Patrick Conway's Hearing
"CLIA"
Before
E&C Health Subcommittee
November 17, 2015

Attachment — Additional Questions for the Record

The Honorable Marsha Blackburn

1. **Dr. Conway, rather than having an either/or approach to testing oversight, might there be another option?**

Answer: We agree that oversight of laboratory testing need not take an either/or approach in terms of CMS' responsibilities versus those of other agencies. In fact, we believe the most effective approach is to build on the collaborative inter-agency approach that is in effect today. CMS, the Food and Drug Administration (FDA) and the Centers for Disease Control and Prevention (CDC) all work together to assure accuracy and reliability of laboratory testing under CLIA, supplementing FDA's separate responsibility for assuring the safety and effectiveness of laboratory tests. These multi-agency efforts are different in focus, scope, and purpose, but they build on the strengths of each agency and are complementary. The division of labor in administering CLIA was carefully designed to ensure that each agency is using its expertise and infrastructure in a way that is not duplicative.

When CLIA was implemented in the early 1990s, the responsibility for certification of laboratories was a natural fit for CMS because of our survey and certification experience. Other CLIA activities, like the categorization of tests, are better suited to the FDA, which in addition to its CLIA role, is positioned to assess clinical validity, conduct premarket reviews, and perform other necessary oversight activities primarily under the Federal Food, Drug, and Cosmetic Act.

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 laboratories' day-to-day operations today and into the future (including those operations that pertain to laboratory-developed tests).

2. **The American College of Medical Genetics and Genomics has proposed a risk-based oversight system for regulation of genetic Laboratory Developed Tests which entails CLIA enhancement and uses a third-party review system for tests being offered. Since the majority of the work requiring scientific and medical genetic expertise would be performed by 3rd parties, if CMS were to implement such a model, how many additional FTE's would CMS/CLIA need?**

Answer: CMS shares your interest in ensuring that all laboratory-developed tests (LDTs) – including those LDTs using genetic and genomic technology – provide accurate and clinically-relevant results to patients and providers. However, any estimate of resources needed to implement the American College of Medical Genetics and Genomics' proposal would be premature at this time. We are not familiar with the details of the proposal, which could affect agency resources; nor is it possible to estimate the volume of tests that might be involved, how new third-party reviewers would be selected and monitored, and any other new responsibilities that CMS would be required to assume.

We also note potential concerns about proposals that would change the current collaborative framework of responsibilities in laboratory oversight (including for LDTs), which is carefully designed to balance the strengths of each partner agency. For example, the FDA has the expertise and infrastructure to conduct pre-market assessments of LDTs for safety and effectiveness, including clinical validity. In contrast, CMS is responsible for certifying and surveying laboratories under CLIA and has long-standing survey and certification experience.

The Honorable Michael C. Burgess

1. **In a June 2006 GAO Report, the GAO indicated that the CLIA program "had a carryover balance of $70 million" as of September 30, 2005. Please detail for the Committee the current funding status of the CLIA program, including a breakdown of revenues (i.e. user fees or other appropriations) and outlays (i.e. detailing administrative outlays, salary outlays, and those outlays attributable to inspection activities, or other) in 2014, and whether the CLIA program still maintains a carryover balance.**

Answer:

A. Cash Balance: As a result of careful stewardship of CLIA funds, together with consistency in the workload, CMS has consistently maintained a cash balance in the CLIA user fee fund. This has enabled CMS to avoid any fee increase for laboratories under CLIA for more than 16 years.

However, in recent years, the total revenue received each year has not fully paid for the total CLIA costs, thus reducing the cash balance in the CLIA user fee fund.

The most recent annual financial gap ranges from $5.9 million in FY2014 to $10 million in FY2016.

As a result of the growing gap in revenues versus expenses, the CLIA cash balance that is carried over from one year to the next is gradually declining from $55.6 million in FY2015 to $45.6 million in FY2016.

