



Statement for FDA's Public Meeting on In Vitro Diagnostic Multivariate Index Assays (IVDMIA's)

February 8, 2007

My name is Tom Tsakeris and I am speaking today on behalf of the Coalition for 21st Century Medicine. I am not being compensated by the Coalition or by any of its member companies. We are pleased that FDA is holding this public hearing and welcome the opportunity to comment on the IVDMIA draft guidance document. We are concerned that, in its current form, the draft guidance document will have adverse unintended consequences. In my discussion today, I will identify some of these unintended consequences, stress the need to obtain better clarity from FDA on the scope of its intent to regulate IVDMIA's, and present alternatives to the draft guidance we believe FDA should consider.

The Coalition represents innovative diagnostic technology companies, clinical laboratories, researchers, physicians, venture capitalists, and patient advocacy groups who believe in a common mission to develop and offer specialized diagnostic testing to improve the quality of healthcare for patients. Innovation and quality patient care are the key objectives for 21st century medicine. The timely development and availability of high quality, innovative diagnostic tests and services meets today's needs for personalized medicine and therefore public health.

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The Coalition has identified several serious adverse consequences that may likely arise from implementation of the draft guidance. These are: (1) active FDA regulation of so-called IVDMIAs will impede the innovation of new tests and services while precluding improvements from being made to existing tests and services; (2) implementation of the guidance will impose undue regulatory burden on clinical labs by adding new regulatory requirements that conflict with existing CLIA requirements; and (3) implementing the guidance will preclude tests and services from being reimbursed by health plans thereby creating disincentives for future research investment in new diagnostic technology. I will now elaborate on these points.¹

In its current form, the draft guidance will significantly affect the ability and incentives for clinical labs to develop new diagnostic test services that build on current medical knowledge. Innovation in diagnostic testing traditionally has been a key attribute of clinical labs. The draft guidance extends the scope of FDA regulation to certain clinical laboratory developed tests, referred to by FDA as IVDMIAs, on the premise that IVDMIA test results (and I am quoting directly from the draft guidance) “cannot be interpreted by the well-trained health care practitioner using prior knowledge of medicine without information from the test developer regarding its clinical

¹ Although laboratory developed tests have historically been outside the scope of FDA’s regulatory authority, at this meeting we will not address the question of FDA’s authority to regulate laboratory developed tests.

performance and effectiveness.”² On the contrary, the Coalition believes FDA should be clear that the primary incentive for clinical labs to develop technologically new diagnostic testing capability derives from the demand from physicians and other health care providers to obtain new innovative testing services commensurate with their advancing knowledge of the potential usefulness of such testing to laboratory medicine and not vice versa. In short, the Coalition believes that clinical labs which offer new tests, IVDMIAs or otherwise, are typically serving informed physicians who are sufficiently knowledgeable about a given test’s technology and its potential clinical utility to seek its availability. The Coalition believes that subjecting clinical labs to the added burden of complying with FDA regulatory requirements will result in physicians and patients experiencing either unnecessary delay or doing without access to important tests in rapidly advancing fields, such as genetics, oncology, and infectious disease.

As written, the draft guidance introduces additional, unnecessary regulatory burdens on already highly regulated clinical laboratories. Clinical labs are currently regulated by CMS under CLIA. The regulations under CLIA are comprehensive, and include detailed requirements to ensure consistent laboratory testing and the reporting of reliable test results to physicians. CLIA has comprehensive requirements for laboratory personnel, quality control procedures, quality assessment measures, performance testing, performance specifications, procedure manuals, and records retention, among other requirements. These requirements differ from FDA’s QSR requirements as they are

² FDA, Draft Guidance for Industry, Clinical Laboratories, and FDA Staff: In Vitro Diagnostic Multivariate Index Assays, at 3 (Sept. 7, 2006), available at <http://www.fda.gov/cdrh/oivd/guidance/1610.pdf>.

structured to focus on labs developing good quality laboratory practices. Under the draft guidance, laboratory tests and services that are already subject to CLIA's Quality Standards would now also be subject to FDA's QSR requirements, which are tailored for traditional medical device manufacturing operations. For laboratories to develop systems that comply with FDA's QSR requirements while continuing to comply with CLIA could take years, would be prohibitively costly, and will likely drive up healthcare costs. In short, what would result for both existing and prospective clinical labs is, at best, an untenable business model.

