Comments to the Food and Drug Administration (FDA) on the Draft Guidance for Industry, Clinical Laboratories, and FDA Staff on In Vitro Diagnostic Multivariate Index Assays (IVDMIAs)

Issued on July 26, 2007

Dear Sir or Madam:

Thank you for accepting comments in response to the revised draft guidance on In Vitro Diagnostic Multivariate Index Assays ("Guidance"). These comments represent a consumer/patient/advocate perspective, crafted by Genetic Alliance. Genetic Alliance is a coalition of more than 650 disease-specific advocacy organizations.

We appreciate the extension to the comment period.

We submitted comments on the first draft guidance and believe that most of them are still relevant.

We recently convened a genetic testing summit called Eyes on the Prize: Truth Telling about Genetic Testing. It was clear that this was a much needed forum, and more dialogue is needed and so we ask that FDA and the Department of Health and Human Services (HHS) convene public meetings to invite all stakeholders to dialogue about effective and efficient approaches to meet the common objective to assure quality and innovation in advanced diagnostic testing.

We recommend:

A clear definition of IVDMIAs. This is not a term found in the FFDCA. The second guidance does not define these tests unequivocally. In fact, the second guidance removed the term 'in vitro assay' and may in fact apply to many more tests than are intended.

A clear distinction between laboratory-developed tests (LDTs) that will be subject to FDA regulation as medical devices under the IVDMIA policy and those that will not. Laboratories need certainty in order to develop diagnostics that have a clear regulatory pathway.

The 2007 Draft Guidance focuses on derivation or verification by the end-user. The end-user for IVDMIAs is generally the treating physician. We think that it is unrealistic to expect the treating physician to engage in derivation or verification. Instead, laboratory physicians and scientists already take the lead, as required by CLIA, in assuring analytic validity and providing consultations to clinicians about proper use of each test. In fact, it is our recommendation that the regulatory system acknowledge the increasing complexity of diagnostics in the realm of personalized medicine, and the need for access to these quality tests by healthcare professionals.

We agree that tests should be subject to transparency, and recommend that when test development and validation is transparent, they not be subjected to burdensome regulation that will limit their access and/or their ability to be improved iteratively as new information is acquired.

Further, FDA in collaboration with CMS should provide a clear distinction as to whether a test is subject to regulatory requirements under the Federal Food, Drug and Cosmetic Act (FFDCA) or CLIA. The 2007 Draft Guidance indicates that the device includes "all elements necessary for obtaining the result." This overlaps CLIA's domain and will create confusion for the labs being subjected to the two regulatory regimes.

FDA should allow a reasonable transition period following publication of any final policy on regulation of IVDMIAs to allow laboratories to come into compliance with the substantial new regulatory burdens that would be imposed, and FDA should not require laboratories to label IVDMIAs as "Investigational Use Only" during such a transition period.

FDA regulation should allow for clearance/approval of clinically meaningful intended use claims under the least burdensome means. Requiring limitations on intended use claims against use in treatment selection can render a test of little clinical usefulness to physicians or their patients and will result in payer denials of the test as "not medically necessary."

Finally, and of great significance to our community is the intent of the guidance to regulate tests applying the Humanitarian Use Device definition. This is unacceptable, since HUD applies to devices for conditions that affect fewer than 4,000 people in the United States. The rare disease community uses the Orphan Drug Act definition: an orphan or rare disease is considered to have a prevalence of fewer than 200,000 affected individuals in the United States. There are more than 7,000 rare diseases, for which more than 1,300 genetic tests are currently available. The number of tests increases dramatically every year. The complexity of these tests will also increase dramatically as various gene interactions are understood and single gene disorder are understood in terms of a primary gene and multiple modifying genes, all of which need to be measured for prognosis, genotype/phenotype correlations and treatment decisions. As personalized medicine progresses, and genetic and genomic tests differentiate common conditions into thousands of conditions, all diseases will be 'rare' and need the special considerations of the orphan drug act. This is the standard that should be applied to tests.

Please give all of these recommendations serious consideration. We are the men, women and children whose lives hang in the balance as FDA attempts to apply the best regulatory paradigm to IVDMIAs. It is time that the regulatory schema enhances and in fact supports access to quality diagnostics in a thoughtful and clear manner. The right balance will support innovation and accelerate the development of the diagnostics we so desperately need.

Please feel free to contact us for further clarification or information.

Sincerely yours,

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