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ON

“EXAMINING THE REGULATION OF DIAGNOSTIC TESTS

AND LABORATORY OPERATIONS”

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Statement of Patrick Conway, MD, MSc
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Chairman Pitts, Ranking Member Green and Members of the Committee, thank you for the opportunity to talk about our work at the Centers for Medicare & Medicaid Services (CMS) related to ensuring accurate and reliable laboratory testing. The Clinical Laboratory Improvement Amendments of 1988 (CLIA)¹, over which CMS has primary jurisdiction,² created minimum standards of quality for all clinical laboratories in the United States, leading to improved patient safety and better, more effective care for all Americans.

CLIA established quality standards for all laboratory testing performed on human specimens for the purpose of providing information for the diagnosis, prevention, or treatment of disease, or assessment of health. In the late 1980s, laboratories’ inaccurate reading of Pap tests contributed to potentially preventable harm from cervical cancer.³ In response, Congress enacted CLIA to address concerns about the rapid growth in unregulated laboratories and, in particular, the lack of workload limits for individuals reading Pap tests – an important patient safety issue associated with laboratory testing.⁴

CLIA has successfully worked for nearly 25 years, contributing to major improvements in the quality of clinical laboratories, promoting more accurate testing, and improving patient safety. Due to the long and consistent operation of the program, the vast majority of laboratories understand, appropriately implement and use CLIA requirements to enhance the quality of their laboratory testing. As of July 2015, there were roughly 250,000 laboratories that had registered with CMS and held CLIA certificates. Because of CMS’ extensive education efforts with

¹ Public Law 100-578 <http://www.gpo.gov/fdsys/pkg/STATUTE-102/pdf/STATUTE-102-Pg2903.pdf>

² The Centers for Medicare and Medicaid Services, the Food and Drug Administration, and the Centers for Disease Control and Prevention all have specific roles in assuring quality laboratory services under CLIA.

³ Bogdanich W. Lax Laboratories: The Pap Test Misses Much Cervical Cancer through Labs’ Errors. Wall Street Journal. Nov. 2, 1987: 1,20.

⁴ Congressional Research Service Report ‘Regulation of Clinical Tests: In Vitro Diagnostic (IVD) Devices, Laboratory Developed Tests (LDTs), and Genetic Tests’ December 17, 2014

laboratories, only 90 were subjected to sanctions for non-compliance in the previous year.⁵ In addition, laboratories continue to improve their performance on proficiency tests (PT), which are important quality improvement tools that help laboratories verify that their test results are accurate and reliable. Over the past 10 years, PT “failure rates”⁶ have steadily decreased from nine percent in 2005 to three percent in 2014.

CLIA Standards and Laboratory Oversight

CLIA, and the regulations that implement it, created a system of laboratory oversight that is primarily based on test complexity. CLIA responsibilities are currently divided between three agencies: CMS, the Centers for Disease Control and Prevention (CDC), and the Food and Drug Administration (FDA). CMS conducts laboratory inspections to make sure that laboratories have appropriate controls, expertise, training, and procedures to ensure that test results are accurate and reliable. CMS also manages the approval of accreditation organizations and the certification of laboratories. CDC has shared responsibility with CMS for CLIA technical standards development and revision and for performing regulatory impact analyses. CDC’s role also includes conducting laboratory quality improvement studies that guide policy determination and development of laboratory practice guidelines (*e.g.*, best practices). In addition, CDC monitors PT practices, develops and distributes educational resources to laboratory professionals, and manages the Clinical Laboratory Improvement Advisory Committee (CLIAC), which advises the Federal Government on CLIA issues.

FDA’s primary responsibility under CLIA is to classify clinical tests into one of three categories (waived, moderate-complexity and high-complexity) based on their level of complexity and risk to patients. All tests introduced in the United States are high-complexity by default unless FDA categorizes a test as moderate or waived complexity. FDA does not categorize tests developed by and used within a single laboratory, known as laboratory-developed tests (LDTs). Thus, by default, they are considered to be high-complexity tests.

