PERSONALIZED MEDICINE COALITION

August 20, 2018

The Honorable Larry Bucshon
U.S. House of Representatives
1005 Longworth House Office Building
Washington, D.C. 20515

The Honorable Diana DeGette
U.S. House of Representatives
2111 Rayburn House Office Building
Washington, D.C. 20515

RE: Request for Comment on U.S. Food and Drug Administration Technical Assistance on the "Diagnostic Accuracy and Innovation Act" Discussion Draft

Dear Representatives Bucshon and DeGette:

On behalf of the Personalized Medicine Coalition (PMC), which represents innovators, scientists, patients, providers, and payers to promote the understanding and adoption of personalized medicine concepts, services, and products for the benefit of patients and the health care system, I am writing to share PMC's appreciation for the opportunity to provide initial comments regarding the U.S. Food and Drug Administration's (FDA's) technical assistance (TA) on the "Diagnostic Accuracy and Innovation Act" (DAIA) discussion draft.

PMC defines personalized medicine as an emerging field that uses diagnostic tools to identify specific biological markers, often genetic, to help determine which medical treatments and procedures will be best for each patient. By combining this information with an individual's medical history and other clinical information, personalized medicine allows doctors and patients to develop targeted prevention and treatment plans. The goal is to provide the right treatment in the right dose to the right patient at the right time.

Our interest in the FDA's TA on the DAIA discussion draft pertains to how legislation can best support this emerging field. We seek to ensure that the field can move forward in enhancing patient care and improving the quality, safety, accuracy, and effectiveness of treatments, with the acknowledgement that innovation and access should be balanced with patient protections. While we understand that FDA's submission of the TA to your office represents an important step in moving legislative discussion forward, the TA is in effect a new bill which includes ideas that must be properly vetted to assess the impact they could have on innovation and patient access. PMC recommends that you provide ample time for stakeholders to provide feedback on FDA's proposal and any potential revisions to DAIA. We also encourage you to solicit a response for TA from the Centers for Medicare & Medicaid Services (CMS) on how DAIA and FDA's TA on the DAIA discussion draft would impact the Clinical Laboratory Improvement Amendments (CLIA) program.

Personalized Medicine Coalition
personalizedmedicinecoalition.org
1710 Rhode Island Ave., NW, Suite 700
Washington, DC 20036
P: 202.589.1770
F: 202.589.1778

Many of PMC's members will present their own responses to the FDA's TA on the discussion draft and will actively advocate for those positions. To support the work of our member organizations, we therefore note the following disclaimer: nothing in these comments is intended to impact adversely in any way the ability of individual PMC members, alone or in combination, to pursue separate comments. Additionally, PMC does not hold a position on whether laboratory-developed tests (LDTs) should be regulated by the FDA or by the CLIA program at CMS. PMC's comments are focused exclusively on personalized medicine issues and are designed to communicate areas of consensus with regard to LDTs, which may be applicable to in vitro clinical tests (IVCTs).

In 2016, PMC moderated a series of discussions on potential legislative solutions with representatives from the diagnostics community, including but not limited to those with an interest in personalized medicine. Six consensus principles emerged from those conversations, which we highlighted in comments submitted to you in July of 2017. We will reiterate these principles because we believe they are critical for you to consider as you review the FDA's TA, conduct further stakeholder discussions, and pursue additional legislative activity.

1. Protect public health labs.

Public health labs should be protected by any regulatory paradigm, which means that sentinel, infectious disease, and public health labs must be able to design, deploy, and use rapidly developed diagnostics to address critical public health needs. DAIA clearly indicates that any FDA review requirements should not apply to tests intended to be used solely for public health surveillance. We appreciated the inclusion of this language in the DAIA discussion draft and we urge you to retain these provisions in any future versions of the legislation.

2. Allow flexibility and efficiency when managing modifications.

As test developers have long argued, the way test modifications are managed by a regulatory system should be flexible and efficient to allow diagnostic tests to evolve with the clinical science that underpins them. The DAIA draft legislation would give FDA the flexibility to approve IVCTs with associated processes for allowing certain modifications, including specimen type, to take place without additional premarket review. PMC believes this is an important feature to include in any future versions of the legislation so that improvements can be made without delaying access and increasing regulatory costs.

