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BY ELECTRONIC DELIVERY

Division of Dockets Management (HFA-305)
Food and Drug Administration
56350 Fishers Lane
Room 1061
Rockville, MD 20852

Re: Docket No. 2006D-0347, Federal Register: July 26, 2007 (Volume 72, Pages 41081-41083)

Dear Sir/Madam,

The following comments are provided by the Biotechnology Industry Organization (BIO). BIO represents more than 1,100 biotechnology companies, academic institutions, state biotechnology centers and related organizations across the United States and 31 other nations. BIO members are involved in the research and development of healthcare, agricultural, industrial and environmental biotechnology products. BIO also produces the annual BIO International Convention, the global event for biotechnology. BIO appreciates the opportunity to comment on the Food and Drug Administration's (FDA's, the Agency's) *Draft Guidance for Industry, Clinical Laboratories, and FDA Staff: In Vitro Diagnostic Multivariate Index Assays*.

BIO appreciates the additional clarification provided by the FDA in the revised draft Guidance. We specifically note the revised definition of In Vitro Diagnostic Multivariate Index Assays (IVDMIAAs) and the identification of a transition period in which enforcement discretion will be exercised. We respectfully submit the following comments on the July 26, 2007 draft Guidance.

General Comments:

IVDMIA regulation in the broad context of genetic testing and personalized medicine

BIO believes there is an interdependency between the draft IVDMIA guidance and other related regulatory documents that are currently being considered and developed. Specifically, we note the intersection of: (1) the draft IVDMIA Guidance; (2) Draft Guidance for Industry and FDA Staff, Commercially Distributed Analyte Specific Reagents (ASRs): Frequently Asked Questions; and (3) the pending guidance to assist laboratories that manufacture IVDMIAs in complying with Quality System (QS) regulations, including how Clinical Laboratory Improvement Amendments (CLIA) requirements may partially fulfill QS requirements. For many companies, a comprehensive understanding of the regulatory environment created by these documents is necessary to efficiently and responsibly plan for and incorporate regulatory expectations into manufacturing and other business practices. This is needed to foster an environment in which technologies can be supplied in a compliant manner with minimal interruption to patient populations. It is important to note that there are patient populations dependent upon many products currently marketed that will be affected by changes to the regulatory environment contemplated by these draft and pending Guidances.

Recommendation: We encourage the agency to consider this interdependency as it develops final guidance and implements its policies. At a minimum, we encourage open, in-depth, public forums with stakeholders during the implementation period. We recommend that FDA continue to engage stakeholders in a formal, deliberative and interactive process to enhance understanding and transparency of the broad regulatory environment for genetic tests. We recommend that a formalized structure and rationale be developed for the classification and regulation of specific subsets of in vitro diagnostics, including all genetic tests and molecular diagnostics. We expect that it would benefit this process to be informed by other expert assessments and advisory reports to be released in the near future.

Ongoing Industry–Stakeholder–FDA Dialogue

In addition to initiating the regulatory discussion recommended above, FDA should continue to interact directly with stakeholders, including industry, in an organized forum to publicly examine the impact of and to address ongoing questions surrounding the implementation of the IVDMIA Guidance. This will be highly instrumental in identifying the least burdensome approach to compliance for the newly regulated entities.

Recommendation: BIO proposes the FDA partner with industry to coordinate an outreach and educational program to bring industry and the broader community of stakeholders – including patients, physicians, and payers – to a clearer understanding of the changes proposed and the requirements to achieve compliance in an orderly manner.

Specific Comments:

Definition and Regulatory Status of IVDMIAs

The draft Guidance states that an IVDMIA “[p]rovides a result whose derivation is non-transparent and cannot be independently derived or verified by the end user” and describes several types of devices that would meet this definition. Some ambiguity remains as to the examples provided and the threshold of “transparency” required for a test to be exempt from regulation under the guidance or to remain clear of regulatory enforcement action.