⁵ 194 laboratories were *proposed* for sanctions in 2014 but only 90 were actually subjected to sanctions. The others were able to improve their processes to demonstrate compliance.

⁶ Failures occur when a laboratory’s submitted proficiency testing results are inaccurate or not reliable. Low failure rates indicate a high level of consistency, accuracy and reliability in testing.

Standards that laboratories must meet under CLIA are based on the complexity of tests they perform – laboratories that perform more complex tests must meet higher standards. Laboratories that perform moderate- and high-complexity tests must meet requirements on quality assessment, quality control, personnel qualifications and education, general laboratory systems, and proficiency testing, among others. Laboratories that perform only waived tests – which are cleared by FDA for home use, and either are simple and accurate with a negligible risk of erroneous result or pose a low risk to patients should they be performed incorrectly⁷ – are exempt from most CLIA requirements. Examples of waived tests include blood glucose testing using monitors that have been cleared for home use, urine pregnancy tests, and other urine dipstick tests.

Further, laboratories performing the same test must meet the same standards, whether located in a hospital, doctor's office, or other site. This framework is designed to reduce the risk of potential patient harm and ensure patients receive the same high quality clinical laboratory testing no matter where their test is performed. CLIA's provisions apply to all laboratories in the United States, not just those that receive Medicare payment, in order to ensure uniform quality across all laboratories.

It is important to note that FDA has regulatory authorities, apart from CLIA, governing the quality of laboratory tests. These multi-agency efforts are different in focus, scope, and purpose, but they are intended to be complementary in assuring safe and high quality laboratory services. The joint efforts of CDC, FDA, and CMS have resulted in improved clinical laboratory operations.

Laboratory Certification

CMS enforces CLIA standards by requiring laboratories to obtain a certificate in order to operate.⁸ Laboratories that perform moderate and high complexity tests need to obtain a Certificate of Compliance (COC) or a Certificate of Accreditation (COA), demonstrating that they adhere to all CLIA requirements. CMS conducts on-site surveys prior to issuing a COC to

⁷ 42 CFR 493.15

⁸ There are five types of certificates: Certificate of Waiver; Certificate for Provider-Performed Microscopy Procedures (a type of moderate-complexity test); Certificate of Registration (COR); Certificate of Compliance; and Certificate of Accreditation.

confirm a laboratory's compliance with the requirements.⁹ The surveys also assist laboratories in improving patient care through education and by emphasizing requirements that directly impact the accuracy and reliability of the laboratory's test performance.

Laboratories holding COCs are surveyed against CLIA regulations every two years. Although CMS has Federal surveyors, which perform on-site CLIA surveys of laboratories across the country, most laboratories are surveyed by state-health-department representatives who coordinate their reviews with CMS.

Laboratories may also receive CLIA certification by virtue of obtaining accreditation (under a COA) from one of seven private, non-profit accreditation organizations approved by CMS. The accreditation organization also inspects laboratories once every two years. To receive CMS approval, the non-profit accreditation organization's requirements must meet or exceed CLIA program condition-level requirements. Periodically, each organization must receive re-approval to ensure it maintains standards that are equal to or more stringent than CLIA regulations.¹⁰ The re-approval review also includes an on-site visit to evaluate the accreditation organization's laboratory oversight practices. In addition to the re-approval process, CMS evaluates each accreditation organization's performance through a validation survey where we compare the results of the most recent survey performed by the accreditation organization to a survey performed by CLIA surveyors.

Laboratories that only perform waived tests receive a Certificate of Waiver (COW). On-site surveys are not required for a COW laboratory unless there is a complaint. In addition, laboratories that perform only waived tests and certain moderate complexity microscopy procedures can receive a Certificate of Provider-Performed Microscopy Procedures (PPM).¹¹ As with waived tests, routine on-site surveys are not required for laboratories with a Certificate of PPM. However, a PPM laboratory may be subject to surveys if a complaint is received.