Year	Revenues	Outlays	Net Annual	Balance

FY2013				**$68.2**
FY2014	**$54.0**	**$59.9**	**($5.9)**	**$62.3**
FY2015	**$53.7**	**$60.3**	**($6.7)**	**$55.6**
FY2016	**$52.1**	**$62.1**	**($10.0)**	**$45.6**

B. Types of Expenses: CLIA is administered through a collaboration of three federal agencies (CMS, FDA and CDC) and State Survey Agencies (SAs).

The State SAs and other contractors perform most of the onsite surveys and complaint investigations of laboratories that hold a certificate of compliance or certificate of registration, as well as validation surveys that check on the adequacy of surveys conducted by CMS-approved accrediting organizations for laboratories that hold a certificate of accreditation.

CMS maintains the CLIA regulations and policies, and monitors the work carried out by State SAs' surveyors, as well as carrying out enforcement actions when State SA or other contractor surveys identify deficiencies in laboratory compliance with CLIA regulations.

The FDA administers the classification system by which tests are categorized as waived, moderate, or high complexity tests. CLIA requirements are calibrated to the degree of complexity involved in each type of test. The FDA may also perform premarket review, and analyze clinical validity and analytic validity of tests, but does so primarily under the Federal Food, Drug, and Cosmetic Act.

The CDC conducts research, staffs the Secretary's Clinical Laboratory Improvement Advisory Committee, and other functions. Below is the FY2016 budget for each agency. The table below does not include the 6.8% sequestration reduction.

Major Category of Expense (millions)	FY2016
Costs - State Survey (Inspections)	$19.29
Costs - CDC	$11.73
Costs – FDA	$4.09
Costs - CMS	$23.55
TOTAL	$58.66

C. Administrative Expenses. The table below shows CMS' administrative expenses, excluding costs of the State-conducted onsite surveys. The expenses encompass both CMS central and regional office expenses, contracts, agency overhead, the information systems and databases through which all State and CMS surveys are documented and maintained, the CLIA regulations and policies, monitoring the work carried out by State SAs' surveyors, as well as carrying out enforcement actions when State SA or other contractor surveys identify deficiencies in laboratory compliance with CLIA regulations.

CMS Administrative & Oversight Expenses (millions)	FY2016
Salaries	$9.89
Overhead	$7.45
CLIA Data System Contract	$2.67
Other- Specialty Inspection Contracts	$0.80
Cytology- Specialty Inspection Contract	$1.55
Administrative-Other	$1.19
TOTAL	$23.55

2. Regarding CMS-conducted laboratory inspections under CLIA, please provide the following:

a. The primary inspection objectives for an inspector;

b. The number of CMS laboratory inspections conducted per year (not including those inspections conducted by deemed organizations); and

c. The number of inspection findings by CMS per year that the agency would deem as "serious," that "create a probability of risk to patients," or that warrant the sanctioning or closure of a CLIA laboratory. Additionally provide a categorical breakdown of the types of such findings.

Answer:

a. The primary objectives for a laboratory surveyor (the CLIA program's term for an inspector) are described in Appendix C of the State Operations Manual. They include determining the laboratory's compliance with CLIA requirements, and assisting laboratories in improving patient care by emphasizing aspects of the regulatory provisions that have a direct impact on the laboratory's overall performance. CMS promotes the use of an educational survey process, especially on initial laboratory inspection, to help laboratories understand and achieve the minimum quality standards established by CLIA. The surveyor is responsible for assessing the laboratory's performance based on review of the laboratory's past and current practices, interviews with the laboratory's personnel, and review of the laboratory's records. CLIA surveyors meet these objectives by employing an outcome-oriented approach focused on the overall performance of the laboratory and the way it monitors itself, rather than a methodical evaluation of each regulatory requirement (apart from "condition-level" deficiencies, discussed further below).

b. Each year, CMS conducts initial surveys of laboratories seeking a CLIA Certificate of Compliance (CoC), which are resurveyed every 2 years for recertification purposes. CMS also conducts validation surveys in a sample of laboratories deemed to meet CLIA requirements through accreditation by an approved private accrediting organization. Laboratories that only perform tests categorized as waived obtain a CLIA Certificate of Waiver (CoW), and are not subject to the CLIA nonwaived testing requirements, such as mandatory on-site surveys every two years. Laboratories holding a CoW may receive voluntary surveys (conducted in conjunction with the CDC). Additional surveys may be initiated based on complaints from the public, or unsuccessful proficiency testing by the laboratory. Finally, surveys of laboratories performing cytology testing are conducted by a specialized CMS contractor.

