pending the outcome of the review.

Section 8: Exemptions

- LDPs 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.
- All Low Risk LDPs shall be exempt from all LDP Publication and Review requirements (Section 4 and Section 5).
- All Moderate Risk LDPs introduced prior to enactment are exempt from the LDP Review requirements (Section 5) and those introduced prior to April 24, 2003 are exempt from both LDP Review and LDP Publication requirements (Section 4 and Section 5).
- All LDPs that have approval from a state that has exempt status under the CLIA regulations and that requires pre-introduction review of analytical and clinical validity data will be exempt from the LDP Review requirements but will be required to submit LDP information for publication as required in Section 4.1.
- Compassionate use under CLIA: A single patient with suspected or established serious or immediately life threatening condition may be offered an LDP that has not been approved as long as the ordering physician has been notified in writing that the LDP has not been approved, and the physician provides the order to proceed. The compassionate use order must be documented by the laboratory.

“Grandfathering” Summary:

Low Risk & surveillance LDPs	N/A: Exempt from both LDP Publication & Review requirements
Moderate Risk	<ul style="list-style-type: none"> • Introduced prior to enactment: exempt from LDP Review (subject to LDP Publication requirements only) • Introduced prior to April 24, 2003: exempt from both LDP Review & Publication requirements
High Risk	No grandfathering: Subject to both LDP Review & Publication requirements

Section 9. Minimum requirements for CMS-approved accrediting organizations' laboratory inspectors and the inspection process

Rationale: CMS should require minimum requirements for CMS-approved accrediting organizations' laboratory inspectors and the inspection process to reduce variability in oversight among the various accrediting organizations.

Relevant code: 42 CFR 493.903; 42 USC 263a(f); 42 USC 263a(e)

Section 9.1: Inspector selection and training

- Require that CMS develop:
 - o Minimum qualifications for inspector selection.
 - o Minimum requirements for inspector training.
 - o Consistent and ongoing training for inspectors.

Section 9.2: Inspection teams

- Require that CMS-approved accrediting organizations use teams of relevant experts to inspect laboratories.
 - o Require that teams include experts relevant to each specialty or subspecialty including statisticians, IT experts, etc. when appropriate (*e.g.*, for MAAAs).

Section 9.3: Feedback mechanism

- Require that CMS develop a mechanism for laboratories to provide direct feedback to CMS on the inspection process.

Section 9.4: Records

- Require that CMS-approved accrediting organizations and proficiency testing programs maintain records and provide these to CMS on a yearly basis.
 - o These records should include:
 - Any complaints, investigations, and conclusions regarding programs and services, and
 - Any corrective action taken.
 - o Require that CMS use these materials in their assessment of each accreditation and/or proficiency testing program.

Section 10: Update list of analytes for which proficiency testing is required to ensure that the performance and validity of all laboratory developed testing procedures meet accepted standards

Relevant code: 42 CFR 493 Subpart H & I; 42 USC 263a(f)

Rationale: CMS's list of analytes for which proficiency testing is required is outdated and does not include many analytes that are routinely used in standard patient care and includes others that are no longer used. All laboratory developed testing procedures (LDPs; which are considered to be high complexity by current CLIA regulations) should be subjected through a CMS-approved proficiency testing program, sample exchanges, or

alternative assessment (*i.e.*, when formal proficiency testing for the analyte does not yet exist) to ensure that LDPs are both accurate and precise.

Section 10.1: Require regular list updates

- Require that CMS update 42 CFR 493, Subpart H & I, using a public process that involves input from relevant clinical laboratory professionals to ensure appropriate oversight keeps up with advances in scientific knowledge and standards of care.
- Require that the list of analytes for which proficiency testing is required through an approved program is reviewed biennially (every two years) and updated no less frequently than every five years.

Section 10.2: Utilization of advisory boards

- Require that CMS develop a mechanism for reviewing and updating the list of analytes for which PT is required through an approved program that involves utilizing outside expert advisory boards that includes relevant laboratory professionals.
 - o Require that the mechanism use separate specialty public advisory boards made up of the following:
 - No fewer than four subject matter experts familiar with relevant LDPs each, and includes representatives from medical center, public health and commercial reference laboratories, and;
 - Third Party Reviewers and CMS-approved accreditation organizations.
 - o Require CMS to appoint subject matter expert members of the advisory boards using a nomination process that includes professional associations.
 - o Require that members of advisory boards have term limits.
- Specify that the advisory boards are tasked with generating a recommended updated list of analytes for which PT is required through an approved program by identifying changes (*e.g.*, additions and deletions) that should be made to reflect advances in scientific and medical knowledge and the current standard of care.
- Require that CMS review the recommendations of each advisory group, consider recommendations from the CDC Clinical Laboratory Improvement Advisory Committee, and adopt an updated list of analytes for which PT is required through an approved program.

Section 10.3: Proficiency testing or alternative assessment for all LDPs

- Clarify language in 42 USC 263a to require that CMS update the CLIA regulations to clarify that all LDPs shall be subjected to proficiency testing or alternative assessment.
 - o Specify that laboratories that have on its test menu an LDP for a least one analyte on the CMS list of analytes for which proficiency testing is required through an approved program must participate in proficiency testing, or alternative assessment if a formal proficiency test for an analyte does not exist.
 - o Specify that, for the remaining analytes, laboratories must participate in proficiency testing through a CMS-approved program, or alternative assessment.
 - o Specify that alternative assessment can involve:
 - Conducting comparative testing using samples, specimens, contrived specimens that have been split between two individuals in the same laboratory, or

- Conducting comparative testing by exchanging samples, specimens, or contrived specimens with other laboratories.