⁹ A COR provides temporary certification for a laboratory to conduct moderate and high complexity tests while it completes the certification process. The COR expires after the earlier of two years or when the laboratory meets certification requirements.

¹⁰ 42 USC 236a. (e)(2)(A)(ii)

¹¹ As of July 2015, 174,122 laboratories performed only waived tests and had received a COW, 18,505 laboratories have received a COC, 16,431 have been accredited and received a COA, and 35,150 have received a Certificate of PPM. Link: <http://www.cms.gov/Regulations-and-Guidance/Legislation/CLIA/Downloads/statupda.pdf>

Proficiency Testing

CMS' laboratory operations oversight activities include monitoring laboratory performance on PT. CMS requires laboratories conducting moderate or high complexity testing to participate in PT for certain tests. A CMS-approved PT program sends the laboratory a set of blind samples roughly three times per year. The laboratory tests the samples in the same manner as it tests patient specimens and reports the results back to the PT program. The PT program grades the results and sends the laboratory scores reflecting how accurately the laboratory performed the testing. PT programs undergo annual and ongoing regulatory review by CMS.

A CLIA Performance Goal study was conducted in 2003 on the number of laboratories properly enrolled and participating in PT and PT performance (*i.e.*, the number of laboratories enrolled in PT with no failures) from 1995 through 2003. The study showed a significant increase in PT enrollment, from 89.6 percent in 1995 to 97.2 percent in 2003, and significant improvement in PT performance, from 69.4 percent in 1995 to 92.8 percent in 2003. A 2010 CDC Report¹² on PT performance also showed improvement in PT performance scores for approximately 30,000 laboratories.

CMS also has worked to clarify aspects of the PT program in response to stakeholder questions, and has implemented several revisions to the requirements. In May 2014, CMS issued a final regulation¹³ to promote program efficiency and reduce burden, including under CLIA. We issued separate regulations in July 2014 to implement the Taking Essential Steps for Testing Act¹⁴. Together, these rules clarified specific types of PT referral (when a laboratory sends a PT sample to another laboratory for analysis) and increased flexibility in enforcement for laboratories that engage in this practice.

Laboratory-Developed Tests

FDA defines an LDT as an in vitro diagnostic test device that is intended for clinical use and designed, manufactured, and used within a single laboratory (*i.e.*, a laboratory with a single CLIA certificate). These tests are also sometimes called “in-house developed tests.” LDTs are

¹² <http://www.ncbi.nlm.nih.gov/pubmed/20441507>

¹³ <http://www.gpo.gov/fdsys/pkg/FR-2014-05-12/pdf/2014-10687.pdf>

¹⁴ Public Law 112-202

“devices,” as defined by the Food, Drug and Cosmetic Act, and are therefore subject to regulatory oversight by FDA. However, as noted above, FDA currently exercises its enforcement discretion with respect to LDTs.

Under CLIA, when a laboratory uses a test system that has not received FDA clearance or approval, such as an LDT, the laboratory treats the test as a high-complexity test. CLIA does not require premarket review of LDTs; the law merely regulates how and by whom the test is conducted and reported out, rather than the scientific principles behind or the clinical validity of the test system itself.

As with all high- and moderate-complexity testing, a laboratory may not release any high-complexity or moderate-complexity test result, including an LDT test result, prior to establishing certain performance characteristics relating to analytical validity for the use of that test system in the laboratory’s own environment.¹⁵ These performance-specification assessments measure the test’s: (1) accuracy (whether the test correctly measures the specific analyte when compared to a standard/reference); (2) precision (whether the test result is reproducible when repeated); (3) reference range (whether the normal range of results is based on the laboratory’s specific patient population); (4) reportable range (the lower and higher limits that the test can accurately report); (5) analytic sensitivity (minimum detection limits or how much of the analyte must be present to be measured); and (6) analytic specificity (the extent to which the method measures the analyte for which it is reporting results) that can be achieved using the given test system in that laboratory’s physical environment. The results can then be compared to the manufacturer’s expected performance specifications, and ultimately be used by the laboratory director as a basis for rejecting or accepting use of that test system in that laboratory.

