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July 8, 2005

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

Re: Docket# 2004N-0279

The American Association for Clinical Chemistry (AACC) welcomes the opportunity to comment on the Food and Drug Administration's (FDA's) "Drug-Diagnostic Co-Development Concept Paper," which describes the Agency's preliminary thoughts on how drugs and laboratory tests could be co-developed, prospectively. AACC offers the following comments on the paper.

General Comments

AACC supports the FDA's goal of encouraging the co-development of drugs and laboratory tests to improve patient care and outcomes. Further, we agree with the Agency's current approach—developing guidance rather than regulation—which will provide the FDA greater flexibility in overseeing this new and promising field.

AACC recognizes that other federal agencies are involved in varying aspects of pharmacogenomic testing. For example, the Centers for Medicare and Medicaid Services is responsible for assuring the quality of testing and reimbursement, while the National Institutes of Health and Centers for Disease Control and Prevention are gathering population data that can be used to assess the utility of drugs for differing subgroups. We urge the federal agencies to coordinate their efforts to ensure that the regulatory approaches are streamlined and complementary.

1.3 Scope

The document states that the concept paper addresses the development of "a single test in conjunction with a single drug." In many combination drug/test studies, however, the test may actually be multiple biomarkers due to the involvement of multiple genes, enzymes or metabolites. For example, traditional pharmacogenomic studies seeking to correlate the drug metabolizing enzyme phenotype to genotypes often test for several genetic polymorphisms using multiplex technology to provide a result. Furthermore a drug may require the assessment of multiple drug metabolizing enzymes (2C19, 2D6, 3A4, etc.). Similar examples exist as DNA SNP haplotypes and also protein profiles. AACC requests that you clarify when a "single test" implies a single analyte versus a single test result (potentially multi-analyte with associated algorithms).

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3.3 Analytical Studies

The concept paper states that “Analytical validation studies are recommended to evaluate the following performance characteristics of the assay, where applicable, for each analyte claimed in the clinical use statement.” These characteristics include: test performance; sample requirements; analyte concentration specifications; cut-off; controls and calibrators; precision; analytical specificity; assay conditions; sample carryover; and device limitations. We agree that these types of analytical studies are appropriate once it is known that the test will be developed.

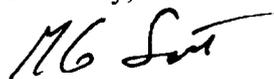
In a co-development environment, however, the potential value of the test will not be known until the clinical validation has been gathered and assessed. Furthermore, the goal of identifying markers early in the human clinical trials or even prior to human clinical trials may be at odds with analytical sensitivity evaluation prior to clinical trial implementation. AACC believes there may need to be an interim step of pre-analytical assessment before committing to a comprehensive analytical validation study in a clinical setting.

6.1.2 Clinical Trial Design Consideration

The FDA mentions repeatedly that the sponsors may wish to use “enriched study populations.” We recommend that the Agency more fully discuss the purposes and value of such studies, particularly in relation to biomarker discovery versus biomarker clinical validation. In addition, we suggest that the FDA elaborate on the advantages and limitations of the enriched population approach, as well as the possible need for a follow-up study to evaluate the general population.

By way of background, AACC is the principal association of professional laboratory scientists--including MDs, PhDs and medical technologists. AACC’s members develop and use chemical concepts, procedures, techniques and instrumentation in health-related investigations and work in hospitals, independent laboratories and the diagnostics industry worldwide. The AACC provides international leadership in advancing the practice and profession of clinical laboratory science and its application to health care. If you have any questions, please call me at (314) 362-1503, or Vince Stine, Director, Government Affairs, at (202) 835-8721.

Sincerely,



Mitchell G. Scott, PhD