3. Mitigate regulatory burdens for government and industry.

To reduce burdens on government and industry, regulatory agencies should recognize when certain safeguards are already in place. These mitigation strategies can help regulatory bodies keep pace with the rapidly evolving science of personalized medicine diagnostic testing. The DAIA discussion draft attempted to clearly delineate between FDA- and CLIA-associated activities. FDA's views on an approach to adverse event reporting are included in the TA but we encourage you to further explore with the community and CMS how reporting systems should be harmonized to prevent unnecessary administrative burdens on what types of information should be reported to whom.

4. Design a grandfathering provision for tests already on the market along with a risk classification system for novel tests.

Tech firm Concert Genetics estimates that as of March 1, 2018 there are nearly 75,000 personalized medicine diagnostics offered by labs, with another fourteen coming to market each day.[i] To manage such an enormous workload, a regulatory agency must design a grandfathering system that will allow most tests to remain on the market unless there is a compelling reason to remove them.

The DAIA discussion draft grandfathered all LDTs first offered more than 90 days prior to the date of enactment, but required that developers of non-reviewed, high-risk tests submit certain data to FDA within five years of the bill's enactment. PMC believes this approach lessens the burdens on FDA and laboratories significantly, while also seeking to protect patients by reviewing information associated with tests that could cause a patient serious or irreversible harm, prolonged disability, or death if there is a clinically significant, inaccurate result that goes undetected when the test is used as intended. In addition, the discussion draft sought to prevent duplication of state activities for grandfathered tests by exempting tests that have already been reviewed by the New York State Department of Health. This least burdensome approach to grandfathering that prevents duplication should be carried forward in any future versions of the legislation.

Likewise, it is critical that a consistent and transparent risk classification system be agreed to and described before enactment of new legislation governing the oversight of IVCTs. The FDA's TA eliminates one of three risk categories (moderate risk) from the discussion draft, which makes it unclear how a significant number of diagnostic tests would be regulated and could have significant unintended consequences.

We are also concerned that the FDA's TA provides a drastically different definition for IVCTs than is included in the DAIA discussion draft. It is broadened to include components, parts, and software used for the purpose of disease detection, diagnosis, screening, prediction, and monitoring, and for selecting treatment based on analysis of human samples.

PMC is still evaluating the impact that these substantial changes proposed by the FDA would have on our members.

5. Ensure regulatory burdens reflect testing volumes.

Regulatory burden must reflect testing volume. For example, diagnostics designed for rare and unmet needs should be given careful and different consideration to ensure that tests are developed for micromarkets. PMC appreciates that the draft legislation designs a special pathway for tests that fill unmet needs, and provides carve-outs for custom IVCTs and tests for rare diseases. However, the TA definition of a test for rare diseases would be based on the number of individuals who would be subject to testing, which may not be knowable, rather than being based on disease incidence. PMC urges you to work with stakeholders to find a reasonable solution to this issue.

6. Accept valid scientific evidence for regulatory purposes — even if that evidence does not include data from a randomized, controlled trial.

Personalized medicine challenges how health care products and services are conceived, developed, regulated, covered, paid for, and used by physicians. Evidentiary requirements for regulatory review must also evolve. The community agrees that, regarding diagnostics, valid scientific evidence should be acceptable for regulatory review even when that evidence does not include data from randomized, controlled trials. The DAIA discussion draft outlined various types of evidence to demonstrate analytical and clinical validity, including peer-reviewed literature, clinical guidelines, case studies or histories, consensus standards, and reference standards. This approach would not seem to be supported by the FDA's TA. We urge you to retain language included in the March 2017 DAIA discussion draft on acceptable sources of evidence to demonstrate analytical and clinical validity in any future version of the legislation.

PMC is committed to working with you and your colleagues to advance these principles and find additional areas of consensus. We welcome the opportunity to provide ongoing input to you as you work to strike the appropriate balance between regulation, innovation, and access to personalized medicine diagnostic tests. If you have any questions about the content of this letter, please contact me at cbens@personalizedmedicinecoalition.org or 202-589-1769.

Sincerely,

Cynthia A. Bens
Senior Vice President, Public Policy

CC: Senator Orrin Hatch
Senator Michael Bennet

[i] Concert Genetics. *The Current Landscape of Genetic Testing: 2018 Edition*. Accessed; August 18,2018. http://www.concertgenetics.com/wp-content/uploads/2018/04/12_ConcertGenetics_CurrentLandscapeOfGeneticTesting2018.pdf