If the draft guidance is implemented immediately, existing products regulated as IVDMIA's will become illegal unless they obtain FDA clearance or approval. Labs will not be able to complete the review process for a period of time. Offering tests that are deemed "illegal" raises serious risks to lab licensure and accreditation and exposes labs to unnecessary liability risks. Of even greater concern, labs may also be prevented from being reimbursed by federal, state, and private insurance coverage. The lack of coverage, along with other increased regulatory obligations, will hinder the ability of clinical labs to maintain current operations as well as attract adequate financial capital to support research and development of new tests and technologies.

The Coalition is also concerned by the ambiguities that exist under the current draft guidance. The definition of an IVDMIA itself is ambiguous and introduces new terms that are not included in FDA's existing regulations. This ambiguity creates uncertainty as to which tests are IVDMIA's subject to regulation by FDA. As written, the definition could be interpreted to include a broad array of tests, including standard

medical treatment algorithms. The Coalition has identified scores of algorithms that are now in use, and many more are being published each month. FDA could be faced with regulating hundreds of IVDMIAAs. This will require a tremendous amount of Agency resources, diverting personnel from reviewing new marketing applications from manufacturers of assays.

The draft guidance sets forth a major change in laboratory regulation and establishes an entirely new regulatory regime. Yet, remarkably, the document is only five pages long. In those five pages, there is very little detail about the proposed new regulatory path or any mention of FDA enforcement policy. In short, labs need far more clarity than has been provided in the draft guidance.

We believe FDA should adopt alternative paths. The Coalition has developed several possible alternatives to the IVDMIA Draft Guidance. For purposes of this meeting, we will focus on four important alternatives.

First, FDA should not pursue regulation of IVDMIAAs via the draft guidance route. Rather, the Agency should propose new regulations that are detailed, clear, predictable, and establish the least burdensome regulatory controls in light of the actual risks and benefits of IVDMIA testing. FDA's exercise of authority over laboratory developed tests represents a substantial change in the regulation of labs and needs to be implemented through new regulations, not a guidance document. This will ensure the maximum public participation and scrutiny. Given the precedent that is being set, full rulemaking is necessary.

Second, FDA should base any level of regulation of IVDMIAAs on risk. The level of risk is higher for IVDMIAAs that are predictive and that result in a binary therapy recommendation – to treat or do not treat – based solely on the IVDMIA outcome. Other IVDMIAAs, whether predictive or prognostic, advisory or adjunctive, that do not give binary therapy recommendations are lower risk. These types of IVDMIAAs should not be held to the same regulatory standards. A risk-based approach would lead to a more appropriate allocation of regulatory effort, both by labs and FDA.

Third, there needs to be a transition period to enable labs with IVDMIAAs to adjust from the current CLIA regulatory path to a CLIA-plus-FDA regulatory path. The lack of a transition period could severely disrupt the availability of tests. If FDA imposed the device requirements on labs without any transition period, it could halt the use and development of tests, as well as improvements to existing tests. If, based on risk, an IVDMIA is subject to FDA regulation, a lab should have between two and four years to submit an application to FDA. During the transition period, FDA should not require that labs label the IVDMIAAs as “investigational” and IDEs should not be required. Note that in 1998, FDA released its Draft Compliance Policy Guide entitled “Commercialization of IVDs Labeled for Research Use Only and Investigational Use Only” which permitted a transition period for subject IVD companies to come into compliance with the Agency’s premarket submission requirements. A similar transition period should be applicable for IVDMIAAs as well.

Fourth, FDA could institute a disclosure program, like a registry. This registry could provide reliable information about the strengths and limitations of particular

IVDMIA, and allow FDA to understand better the scope of IVDMIA. The information available through the registry could help FDA to create a more specific definition of an IVDMIA, and could help shape how IVDMIA should be regulated. This would facilitate FDA's regulatory approach.

In conclusion, we believe that if the draft guidance is implemented in its current form, important medical tests may become unavailable, be frozen at their current technological state, become more expensive, or potentially lose insurance coverage. None of these outcomes benefit patients. Labs have been a significant source of innovation for decades. Laboratory developed tests, including tests and services that would be considered IVDMIA under the draft guidance, are an essential part of public health and are the future of personalized medicine. To preserve this future, FDA should go through formal rulemaking procedures and carefully consider the alternatives we have presented.

Again, on behalf of the Coalition for 21st Century Medicine, I thank you for the opportunity to speak about the regulation of IVDMIA.