   Table 1, below, shows the average number of surveys conducted each year, in each category, from fiscal year (FY) 2011 through FY 2015 (not including surveys conducted by private accrediting organizations):

Table 1: Surveys Conducted (FY 2011–FY 2015)

Survey Type	Average annual number performed
Initial surveys of CoC laboratories	1,221
Recertification surveys of CoC laboratories	8,244
Validation surveys	356
Certificate of Waiver voluntary surveys	1,975
Complaint surveys	178
Unsuccessful proficiency testing surveys	2,548
Specialized cytology surveys	47

c. When a CLIA survey identifies a deficient practice in a laboratory, the surveyor cites the appropriate requirement in the CLIA regulations with which the laboratory is non-compliant. A "condition-level" deficiency is more serious than a "standard-level" deficiency, and must be corrected for the laboratory to continue patient testing. If sufficient correction is not demonstrated, CMS may initiate enforcement actions that could lead to termination of the laboratory's CLIA certificate (without which it may not operate). Table 2, below, shows the top 10 condition-level deficiencies cited nationally, based on survey data for 17,389 laboratories holding a Certificate of Compliance (CoC) as of December 2015. The survey data reflect surveys that occurred in FY2014 and FY2015 since laboratories are on a two-year survey cycle. The data represent the number of laboratories cited for each condition-level deficiency, and one or more conditions may be cited for each laboratory. For example, 555 CoC laboratories were cited for the first condition-level deficiency (Requirements for Moderate Complexity Laboratory Director) listed in Table 2. Some of those same laboratories may also have been cited for one or more of the other condition-level deficiencies listed in this table.

Table 2: Top 10 Condition-level Deficiencies (FY2014 & FY2015)

Condition Cited	Total Number of LabsCited Nationally	Percentage (%) of National Total*
Requirements for Moderate Complexity Laboratory Director	**555**	**3.2**
Requirements for Successful Proficiency Testing (PT) Participation	**375**	**2.2**
Requirements for High Complexity Laboratory Director	**262**	**1.5**
Monitoring of Analytic Systems	**236**	**1.4**
Requirements for PT Enrollment and Testing of PT Samples	**220**	**1.3**
Requirements for Technical Consultant – Moderate Complexity	**165**	**0.9**
Requirements for Laboratory Personnel – Moderate Complexity	**160**	**0.9**
Hematology Quality Control	**92**	**0.5**

Requirements for Testing Personnel – High Complexity	**90**	**0.5**
Requirements for Technical Supervisor – High Complexity	**61**	**0.4**

*****This column represents the percentage of the labs cited for each of the top 10 identified condition-level deficiencies cited nationally out of the total number of CoC laboratories (17,368) surveyed during one survey cycle in FY 2014 & FY2015).

The CLIA statute contains special rules for cytology testing including workload limits, specialized proficiency testing and personnel standards, and quality control procedures, reflecting Congress' particular concern about such testing when CLIA was enacted in 1988. Laboratories that perform cytology tests are surveyed by a specialized CMS contractor, which selects a sample of these laboratories to survey each year. An average of 47 specialized cytology surveys were conducted each year from FY 2010 through FY 2014. During that period, 37.3% of the cytology laboratories surveyed were cited for condition-level deficiencies. Table 3, below, shows the top 5 condition-level deficiencies cited at cytology laboratories surveyed by the CMS contractor for FY 2010 through FY 2014.

Table 3: Condition-level Deficiencies in Cytology Laboratories (FY 2010-FY 2014)

Condition Cited	Total Number of Times Cited Nationally
Requirements for High Complexity Laboratory Director	**66**
Requirements for specialty of Cytology	**40**
Requirements for Technical Supervisor – High Complexity	**27**
Requirements for Proficiency Testing (PT) Enrollment and Testing of PT Samples	**14**
Requirements for Successful PT Participation	**9**

3. Dr. Conway's written statement indicates that "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." However, as CMS acknowledges on CMS.gov, "the objective of the CLIA program is to ensure quality laboratory testing." How does CMS accomplish this mission without the ability to determine whether a test is difficult to carry out or likely to harm a patient?

