October 15, 2014

American Clinical Laboratory Association

Sydne Harwick
Legislative Clerk
Committee on Energy and Commerce
2125 Rayburn House Office Building
Washington, D.C. 20515

Via USPS and Electronic Mail to: sydne.harwick@mail.house.gov

RE: 21st Century Cures: Examining the Regulation of Laboratory Developed Tests - Questions for the Record

Dear Ms. Harwick,

Per your letter dated September 30, 2014, attached are my responses to the additional questions for the record brought forth by the Honorable Michael C. Burgess.

ACLA greatly appreciated the opportunity to participate in the September 9, 2014 21st Century Cures hearing, "Examining the Regulation of Laboratory Developed Tests". The 21st Century Cures Initiative hosted by Chairman Fred Upton and Rep. Diana DeGette has been a critical dialogue between Congress and health care stakeholders on ensuring medical innovation continues in the United States to improve the quality and access of care available to patients.

As has been mentioned in multiple Cures hearings and roundtables, clinical laboratory diagnostics, including molecular and genomic testing, play a crucial role in diagnosing and characterizing diseases so that patients can receive the best treatment sooner. Laboratory developed tests (LDTs) have been at the forefront of this innovation, lowering costs and saving lives. The FDA's proposal to newly apply the FDA medical device oversight framework to LDTs and laboratories threatens this innovation by duplicating costs and standards that already exist under the Clinical Laboratory Improvement Amendments and by creating new barriers to patient access.

ACLA looks forward to continuing work with the Committee to ensure robust innovation in clinical laboratory diagnostics that will lower health care costs and improve the quality of care available to patients.

Sincerely,

Alan Mertz
President
American Clinical Laboratory Association

The Honorable Michael C. Burgess

1. **Some advocates in favor of the FDA intervening in LDTs have suggested that laboratory tests are unregulated (or inadequately regulated) because they have not been required to go through FDA review. Is this the case? Have LDTs been unregulated all these decades that FDA claims to have been exercising "enforcement discretion?"**

No, this is not the case.

The clinical laboratory industry has been extensively regulated for decades under a comprehensive, interlocking framework of federal laws, state laws, and peer review "deemed" authorities. The primary federal law governing labs has been the Clinical Laboratory Improvement Amendments (or CLIA), specifically the Clinical Laboratory Improvement Amendments of 1988. CLIA creates stringent requirements governing the operation of clinical laboratories to ensure the safe and accurate function of laboratories and the testing services they provide. These requirements cover the laboratories themselves, the necessary certifications for laboratory personnel from pathologists and geneticists to technicians, and the documentation of procedures for individual clinical laboratory tests. In addition, laboratories are also subject to inspections under both CLIA and state law.

Further, moderate and highly complex laboratories, including all ACLA members, can submit to additional oversight through deemed peer review authorities, such as the College of American Pathologists, the Joint Commission, and others, which add additional expertise in reviewing both the operation of the laboratory and the analytical and clinical validity of individual tests. This additional oversight for moderate and high complexity laboratories also involves the use of proficiency testing to ensure the accuracy of testing results.

A group of 23 lab directors from the nation's leading academic medical centers wrote to the Acting Director of the Office of Management and Budget on July 16, 2014 and stated that "as part of this oversight, clinical laboratory physicians and scientists, including most of the signatories to [the] letter, perform careful inspections of laboratory facilities, exhaustive review of test protocols and validation, and continually monitor laboratory performance. This regulatory framework requires both extensive validation and continuous monitoring to ensure the performance, quality, and reliability of diagnostic services, yet allows laboratories the flexibility to develop and validate lab tests quickly and, thus, more quickly adopt new scientific knowledge and rapidly respond to unmet public health needs."

Operating under this comprehensive yet flexible LDT oversight framework, the field of laboratory medicine has thrived, producing some of the most spectacular advances in medicine to occur in the last century. As highlighted in the aforementioned academic medical center lab director letter to OMB, "LDTs have long addressed emerging public health risks, such as HIV. For example, no HIV-1 antibodies confirmatory test was available when the HIV-1 screening test was introduced in 1985. Clinical laboratories developed and validated an LDT Western blot to meet the critical need to establish definitive diagnoses of HIV-1. It took two years before an FDA-approved Western blot test became available. Even now, the FDA-approved Western blot kit has not significantly changed since its first approval. Because obtaining additional FDA approvals for test modifications would be so burdensome, the manufacturer has not modified the test to keep up to date with the medical science." Advances such as theses "came about because of, and would not have been possible without, the current regulatory framework governing LDTs."

