

February 27, 2007

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

[Docket Number 2006D-0347 - Draft Guidance for Industry, Clinical Laboratories, and Food and Drug Administration Staff on In Vitro Diagnostic Multivariate Index Assays; Availability; Extension of Comment Period]

Dear Sir or Madam,

BioSignia, Inc. is a company in Durham, NC that provides predictive models to various segments of the healthcare industry. Physicians and others use these tools, via the internet, to assess the chronic disease risks (cardiovascular diseases and cancers) of their patients and to recommend preventive strategies. As an example, we have used the well-known multivariate Framingham Heart Disease Risk Score to assess the risk of heart disease in patients. This model uses 2 laboratory tests, for total and HDL cholesterol, with other clinical information to produce a 5-year risk of having heart disease. We have a proprietary procedure to augment this established model with other well-established risk factors such as a family history of heart disease and body mass index (BMI). We have also developed other proprietary disease models of our own to aid physicians in recognizing those at risk of common chronic diseases, including chronic obstructive pulmonary disease, colon cancer, and type 2 diabetes.

We are in support of the effort by the FDA, represented by the Draft Guidance, to bring regulatory oversight to this new field of *in vitro* diagnostics that are rapidly being developed as a result of the revolution in genomics and other “omics”. While these multivariate assays and their required algorithms have the potential to greatly enhance the practice of medicine, a new level of regulatory oversight is needed. The required algorithms associated with the laboratory tests effectively prohibits the physician from making an independent evaluation of the patient’s condition based on the laboratory data alone.

Our specific concern is the definition of “*in vitro* diagnostic multivariate index assays” (IVDMIA) and what types of procedures will be covered. The definition clearly intends to cover a “test system at employs data, derived ... from one or more *in vitro* assays, and an algorithm ... to generate a result that ... is used in the ... prevention of disease.” This

definition includes the Framingham model described above, which is an algorithm that utilizes data, including the results of two laboratory test, to inform the user of the risk of heart disease and is used in the prevention of that disease. This model has been available since 1988 and is widely available in paper forms and on the internet. Other disease prevention models, such as those that BioSignia uses, would also be covered. These tools have generally bypassed FDA oversight as educational tools, not intended for diagnostic use.

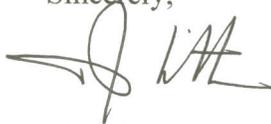
We are not opposed to bringing these older tools under FDA oversight if that is the intended purpose. We are only concerned that the definition may be boarder than was intended. If, intentionally or unintentionally, this definition stands and these older preventive risk tools are included, then the consequences need to be considered.

We suggest a possible change in the definition that would help to clarify the distinction between the older risk models and the newer ones. This change would be to emphasize the necessary tight linkage between the assays and the algorithms in the new generation of multivariate tests. The laboratory results of these assays are quite impossible to interpret without the associated algorithm. In contrast, the individual components of the older models are all “free standing” in the sense that a physician is free to interpret them individually based on his or her own experience. All of the laboratory tests are already FDA approved assays that are commonly part of current laboratory reports. Furthermore, the use of tools such as the Framingham model are confined to long-term disease prevention for which the usual prescriptions are not novel, but include such common-sense interventions as cholesterol lowering and weight loss. These strategies have long been associated with minimal potential harm and maximal preventive efficacy.

In summary, we are asking that the effect of the current definition of IVDMIA on older multivariate models be considered and clarified.

Further clarification can be obtained from our Director of Research, Dr. Martin Root, at 919-933-2021 or [mroot@biosignia.com](mailto:mroot@biosignia.com).

Sincerely,

A handwritten signature in black ink, appearing to read 'T. Smith', with a stylized flourish at the end.

Timothy Smith, PhD  
CEO, BioSignia, Inc.