Answer: As noted, CMS is responsible, under CLIA, for oversight of laboratories' day-to-day operations and procedures, including qualifications, training and proficiency of their personnel, performance assessments of their equipment, proper handling of specimens, etc.

This function is distinct from assuring the safety and effectiveness of laboratory tests, and does not include premarket review of laboratory tests, for which the FDA has the necessary authority (primarily under the Federal Food, Drug, and Cosmetic Act), and expertise.

FDA is also a critical partner in administering CLIA, which created a system of laboratory oversight based on test complexity. FDA's primary responsibility under CLIA is to classify clinical laboratory tests into one of three categories (waived, moderate complexity, and high complexity) based on their level of complexity and risk to patients if performed incorrectly. All tests introduced in the United States are considered high complexity by default unless FDA categorizes a test as waived or moderate complexity. FDA does not categorize tests that are designed, manufactured, and used within a single laboratory, known as laboratory-developed tests (LDTs). Thus, by default, they are considered to be high complexity tests.

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 for 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, or are simple and accurate with negligible risk of an erroneous result and pose a low risk to patients if performed incorrectly – are exempt from most CLIA requirements.

CMS enforces CLIA standards by requiring laboratories to obtain a certificate in order to operate, and conducting on-site surveys. Laboratories performing the same test must meet the same standards, whether located in a hospital, doctor's office or other site. 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.

4. During the hearing, Dr. Conway indicated that seven organizations are currently deemed authorities under CLIA. Please provide the following:

- **a. The names of each of the deemed authorities;**
- **b. The number of inspectors fielded by each organization as compared to CMS;**
- **c. The types of expertise and qualifications of the inspectors of each organization as compared to inspectors fielded by CMS;**
- **d. The number of laboratory inspections per year, per organization as compared to CMS; and**
- **e. A description of how inspections by a deemed organization may differ from an inspection conducted by CMS.**

Answer: The following table presents information on each of the seven accrediting organizations currently approved by CMS under CLIA. This information was provided by the accrediting organizations; thus we note that not all information is described consistently across entities, and may represent different time periods. The last column shows comparison information for surveys conducted by CMS or its contractors.

	A2LA	AABB	AOA/HFAP	ASHI	CAP	COLA	T
Organization Name	American Association for Laboratory Accreditation	Formerly known as the American Association of Blood Banks	American Osteopathic Association/ Healthcare Facilities Accreditation Program	American Society for Histocompat-ibility and Immunogen-etics	College of American Pathologists	Formerly known as Commission on Laboratory Accreditation	Th Co
Number of Inspectors	19	5 AABB employees (team leaders), and approx. 700 volunteer inspectors	16	150	25 CAP employees (staff inspectors and techs), and about 9,700 volunteer inspectors	24	
Inspector Expertise/ Qualifications (as described by each organization)	Bachelor's degree, 10 years experience.	Bachelor's degree in medical technology or related discipline, 3 years experience, in-depth knowledge of specialty areas. Training to maintain their competency to inspect.	At least a Bachelor's degree with certification as a medical technologist by the American Society for Clinical Pathology.	Employed at ASHI-accredited laboratories and familiar with all tests of each laboratory they inspect.	Practicing laboratorians trained to do inspections. Includes pathologists, Ph.Ds, medical technologists, respiratory therapists, histotechs, geneticists.	10-30 years experience. Ongoing training. Subject matter experts hired as needed.	Me Te w/ deg rel dis Pro lic rec law wi na ac org ex or tec sp set mu at of ma ex
Laboratories Inspected each	2[1]	100	90	100	4,000	4,000	

[1] A2LA is a recently approved accreditor; thus they had completed considerably fewer surveys than the other accreditors at the time this information was reported.