2. **Reimbursement for most diagnostic tests is very low. If the anticipated revenue for a test over time is lower than what a company would need to spend for FDA pre-market approval will companies now abandon development of tests that can benefit our healthcare system?**

Reimbursement for diagnostics has experienced extreme downward pressure in both the private and public payer settings over the last few years. Many laboratories, particularly those in the molecular and genetic testing space which has been so crucial to the personalized medicine revolution, have faced unsustainable reimbursement rates that in some cases do not cover the basic costs of performing the tests. Certainly layering additional burdensome and duplicative regulatory requirements on top of the exiting oversight framework will dramatically increase the cost of development for any test, and will likely prevent laboratories from moving forward with many promising new tests for which they are already unlikely to recoup the cost of investment, even without the additional layer of regulation under the FDA.

Many tests today are available only as LDTs. The reasons vary. In some cases, there is no financial incentive to perform clinical trials and seek FDA approval or clearance of a test for a well-accepted, clinically recognized biomarker, because the test will serve only a small patient population. In other cases, a kit has not yet completed the FDA authorization process.

With evolving medical technology, clinical laboratories are well positioned to develop more novel LDTs that will diagnose or otherwise allow evaluation of other diseases and conditions for which there is no available IVD test kit. But if FDA moves forward in regulating this testing under its device authorities, many of the tests will become unavailable, with adverse effects on patient care. Some of these tests will never generate the financial returns needed to justify the costs of obtaining FDA clearance or approval, notwithstanding well-accepted and recognized clinical support in the form of peer-reviewed research and/or laboratory-based studies. Clinical laboratories currently are filling a significant gap for individuals with these diseases, and FDA regulation would preclude them from service these medical needs. Even if some laboratories elect to pursue the FDA authorization process rather than discontinuing their tests, they would need significant time to generate data needed to support a submission and to obtain approval of that submission. During this time, FDA regulation could preclude availability of these LDTs, which would compromise patient care.

3. **How will the FDA proposed LDT regulations impact current CLIA certification process? Will it weaken CLIA or cause duplication, redundancy and excessive administrative burdens on small companies?**

Presently, it is difficult to see how the FDA's proposed LDT regulations will impact the current CLIA certification process, as there is no discussion of how any additional regulation by the FDA would interact with the regulation already in place under the CLIA program, including those functions performed by deemed authorities. There are many areas of commonality and overlap, specifically with respect to validation, inspections, and Quality Systems Regulation (QSR), and yet there is no discussion of how the two separate regulatory authorities would regulate the laboratory industry in a way that would not impede innovation. The Agency, apparently acknowledging the very clear potential for overlapping and duplicative regulatory requirements, had discussed a third guidance document that it planned to release with the actual draft guidance which was to specifically address how the QSR requirements applicable to devices under the FDA would interplay with the quality requirements under CLIA. The Agency did not release such a document with the formal release of the Draft Guidance

documents, and has stated that it no longer plans to release such a guidance document. Rather, it has said that it will rely on a third-party organization to explain how CLIA and FDA's QSR requirements could be reconciled. ACLA believes that it is wholly inappropriate for FDA to leave such a vital issue to an unaccountable third party to resolve.

Laboratories would bear substantial burdens in seeking to comply with FDA requirements applicable to devices, even if only a subset of LDTs were determined to be subject to premarket review. Laboratories likely would need to adopt wholly new procedures and processes to comply with FDA's QSR requirements, which would pose special challenges because FDA has not defined how QSR requirements would apply in the laboratory context. Laboratories also would need to comply with adverse event reporting, labeling, and promotional requirements. These requirements would apply even if FDA regulated only one of a laboratory's LDTs. Laboratories also would be likely to encounter challenges in complying with both CLIA and the FDCA. For example, it could be difficult to comply with FDA promotional requirements while fulfilling CLIA requirements to offer consultation on interpreting test results. And although CLIA regulations require laboratories to provide pertinent updates on testing information as soon as it is available, FDA requirements for obtaining approval or clearance of labeling changes could preclude this action. Laboratories also would encounter duplicative regulation, such as inspection by both FDA and CMS. This additional regulatory burden would be both costly and unwarranted, and particularly onerous for smaller laboratories.