Again, other than requiring that lab directors ensure that the test systems they select meet performance specifications that will ensure quality results, CLIA does not regulate the scientific principles behind or the clinical validity of any test – that is, the ability of the test to identify, measure, or predict the presence or absence of a clinically relevant condition or predisposition in a patient. FDA is authorized to evaluate the clinical validity of a test under its premarket clearance and approval processes, as part of its responsibility for assuring the reasonable safety

¹⁵ 42 CFR 493.1253(b)(2) Establishment of Performance Specifications.

and effectiveness of medical devices, generally. As a result, FDA has built substantial experience and expertise in this area, and CMS has generally deferred to FDA on how best to ensure the clinical validity of test systems.

Moving Forward

CMS is committed to ensuring high quality, accurate, and reliable laboratory testing by assuring that laboratories have appropriate controls, expertise, training, and procedures. We believe CLIA and our implementing regulations create the necessary framework to effectively oversee laboratory's day-to-day operations today and into the future – including those operations that pertain to the use of high-complexity tests, including LDTs.

In addition, there are several principles, noted below, that help guide our work on CLIA, which may also be useful in informing any future efforts by the Committee in this area.

- First, we aim to prevent duplicative oversight efforts across agencies. CLIA requires effective coordination across CMS, FDA, and CDC. We have worked hard to ensure our oversight efforts are consistent and complementary with other related but distinct regulatory schemes. And, in doing so, we have ensured that we take advantage of the unique expertise of each Agency and its staff.
- Second, we focus on building on our Agency's oversight strengths. When CLIA was implemented in the early 1990s, the responsibility to conduct certifications of laboratories was a natural fit for CMS because of our survey and certification experience.¹⁶ On the other hand, CMS does not have a scientific staff capable of determining whether a test is difficult to successfully carry out or likely to prove detrimental to a patient if carried out improperly. This expertise resides within the FDA, which assesses clinical validity in the context of premarket reviews and other activities aligned with their regulatory efforts under the Food, Drug, and Cosmetic Act.
- Third, we value our relationship with our private sector accreditation organizations and state-based partners. These organizations play an important role in evaluating and certifying laboratories – roughly 16,400 laboratories performing non-waived testing in

¹⁶ CMS requires other providers – such as hospitals, nursing homes, physician practices and others – to meet CLIA standards and, in some cases, undergo a CMS- or accreditor-led survey.

the United States are certified through an accrediting organization.¹⁷ In addition, laboratories in two states¹⁸ receive exempt status because these states have standards that are at least as stringent as CLIA. We believe it is important to preserve these organizations' ability to use private sector and state-driven approaches to build on the minimum standards established by CLIA.

- Fourth, we take targeted, smart approaches to oversight to improve patient safety without creating burdensome administrative requirements in regard to the areas over which we have authority. We believe the current approach – in which laboratories must meet higher standards if they perform more complex tests – has paid dividends in improving the quality of testing processes.

Thank you, again, for the opportunity to discuss CMS's work related to ensuring accurate and reliable laboratory testing. We look forward to continuing our work with the Committee to promote high-quality laboratory testing for all Americans.

¹⁷ <https://www.cms.gov/Regulations-and-Guidance/Legislation/CLIA/Downloads/statupda.pdf>

¹⁸ New York and Washington. Laboratories in NY have a partial exemption: all Physician Office Labs (POLs) fall under CLIA and are inspected every two years by CLIA surveyors. Any laboratory in NY that is not a POL falls under NY State licensure requirements and these are inspected by NY State CLEP (Clinical Laboratory Evaluation Program) surveyors. There are approximately 4,150 laboratories under the NY exempt state program and 4,023 laboratories under the WA exempt state program.