	A2LA	AABB	AOA/HFAP	ASHI	CAP	COLA	T
year							
Description of Inspections	Consists of defined steps for inspector preparation and on-site inspection.	An in-depth audit of the quality management system and technical requirements as specified in AABB Standards; also incorporates CLIA requirements. The quality system approach is a holistic review of an organization's policies, processes and procedures.	Material reviewed during a survey/ inspection covers all CLIA regulations.	More in-depth review of HLA typing in the laboratory [identifying an individual's unique pattern of HLA antigens]; some standards are more stringent than CLIA.	A team of experts from disciplines of the tests performed in the laboratory uses 21 discipline-specific checklists, including focus on emerging technologies. Instructions suggest open-ended questions, specific documents to sample, tracers to follow, and practices to observe.	Based on CLIA standards plus additional standards. Laboratories with serious or systemic noncompliance are referred to a special technical team that determines additional requirements and next steps.	Su is pa ce ev un sy an op us ap Su tra me re su "t ex a p th or

5. **CMS materials indicate that the States of New York and Washington have "CMS approved laboratory program(s)." Please provide the following:**
   a. Describe the difference in these state laboratory programs from those under CLIA.
   b. Further, the Committee understands New York State also inspects laboratories that are not located in New York State but provide services on patient samples originating in New York. How do these inspections and policies differ and intersect with CMS CLIA operations?

Answer: Washington and New York have CMS-approved state laboratory licensure programs equal to or more stringent than the CLIA program. While laboratories in these states must register with CMS for a CLIA identification number, these state programs have oversight authority for the laboratories located in their respective states.

a. Washington's survey and enforcement process is substantially equivalent to the CLIA process, but includes the following requirements that are different or more stringent than CLIA:

- Washington's enforcement process in regard to proficiency testing (PT) requirements is stricter than CLIA.
- Washington offers new state-inspected laboratories a free technical assistance visit, prior to their first inspection.
- All cited deficiencies must be corrected within 60 days of acceptance of the plan of correction. If the laboratory has repeat deficiencies from its previous 2 surveys, it gets a 1 year on-site follow-up survey for which it is billed. In contrast, CLIA has different timeframes for correction of deficiencies based on severity of the deficiency. Condition-level deficiencies must be corrected within 90 days and standard-level deficiencies must be corrected within 12 months. Repeat deficiencies are evaluated to determine if the level of overall noncompliance should be increased, which may affect enforcement actions.
- Washington surveyors assess whether clinical validity of a laboratory-developed test (LDT) has been established. If the laboratory has no evidence that clinical validity has been established, the surveyor may ask that a disclaimer be placed on the report, stating that the test has not been clinically validated. CLIA surveyors do not evaluate the clinical validity of LDTs, as clinical validity falls under the scope of the FDA, not CMS,

New York State's (NYS) Public Health Law is broader than CLIA in how it defines a "clinical laboratory." For example, NYS regulates forensic identity testing, parentage identity testing, forensic toxicology testing, and tests on some alternative types of samples. Laboratories that perform only the technical component of histopathology testing are also required to obtain a permit. These types of activities are not covered by CLIA. In addition, if a laboratory performs steps in the testing process at multiple locations – for example, processing of the specimen is performed at one location, testing/analysis at another location, interpretation at a third location, and reporting of

results at a fourth location -- each location must obtain a NYS permit. CLIA does not require a certificate for facilities that only perform specimen processing. In addition:

- The NYS law authorizes State experts to review LDTs to determine whether the proposed testing is both analytically and clinically valid, before the testing can be performed on specimens from NYS. CLIA does not address clinical validity.
- A laboratory may not perform testing either in NYS or on specimens from NYS until it has met on-site survey, proficiency testing, and validation requirements, if applicable, and has been issued a NYS permit. In contrast, CLIA allows laboratories to begin testing with a Certificate of Registration prior to the initial survey, which is performed 3-12 months after testing as begun.
- The NYS law defines specific training and education requirements for laboratory directors, which are more stringent than CLIA. For example, the director must have relevant training/experience obtained within the last 6 years to direct testing in a specific specialty/category.
- Some NYS specialty standards, such as for genetic testing, require that all reports be signed by the qualified person who reviewed, approved, and interpreted the test results. In general, CLIA is less prescriptive.
- The NYS law defines a supervisor as a licensed clinical laboratory technologist with 6 years of post-licensure clinical experience. In contrast, CLIA requirements for technical supervisors differ by educational level. The longest period required by CLIA is for Bachelor's degree-level applicants, who must have 4 years of experience in the specialty/subspecialty they are supervising.