Section 11: Mechanism for reporting laboratory errors

Relevant code: 42 CFR 493.2; 42 CFR 493.1233; 42 CFR 493.1291(k)

Rationale: Current CLIA regulations require that each laboratory report test patient result errors to the authorized person ordering the test, maintain a record of those errors, ensure that all complaints and problems reported to the laboratory are documented, conduct investigations of complaints when appropriate, and issue a corrected report. CMS-approved accrediting organizations must notify CMS within 10 days of any deficiency identified in an accredited or CLIA-exempt laboratory if the deficiency poses an immediate jeopardy to the patient or a hazard to the general public. The proposal builds upon these requirements.

Section 11.1: Reporting errors

- Require labs to have ready access to a mechanism for ordering physicians to report possible laboratory/LDP errors.
- Require that any investigations conducted by a laboratory that reveal an error poses immediate jeopardy to the laboratory's patients or a hazard to the general public be reported to CMS directly.
 - o As defined in 42 CFR 493.2, 'Immediate jeopardy' means a situation in which immediate corrective action is necessary because the laboratory's noncompliance with one or more condition level requirements has already caused, is causing, or is likely to cause, at any time, serious injury or harm, or death, to individuals served by the laboratory or to the health or safety of the general public. This term is synonymous with imminent and serious risk to human health and significant hazard to the public health.
- Require that CMS provide this information to the public through the database described in Section 4.

Section 11.2: Further investigation of errors

- Require that CMS request FDA to investigate a modified FDA cleared or approved IVD that has possibly produced erroneous results when there is a sufficient concern. Sufficient concern would be similar to the threshold for when FDA cleared or approved IVDs are investigated.

Section 12: Enable CMS to collect fees to facilitate activities for LDP oversight

Relevant code: 42 USC 263a(m)(2)

Rationale: CMS should be provided the resources required to carry out the new activities outlined above.

- Enable CMS to collect an annual fee commensurate with the number of LDPs the laboratory offers;
 - o In the CLIA regulations, after "The Secretary shall require the payment of fees for inspections of laboratories which are not accredited and for the cost of performing proficiency testing on laboratories which do not participate in proficiency testing programs approved under subsection (f)(3)(C) of this section." Insert "The Secretary shall also require the payment of fees for

submission of LDP information and cost of processing and reviewing the information and maintaining the LDP database.”

- Require that the annual fee be limited to cost recovery
- Require that the annual fee be reviewed and any necessary updates recommended by the advisory board described in Section 10.
- Waive fees for public health laboratories that are outside of the standard fees for accreditation inspections.

Section 13: Ensure adequate scientific expertise

- Require that the CMS division responsible for the implementation of CLIA regulations have in its top leadership a board-certified professional who has served as a laboratory director in a clinical laboratory that performs high complexity LDPs, and understands the special considerations of complex LDPs and a wide range of different types of LDPs.
- Require CMS to develop a mechanism whereby it can utilize the expertise of relevant subject matter experts in the medical and scientific communities.

Section 14: Other entities may not duplicate the activities of CLIA or otherwise require laboratories to submit evidence of an LDP’s analytical or clinical validity to assess whether a test is reasonable and necessary.

Rationale: Medicare Administrative Contractors requirements that laboratories submit data regarding analytical or clinical validity adds a duplicative regulatory system that adds expense to the healthcare system and involves potentially conflicting requirements.

- Insert the following text: “No State, tribal, local government (or political subdivision thereof), or government contractor may establish or continue in effect any requirement related to assessing the analytical and/or clinical validation of an LDP that is different from, or in addition to, the requirements of [the CLIA regulations as amended by this bill] for the purposes of assessing whether the LDP is reasonable and necessary, *i.e.*, for coverage and payment purposes.”
- No federal government entity or entity that sets coverage or payment policy may be a CMS-approved Third Party Reviewer.

Section 15: Exempt status

Rationale: Inspection by the enhanced CLIA regulations should continue to preempt states that are judged to be less stringent than the CLIA regulations. States that currently have exempt status under CLIA, *i.e.*, New York and Washington, will continue to have exempt status.

- CLIA regulations shall continue to preempt states that are judged to be less stringent than the CLIA regulations.

Section 16: In certain situations, LDP protocols may be shared

Rationale: The ability to share protocols is essential to permit CDC and public health labs to respond to public health emergencies. This also facilitates multi-site hospital or reference lab systems to establish procedural conformity.

- Clarify that laboratories within a single corporate entity may share protocols without having to submit information as required in Section 4 as long as the corporate entity controls and specifies all aspects of the LDP, *e.g.*, the instruments and reagents used, and the receiving laboratory verifies LDP performance.
- Clarify that CDC and public health laboratories may share protocols without having to submit information as required in Section 4 as long as the receiving laboratory verifies LDP performance.

Section 17: Standardized reference materials

- Require that CMS collaborate with FDA, NIST, CDC, WHO, and drug developers to facilitate the development of standardized reference materials.
 - Such collaboration could include providing representation on advisory committees.

Section 18: Conforming amendment

- Require CMS to update CLIA regulations to incorporate these new requirements.

Section 19: Timeline

- Updated CLIA regulations will be finalized within two years after the legislation is enacted. Requirements will be effective two years after the regulations are finalized.