Recommendation: BIO proposes that FDA provide a rationale narrative or logic map to make apparent the FDA’s method of IVDMIA assessment and classification, to give industry the ability to independently evaluate regulatory requirements for future product planning. We request further clarity as to what extent an interpretation function would need to be available, published, and/or disclosed in order to be sufficiently transparent under the definition used in the guidance such that a test may not be considered an IVDMIA. Please provide additional specific examples of the types of tests that qualify as IVDMIAs, if possible.

Premarket and Postmarket Requirements for IVDMIAs

We believe the draft guidance should be more explicit regarding FDA’s specific expectations for laboratories to comply with other requirements that currently apply to medical device manufacturers, such as medical device reporting (MDR), registration and listing, and labeling. For example, would a laboratory that offers an IVDMIA have to register and list all tests offered, or only the IVDMIA? We also think there are significant questions remaining in translating the FDA QS regulations and CLIA quality practice requirements that could already be captured under current best practices in CLIA regulation. As noted above, quality practices and other regulatory requirements for IVDMIAs are highly interdependent. Sufficiently analyzing the impact on manufacturing practices will require a comprehensive understanding of the regulatory environment.

Recommendation: BIO proposes that FDA provide further clarity on the specific requirements for laboratories regarding MDR and provide a comparative matrix for QS regulations and operational requirements for dually regulated IVDMIAs under FDA and CLIA.

Timeline for Submitting IVDMIAs for FDA Review

We appreciate that FDA has recognized the need for a transition period for laboratories to come into compliance with the substantial new regulatory requirements under the

Guidance. BIO encourages FDA to fully consider the large impact of this change in the regulatory paradigm, and the capacity of companies, including emerging diagnostics companies, to gain sufficient understanding and clarity with respect to FDA requirements and processes in order to integrate the new requirements into their business practices and clinical research programs. The proposed transition times may not be adequate to achieve these goals.

We are also concerned about the potential disruptive impact on patient care in cases where the timeline provided is insufficient for FDA to complete its review of a currently marketed product. For example, if a manufacturer submits a 510(k) or PMA within the initial 12 month transition period, but the review time exceeds 6 months, an IVDMA that is currently well-established in clinical practice and reimbursed by third-party payers could suddenly be categorized as “investigational” pending clearance or approval, resulting in denial of coverage and limiting access for patients. This issue is even more likely to occur for IVDMIAs that require PMA submissions, since the average FDA review time for PMAs approaches 12 months.

Recommendation: BIO proposes that active dialogue be commenced between the Agency and industry to adequately assess the impact of this change in the regulatory paradigm and the transition period that will be appropriate to ensure that manufacturers can adequately plan for and incorporate changes to ensure there is no disruption in the availability of these important products. In addition, we recommend that FDA review time after submission of a 510(k) or PMA not be included in the transition period.

Least Burdensome Approach and Impact on Innovation and Availability

The draft Guidance represents a significant extension of the regulatory paradigm by extending medical device regulations to IVDMIAs. This shift from the current regulation under CLIA will have an impact on the cost of development and ongoing compliance, and could result in the delay of market introduction of these assays. For some test developers and small business entities, the increased costs and delay in market introduction may make commercialization of the test cost-prohibitive. A direct discussion between industry and FDA about the challenges of adapting to regulatory changes in an emerging marketplace would ensure that these issues are fully considered and help to provide a clear pathway for the least burdensome approach.

Recommendation: BIO proposes that FDA partner with industry to coordinate a workshop on the development and commercialization environment of IVDMIAs in order to identify a least burdensome regulatory approach. Such a forum could highlight the value of innovation in diagnostics and identify policies that support continued innovation and continued availability of safe and effective products.

Respectfully submitted,

A handwritten signature in cursive script, appearing to read "Chris Colwell".

Chris Colwell
Director, Healthcare Regulatory Affairs
The Biotechnology Industry Organization (BIO)