b. In regard to testing performed on patient specimens originating in New York State, the NYS law does not differentiate between laboratories located in NYS and those serving New York residents that are located outside of NYS. Thus, all laboratories performing testing in NYS, or on NYS samples, must meet State requirements to be eligible for a NYS permit. Similarly, since CLIA applies to all laboratories in the U.S., inspections and policies under CLIA are not based on location of the laboratory.

6. On April 16, 2015, the FDA and CMS announced the formation of the "Task Force on LDT Quality Requirements." Please provide the following:

a. The scope of the Task Force's work;
b. When findings or conclusions of the Task Force will be made public and, if not to be made public, the rationale for not making public;
c. The anticipated time period the Task Force is expected to operate; and
d. The extent to which the Task Force is coordinating with industry, and/or provider, and/or patient stakeholders.

Answer: To coordinate efforts across the Department of Health and Human Services, FDA and CMS established an interagency task force in April 2015 to continue and expand on our collaboration related to the oversight of laboratory-developed tests (LDTs). The Task Force, comprised of leaders and subject matter experts from each agency as well as NIH and CDC, is working to address a range of issues, including those involving quality requirements for

LDTs. There is no set endpoint for the Task Force, which will continue operating as long as it is determined to be useful by the participating agencies.

The Task Force goals include:

- Clarifying FDA and CMS roles in the oversight of LDTs and clinical laboratories.
- Addressing the needs and concerns of clinical laboratories in regard to their development of LDTs, and how laboratories would implement the FDA Quality System regulation requirements.
- Investigating how to best leverage joint resources to develop appropriate training, avoid duplication, and maximize efficiency of efforts.

The first product of the Task Force was a joint blog, detailing FDA and CMS responsibilities with regard to LDTs and clinical laboratories. The blog was published on both FDA and CMS CLIA websites on April 17, 2015. FDA also held meetings with each of the CLIA-approved accreditation organizations to review their survey processes.

The Task Force will also seek and facilitate input from a range of stakeholders including industry, providers, and patient advocates, through public forums and other information-sharing processes.

Underlying the Task Force's work is FDA's and CMS' agreement on their complementary roles in regulating laboratories and laboratory tests. CMS, under CLIA, focuses on the laboratories' overall performance whereas FDA, under the Federal Food, Drug, and Cosmetic Act (FFDCA), focuses on the safety and effectiveness of LDTs. , Although each agency's role is different, FDA and CMS share an interest in ensuring effective and efficient oversight of LDTs so laboratories can offer innovative tests to the American public with confidence that they are accurate and provide clinically meaningful information, without unnecessary or duplicative agency oversight.

<u>The Honorable Frank Pallone, Jr.</u>

The Clinical Laboratory Improvement Amendments are quality standards that apply to all clinical laboratories to ensure that test results are accurate and reliable. The standards a lab must meet correspond with the complexity of the test – labs performing more complex tests must meet higher standards – and are focused on personnel qualifications, laboratory systems, quality control and proficiency testing. Some stakeholders have advocated for a modernized CLIA as a way to address gaps in oversight over LDTs.

To better understand the limitations of CLIA's authority in comparison to the FDA's proposed regulatory framework, please respond to the following questions:

1. **Does CMS require labs to provide any evidence that the tests labs are performing are producing accurate results?**

Answer: CMS looks for evidence of test analytical accuracy during the on-site surveys. CLIA requires the laboratory to have documented evidence of analytical validation, proficiency testing, quality control, quality assessment monitors, etc.

2. **Does CMS require labs to provide evidence that would support claims they make about their tests?**

Answer: CLIA does not address clinical claims about tests made by a laboratory.

3. **Does CMS collect or report on any adverse events for tests?**

Answer: No, CMS does not collect or report on any adverse events related to testing devices. We report on laboratories on which sanctions have been imposed related to risk of patient harm due to deficiencies in laboratory operations.