



March 5, 2007

Division of Dockets Management Branch (HFA-305)  
Docket No. 2006D-0347  
Food and Drug Administration  
5630 Fishers Lane, Room 1061  
Rockville, MD 20852

Dear Sir/Madam:

The American Society for Clinical Laboratory Science (ASCLS) is writing in response to the FDA's request for comment on the draft guidance document entitled "In Vitro Diagnostic Multivariate Index Assays (IVDMIAs); Draft Guidance for Industry, Clinical Laboratories, and FDA staff". We applaud the FDA for seeking such broad input and commit to continue to work with the agency on this and other related topics.

ASCLS is the nation's oldest and largest non-registry professional association for non-physician clinical laboratory professionals. The Society's mission includes promoting high standards of practice in the workplace and ensuring professional competence, while its ultimate goal is to ensure excellent, cost-effective laboratory services for consumers of health care. Our membership of nearly 11,000 includes clinical laboratory directors, managers, administrators, supervisors, and staff at all levels of practice.

ASCLS commends the FDA for its attempt to frame the issues surrounding these assays and their thinking on IVDMIAs. We agree with the agency that these assays are medical devices and cannot be classified and regulated under the Analyte Specific Reagent (ASR) rule.

Our members' concerns are two-fold:

- advances in science hold promise for better diagnostic and therapeutic information provided by clinical laboratory professionals at every point in the health continuum and these advances must not be stifled by more regulatory burdens;



- ➡ many of the claims made in the name of advancing science cannot be validated by other than the developer of the test which appears to be a violation of CLIA regulations at the least and sets the stage for potential misinformation for health care providers and our patients. The approach that the scientific community will somehow sort out the real science from the inaccurate supposes that every scientist in every laboratory in this country has the resources to study the test development and method intensely enough to guarantee patient safety and that simply is not the case.

We have reviewed the entire guidance document for IVDMIAs and offer the following comments and suggestions:

#### **DEFINITION AND REGULATORY STATUS OF IVDMIAs**

We support the characteristics that FDA has enumerated to define IVDMIAs. We assume from the language that all three characteristics must be present for a device to meet the definition. If not, some very common algorithms and calculations, developed in-house by laboratories, might be in jeopardy. Therefore, we request clarification on this point.

#### **PREMARKET AND POSTMARKET REQUIREMENTS FOR IVDMIAs**

We recommend that the FDA include descriptions of the 510(k) and PMA processes with some explanation of the differences between them in a bulleted or table format. The web sites for complete explanations of both should be included as was done with the web site for additional information on device classifications. Many clinical laboratories have not been involved in any FDA submissions and the apprehension about proceeding could be a major deterrent to developing new technology and test methods. Any explanations that will simplify and enhance an understanding of what is required will help mitigate the burden of this guidance.

ASCLS also requests that the FDA develop more examples, and over time, a process that will better define whether a device is a Class II or III device. The examples in the current document do not provide enough guidance for laboratorians to predict the class of their test.



## POST MARKET REQUIREMENTS

ASCLS is supportive of FDA's intent to work with clinical laboratory professionals to be in compliance with the Quality System Regulation (QSR) and CLIA. We would ask that FDA not wait for laboratories to identify "instances where they believe compliance with a particular CLIA requirement may demonstrate compliance with a QSR requirement" but to develop a compendium of instances that can be added to over time.

We commend the FDA's plan to provide laboratory professionals with further guidance about complying with MDR provisions that currently apply to manufacturers. Again this is an area that will be completely new for most clinical laboratories and would be burdensome to implement without clear guidance. We believe that this guidance will likely encourage clinical laboratories to develop accurate and safe technologies.

## GUIDANCE VERSUS RULEMAKING

We perceive the use of guidance documents as a way for the FDA to be more responsive to changing technology because the guidance seems to be more easily adjusted. However, there does not seem to be the same level of communication between the agency and stakeholders that we see in a rulemaking process. We do have some concerns about the rather one-sided communication such as the February meeting that does not afford the stakeholders the opportunity to "hear" what the FDA is thinking or to elicit responses to their concerns.

The emergence of IVDMIAs is a testament to the ingenuity, commitment, and technological innovations of laboratory professionals and manufacturers. We believe that we are on the brink of introducing revolutionary technology that can improve laboratory services. The information that will be produced will determine diagnostic and therapeutic pathways, and will be used as a basis for clinical decisions. Therefore, we must formalize a specific process that ensures that the entire health care community has enough information about the method. Claims by laboratories and manufacturers that have not been proven to be accurate and precise, or are not reproducible and easily understood will undermine the quality of laboratory services. We believe that this guidance document provides an approach to ensuring that our services are medically and scientifically sound and we support the concepts of the document.



AMERICAN SOCIETY FOR CLINICAL LABORATORY SCIENCE

ASCLS and its members stand ready to work with the FDA using the knowledge of our members to help enhance this guidance or participate in rulemaking. We thank you for the opportunity to submit our comments.

Respectfully submitted,

A handwritten signature in black ink that reads "Shirlyn B. McKenzie". The signature is written in a cursive, flowing style.

Shirlyn McKenzie, Ph.D., CLS(NCA)  
President, ASCLS