



**BlueCross BlueShield
Association**

An Association of Independent
Blue Cross and Blue Shield Plans

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

Re: Docket Number 2006D-0347

Dear Sir:

The Blue Cross and Blue Shield Association (BCBSA) is pleased to provide comments on the Draft Guidance on In Vitro Diagnostic Multivariate Index Assays. BCBSA is made of 39 independent locally-owned and operated Blue Cross and Blue Shield companies that collectively provide healthcare coverage to 98 million Americans.

We welcome the issuance of this important guidance and strongly concur that IVDMIAAs should meet pre- and post-market device requirements under the Act and FDA regulations, including pre-market review requirements in the case of class II and III devices.

We agree that IVDMIAAs include elements, as described in the section on "Definition and Regulatory Status of IVDMIAAs" in the guidance, that are not among the primary ingredients of in-house tests and that, therefore, raise safety and effectiveness concerns. Moreover, some IVDMIAAs have been developed as the sole testing product of new, stand-alone commercial laboratories. While at least some of these labs have received CLIA approval, they have had neither the history nor the experience of meeting regulatory requirements of laboratories that routinely conduct a wide variety of moderate complexity and high complexity laboratory tests. To ensure patient safety and the use of effective diagnostics

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and lab-based treatment selection methods, IVDMA tests should meet the same regulatory requirements as other commercially manufactured moderately and highly complex laboratory tests. Further, we recommend extending regulation to all "home-brew" testing for similar reasons.

We recommend revising the section that defines IVDMIAs. The first characteristic of "Use clinical data" should be clarified to say: "Empirically identify a set of variables derived from clinical data—including data from individual analytes (e.g. amino acid or nucleic acid sequences) measured in one or more in vitro assays –and, in some cases, demographic data, and derive weights or coefficients for these variables to be employed in an algorithm.

We agree that most IVDMIAs will be either class II or III devices. Pre-market approval is particularly essential when, based on the test result, patients might be administered treatment with potentially harmful side effects that they would not otherwise have received, or might be denied potentially beneficial treatment that they would have otherwise received. However, tests predicting risk alone should be carefully considered for potential harms (e.g. invasive monitoring procedures) that might necessitate Pre-market Approval.

Thank you for your attention to our concerns. If you have any questions, please contact Margaret Piper, Ph.D., at 312.297.5895.

Sincerely,



Allan M. Korn, MD, FACP

Senior Vice President
Chief Medical Officer