



Better health through  
laboratory medicine.

August 20, 2018

Congressman Larry Bucshon  
U.S. House of Representatives  
1005 Longworth House Office Bldg.  
Washington, DC 20515

Congresswoman Diana DeGette  
U.S. House of Representatives  
2111 Rayburn House Office Bldg.  
Washington, DC 20515

Re: FDA Technical Assistance Comments on the Diagnostic Accuracy and Innovation Act

Dear Representatives Bucshon and DeGette,

The American Association for Clinical Chemistry (AACC) appreciates the opportunity to comment on the Food and Drug Administration's (FDA's) technical assistance comments pertaining to the Diagnostic Accuracy and Innovation Act (DAIA). Although we certainly share your desire to improve the quality of patient care, we do not believe this draft legislation, in its current format, accomplishes that aim.

AACC is a global scientific and medical professional organization dedicated to clinical laboratory science and its application to healthcare. AACC brings together more than 50,000 clinical laboratory professionals, physicians, research scientists, and business leaders from around the world focused on clinical chemistry, molecular diagnostics, mass spectrometry, translational medicine, lab management, and other areas of laboratory science to advance healthcare collaboration, knowledge, expertise, and innovation.

AACC agrees that the increase in the number and complexity of laboratory developed tests (LDTs) perhaps warrants a new assessment of regulatory and professional oversight for these tests. Although we agree some adjustments may be necessary, we believe that the current oversight structure is generally adequate and that a major change in policy is unwarranted. Our specific comments follow.

### **Current Regulatory System**

There appears to be a misconception that because the FDA is using its "enforcement discretion" regarding LDTs that these tests are unregulated. This belief is inaccurate. Currently, all laboratories performing LDTs are regulated under the Clinical Laboratory Improvement Amendments (CLIA). These testing facilities are categorized as high complexity laboratories, subject to stringent personnel, quality control and proficiency testing requirements as well as regular inspections.

Many of these same facilities actively participate in the New York State, Joint Commission, College of American Pathologists (CAP) or other oversight programs, where they often must meet requirements more stringent than CLIA. We are concerned that expanding oversight to include another federal agency will, in many instances, add to the regulatory burden and costs of performing LDTs. This may result in many laboratories discontinuing these tests, stifling diagnostic innovation and negatively impacting patient care.

AACC feels it is important to note that the FDA regulatory structure is designed for medical device manufacturers, not clinical laboratories. Manufacturers provide invaluable test kits and instrumentation that assist laboratories in providing accurate test results. Laboratories occasionally modify FDA cleared or approved tests or develop new in-house tests to meet specific clinical needs. The results from these tests are used to diagnose and treat patients. To apply FDA regulatory requirements to hospitals and independent laboratories utilizing LDTs would be misguided and counterproductive to excellent patient care.

#### ***Risk-Based Classification Process***

AACC supports the use of a risk-based approach to stratify LDTs and determine the appropriate level of oversight. The current definitions of high and low risk in the draft document are reasonable, but we are concerned how this language could be interpreted, particularly the term “remote” in the definition of high risk. How “remote” is defined can result in a very large or limited number of tests placed within this category.

From our perspective, the high-risk category should be very narrow in scope. For example, AACC suggests the following criteria for designating high-risk tests:

- the accuracy of the test cannot be independently verified;
- there is a lack of transparency regarding the underlying data to support claims made about the test; and
- the absence of professional consultation/interpretation could lead to serious patient harm.

Examples of high risk tests include In Vitro Diagnostic Multivariate Index Assays (IVDMIAs) and direct-to-consumer genetic tests.

#### **Grandfathering of LDTs and Maintaining Innovative LDTs**

The draft measure would grandfather LDTs that are performed prior to a certain date from having to comply with premarket review requirements. Although AACC does not believe LDTs should be subject to the FDA review process, we oppose efforts to grandfather LDTs within any regulatory scheme. The development of LDTs plays a critical role in providing new innovative technologies that offer hope and assistance to many patients. The clinical laboratory community has historically been quick to respond to changing clinical and service demands, such as meeting the need for more sensitive and specific therapeutic drug monitoring tests and filling the gaps

when FDA-cleared or approved commercial tests are unavailable, for example, new tests for inborn errors of metabolism, Ebola, Zika or H1N1. The best means of maintaining this innovative process is to keep the current regulatory structure in place with only minor modifications—thus excluding grandfathering from any reform initiative.

### **Tests for Rare Diseases**

There are many medical conditions for which it is not cost-effective for an IVD manufacturer to develop a commercial assay. Clinical laboratories have traditionally filled this void through LDTs. The draft bill identifies several testing categories that would be exempt from pre-market review, such as emergency use, low-risk, rare disease, and public health surveillance testing, amongst others, if they meet certain criteria. We agree that these LDTs should not be subject to additional FDA oversight. AACC has real concerns about how the FDA, if it was given authority over this testing, would implement the provisions.

The FDA revised measure does not exempt newborn screening from FDA oversight. Language included under the Public Health Surveillance section seems to imply such an exception, but it is not clear. AACC suggests that a separate section on Public Health Testing be created that specifically exempts newborn screening.

