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August 27, 2007

VIA Electronic Submission

Division of Dockets Management  
HFA-305  
Food and Drug Administration  
5603 Fishers Lane  
Room 1061  
Rockville, Maryland 20850

Re: Docket No. 2006D-0347  
Draft Guidance for Industry, Clinical Laboratories, and FDA staff  
on *In Vitro* Diagnostic Multivariate Index Assays (IVDMIA)

Dear Madam or Sir:

The Personalized Medicine Coalition (PMC), a federation of over 100 organizations representing a broad spectrum of academic, industrial, patient, provider and payer communities, is providing comments on *Draft Guidance for Industry, Clinical Laboratories, and FDA staff on In Vitro Diagnostic Multivariate Index Assays*. Overall we are pleased that this new draft guidance clarifies the definition of IVDMIA, further details the risk-based regulatory intent, acknowledges challenges faced by industry regarding potentially conflicting CLIA and FDA regulations, and outlines a transition timeline. Our suggestions to FDA on advancing personalized medicine are italicized.

FDA has encouraged laboratories to contact them “early and often” as they enter the regulatory process, and we hope that FDA will do the same by engaging industry in an active dialog in the future. The PMC emphasizes that diagnostic platforms, such as IVDMIA technologies and services provided by their use, are critical assets for the individualization of risk assessment, therapeutic selection, and prediction of health and disease intervention outcomes. As a result, these technologies represent a cornerstone for advances to enhance health care through the clinical transformation of science to benefit patients.

We recognize that the IVDMA class of products is among many new areas of medical test development and application that will represent new opportunities for health care, but will also bring new challenges. In this regard, it is important that confidence is built in the processes that are used to provide medical practitioners, consumers, and others with the requisite evidence that test information is valid. The future of personalized medicine depends on these technologies, the information they provide, the transparency of the processes used to apply them, the evidence base that guides their usage, and the oversight of their development and performance.

### **Definition of IVDMIAs**

We appreciate FDA's efforts to revise substantially the draft guidance of September 2006 by clarifying and further defining its descriptive parameters. We believe that the framework suggested in this draft improves understanding of which laboratory- and industry-developed tests will fall under this guidance. By providing additional clarity on the limited scope of tests the FDA intends to regulate, this draft has, to a large extent, alleviated concerns raised in prior public forums and docket submissions that the breadth of tests being addressed by the first guidance was overly expansive. We are pleased that FDA bases its oversight on the risk associated with the health care decision made by the patient in response to test results, and not on the technology behind the test. As the process moves forward, we urge FDA to continue to focus its oversight on risk to patients, not technology.

### **CLIA**

We recognize that a fundamental objective in developing the regulatory environment for these technologies is to provide medical practitioners and patients with assurances of the safety, effectiveness, and quality of these medical products while, at the same time, maintaining parameters that do not place undue restrictions on test developers and stifle innovation through overly burdensome requirements. To ensure patient safety in ways that support timely development and dissemination of these medical products, the FDA should consider more patient and industry participation in the future contemplations of test evaluation parameters and the implementation phase of these requirements. *We suggest that overall FDA and CLIA authorities increase their efforts to interact with genomic test developers and laboratories that perform these tests to provide clear and consistent messages that facilitate better understanding of each party's role in oversight.* The best time for improved communication and understanding is at the early stage of marketplace entry. We therefore believe that the PMC can help its members, the FDA, and others to understand the new regulatory environment by providing a forum for inquiry and discussion as personalized medicine progresses and is adopted.

For example, Quality System regulation (QSR) guidance development offers FDA and the community an opportunity to engage. FDA has indicated that some of the QSR may be partially fulfilled by corresponding QSR in CLIA, and has indicated intention to issue guidance to assist

laboratories and test developers in navigating these two systems. *We urge FDA to maintain its history of robust dialog with industry and to consider hosting a workshop with all interested stakeholders before issuing guidance on QSR. To clarify the relationship between FDA and CLIA regulation for IVDMIAs, we request that FDA publish an analysis and side-by-side comparison between FDA's Medical Device Regulation for Manufacturers of in vitro diagnostic kits (21 CFR Parts 803, 807, 809, 810, 820), and CLIA regulations for laboratories developing diagnostic test services (42 CFR Part 493). To provide industry with greater clarity, FDA should outline specifically what medical device regulations laboratories would be subject to, and which requirements a laboratory is accountable to under CLIA.*

## **Reimbursement**

Many in the community are concerned that as currently marketed and reimbursed IVDMIAs go through this regulatory transition, reimbursement may be unavailable to patients from third-party payers. It is our understanding that when an IVDMIA is submitted to FDA, that test is deemed “investigational” by the FDA until it is cleared and that the device submission and approval process can take many months to complete. Currently, private and government health insurers, (including Medicare, Medicaid and the Federal Employees Health Benefit Plan), rarely cover services that are deemed “investigational” by the FDA. Without health insurance coverage and reimbursement for these currently available tests, only those patients who can afford to pay out-of-pocket for tests will have access to these IVDMIAs in the interim. FDA should work with CMS, commercial payers, and others on developing ways to avoid these possible but unintended outcomes. *We believe that a coordinating policy office at HHS for personalized health care could ease the transition between FDA pre-market regulation and government reimbursement for tests currently on the market, while maintaining the agencies' separate and distinct jurisdictions.*

## **Timeline**

The PMC believes that by defining most IVDMIAs as Class II or Class III devices that require clearance or pre-market approval from FDA, the agency's historical practice regarding the use of laboratory developed tests is changing. FDA has acknowledged the community's concern by offering a timeline for transition. *Recognizing that some laboratories may not have experience with FDA requirements for post-market reporting, we encourage FDA to develop additional materials and provide assistance with examples that outline specifically how Medical Device Reporting requirements can be met without duplication of efforts. Further, although the 12- to 18-month transition period outlined may be adequate, we urge FDA to consider adding time to the transition period (up to one year) that each submission remains under review by the FDA. FDA can demonstrate flexibility and assist industry adjustment to this system through a “grandfathering” process whereby products that are already on the market may use data that have already been developed in the submission process.*

## **Conclusions**

As FDA Commissioner Andrew von Eschenbach has said, personalized medicine is at an “inflection point.” It depends therefore on a reasonable and predictable regulatory environment upon which developers, payers, and patients can rely. We anticipate that there will be a need for continued dialog on IVDMIAs and related genomic technologies. We again offer the PMC as a venue for enhanced communication and understanding of the requirements going forward and underscore how important it is that careful, small steps are taken in the early days of FDA’s oversight of IVDMIAs.

If you have any questions regarding these comments, please contact Dr. Amy Miller, Public Policy Director, (202) 589-1770, or [AMiller@PersonalizedMedicineCoalition.org](mailto:AMiller@PersonalizedMedicineCoalition.org).

Respectfully submitted by,

The Board of Directors  
The Personalized Medicine Coalition  
[www.personalizedmedicinecoalition.org](http://www.personalizedmedicinecoalition.org)