



March 5, 2007

Division of Dockets Management
HFA-305
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

RE: 2006D-0336 (IVDMIA Draft Guidance)

Sir/Madam:

We are writing in response to FDA's plans to implement the draft guidance document on IVDMIA's referenced above. As a diagnostics manufacturer, Ciphergen Biosystems is developing advanced diagnostics that are intended to improve the quality of healthcare for patients by addressing specific clinical needs. We are concerned that this guidance introduces an additional, unnecessary regulatory burden into an area that is currently regulated by the Centers for Medicare & Medicaid Services (CMS) under the Clinical Laboratory Improvement Amendments of 1988 (CLIA). We believe that improvements to the existing CLIA system would provide a clear strategy to improve the quality of care and encourage innovative new laboratory developed tests (LDTs) that are essential to maintaining the ability to provide cutting edge advancements in diagnostics.

As currently configured, the IVDMIA Draft Guidance may place burdensome restrictions on laboratories that far exceed any now in effect and may add undue regulatory burden that delays patients' and physicians' access to important new technology and medical information. Also, these changes are being proposed without following existing rule making procedures thereby denying stakeholders the opportunity to present alternative points of view. Unless significant modifications are made, the IVDMIA Draft Guidance will dampen innovation and likely have a significant, deleterious effect on public health and healthcare in this country by severely limiting introduction of new diagnostic approaches.

During the public meeting on February 8th, it was clear that many similar concerns were shared by a wide range of industry, laboratory and advocacy representatives. Of specific concern to Ciphergen are the following issues:

- If implemented in its current form, the IVDMIA Draft Guidance may significantly stifle innovation and freeze the development of many tests currently in research, development, or production;
- The current IVDMIA Draft Guidance is relatively brief and imprecise and may result in non-standardized interpretation by industry and uneven enforcement by FDA. There is little detail on the proposed new regulatory path or potential unintended and undesired consequences;

- The IVDMIA Draft Guidance, rather than provide a least burdensome approach, may create a new layers of regulation with conflicting and overlapping jurisdiction between FDA and CMS;
- The IVDMIA Draft Guidance could represent a direct intrusion into the practice of medicine by physicians since the reporting of laboratory results is a direct physician-to-physician event;
- The IVDMIA Draft Guidance, if implemented in its current form, will likely reduce the ability of innovative laboratories investing in IVDMIA's to attract adequate financial capital for R&D investment into new tests and technologies;
- If FDA regulation is imposed, important medical tests may become unavailable, be frozen in their current state, become more expensive, or potentially lose insurance coverage;
- If LDTs are subject to FDA regulation as medical devices, laboratories themselves would become medical device manufacturers. Laboratories would be simultaneously subject to FDA and CLIA regulations and standards. This adds an undue regulatory burden. It would be extremely costly and could take many years for a laboratory to develop and implement systems that would comply with FDA's device requirements (such as Quality System Regulation (QSR) compliance). It is likely that very few laboratories would be able to conform to these burdens and would instead opt to discontinue LDTs altogether;
- The IVDMIA Draft Guidance states that most IVDMIA's will either require 510(k) clearance or premarket application (PMA) approval. There is no clarity provided defining what data will be required to support a 510(k) or a PMA; and
- While FDA has said that it does not intend to regulate well-established tests that incorporate algorithms, e.g., the "triple marker screen" for Down Syndrome, it is a practical reality that tests constantly evolve and improve. A fourth marker for Down Syndrome has now been identified and is being widely used. The IVDMIA Draft Guidance would freeze the development of many such tests, and the ambiguities in the guidance would deter improvements of existing tests.

We believe that CLIA provides an adequate basis for regulating LDTs. The more reasonable, less burdensome and most effective regulatory approach would be to strengthen CLIA and its regulations, not to superimpose a new layer of regulation through FDA. The current CLIA regulations can certainly include a provision to include clinical validation in the event that test reports and claims inherently assess outcomes. CLIA should be strengthened through harmonizing quality standards for all LDTs and by the creation of subspecialties as necessary under CLIA that address FDA's concerns regarding IVDMIA's, especially as they relate to the appropriate conditions for clinical validation of diagnostic or predictive claims.

If FDA regulates IVDMIA, there should be a transition period to bring IVDMIA's from the current CLIA regulatory path to a new CLIA / FDA regulatory path. FDA should incorporate a grace period of two years for submission of applications for IVDMIA's requiring a 510(k) and four years for submission of applications for IVDMIA's requiring a PMA into any final guidance or regulation to minimize disruption in the availability of tests. There should also be a similar transition period for GMP compliance requirements by laboratories.

Implementation of these changes by FDA without significant prior dialog and input from stakeholders will lead to disruption of the ability of laboratories to address new diagnostic assays and will markedly diminish patients' access to novel approaches for disease diagnosis and management. There is no doubt that high quality LDTs are necessary yet implementation of these proposed regulations may drive laboratories away from

development of new tests. Undoubtedly the number of laboratories willing to devote effort and resources in this direction will be severely limited going forward.

We are encouraged by the steps FDA has taken to solicit opinion and comments from stakeholders. We look forward to working with all concerned to craft an approach that assures that products manufactured for use in LDTs meet high standards of quality and performance to assure that patient testing results meet appropriate standards of care.

Sincerely,

Gail S. Page
CEO and President