The draft bill also defines a rare disease as testing fewer than 8,000 individuals annually for a condition. This is an arbitrary number, which seems low. Further, the characterization differs from the definition adopted by Congress in the 2002 Rare Disease Act (Public Law 107-280), which specifies that a rare disease is “any disease or condition that affects less than 200,000 persons in the United States.” This provision needs clarification.

### **Precertification**

The FDA is proposing that DAIA include a precertification provision that would allow an individual, if they meet certain criteria, to introduce certain tests without going through the premarket review process. The wording of this section is confusing as it applies to clinical laboratories. This section seems to require a single individual (i.e., test developer) to apply for precertification. It is unclear whether the “test developer” can be an individual, a laboratory or a manufacturer. In addition, once precertification is achieved, it is unclear whether high or low risk tests can be developed or whether any type of review of those tests will be performed.

Regardless of whether the intent is to focus on the individual or the entity, the precertification process appears to be nearly as cumbersome and costly, from a clinical laboratory perspective, as the existing 510(k) review process. According to the document, the applicant would need to seek precertification for each “single technology” and each “single medical specialty.” For many laboratories, this could involve submitting numerous applications affecting many specialties. The ultimate effect of requiring laboratories to go through the 510(k) or precertification processes will be to eliminate many LDTs and stifle innovation. This section re-enforces our underlying premise—clinical laboratories are not medical device manufacturers and that possible

modifications pertaining to regulatory oversight of clinical laboratories should be made within CLIA.

### **Registration and Notification**

The FDA technical assistance document recommends that manufacturers and laboratories register annually with the Secretary if they develop LDTs. In addition, test developers would be required to provide the Secretary with 17 types of data for each test. AACC is concerned that this process is redundant, costly, and presents an undue administrative and financial burden on many testing facilities.

Currently, CMS requires that all CLIA laboratories submit a laboratory activity list to the agency that comprises all the tests it performs, including LDTs, as well as the methodologies utilized. CAP, a key private accrediting body, requires that laboratories provide a specific list of all LDTs they perform. Further, much of the data requested under the draft measure is already collected by CMS and the CLIA program and/or its deemed accrediting bodies. AACC suggests that any additional data be gathered during routine CLIA inspections within the current regulatory framework. At a minimum the paperwork reduction principle should be applied so that laboratories need only submit information once per review cycle and that data should be shared amongst regulatory agencies.

### **Quality System Requirements**

Recently there has been flexibility introduced into laboratories performing LDTs in the form of the Individual Quality Control Program (IQCP) option to meet quality system documentation requirements. We feel that this framework meets many of the intentions of the proposed FDA oversight, and therefore we suggest that IQCP under CLIA be the standard quality system requirement for laboratories performing LDTs.

### **Adverse Event Reporting**

The FDA document states that test developers must “establish, maintain, and implement” a reporting system that notifies the agency of adverse events quarterly, unless the event presents an imminent threat to public health or involves a patient death. AACC does not believe the adverse event framework, which was developed for reporting problems involving medical devices, is appropriate for services provided by clinical laboratories. Results from LDTs do not generally result or contribute to the death or serious injury to a patient.

During a January 2015 FDA Public Workshop on LDTs, the Mayo Clinic reported that over the previous five years it had produced more than 2.5 million LDT-based tests without a single sentinel event (The Joint Commission defines a sentinel event as a safety event that results in death or permanent harm to the patient). One reason for the overall safety of LDTs is that laboratories implement internal quality controls that detect many analytical and pre-analytical errors and prevent wrong results from being reported. The current CLIA regulatory framework also requires laboratories to identify, document and perform corrective measures for any

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laboratory errors, and this would include errors resulting in patient harm if they were to occur. This documentation is reviewed on a regular basis by CLIA or accrediting bodies. AACC recommends that when a laboratory identifies a testing error it should report that mistake to the appropriate oversight body.

### **User Fees**

The draft measure includes a placeholder for additional user fees that can be applied to laboratories performing LDTs. Reimbursement for clinical laboratories is being cut dramatically under the Protecting Access to Medicare Act, while at the same time testing facilities must pay registration/accreditation fees under CLIA as well as incur the costs of on-site inspections and periodic proficiency testing to demonstrate performance. The regulatory requirements outlined in this technical assistance document, along with the additional costs, would assure that only a few, if any, laboratories would continue to offer LDTs. Unfortunately, this outcome would stifle innovation and harm patient care.

On behalf of AACC, I would like to thank you for the opportunity to provide comments on this FDA redlined document regarding DAIA. If you have any questions, please email Vince Stine, PhD, AACC's Director of Government Affairs, at [vstine@aac.org](mailto:vstine@aac.org).

Sincerely,

A handwritten signature in black ink, appearing to read "Dennis J. Dietzen". The signature is fluid and cursive, with a long horizontal stroke at the end.

Dennis J. Dietzen, PhD, DABCC, FAACC  
President, AACC