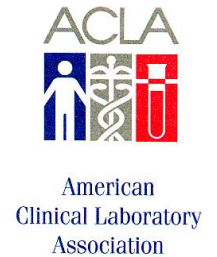


January 29, 2009

Maria Ellis  
Executive Secretary for MEDCAC  
Centers for Medicare and Medicaid Services  
Office of Clinical Standards and Quality  
Coverage and Analysis Group  
Mailstop C1-09-06  
7500 Security Blvd  
Baltimore, MD 21244



Re: Comments to MEDCAC on Genomic Testing

Dear Ms. Ellis:

The American Clinical Laboratory Association (“ACLA”) is pleased to have this opportunity to submit comments to the Medicare Evidence Development and Coverage Advisory Committee (MEDCAC) on requirements for evidence to determine if diagnostic uses of genomic testing in Medicare beneficiaries with signs or symptoms of disease improve health outcomes. ACLA is an association representing independent clinical laboratories throughout the country, including local, regional and national laboratories. Many if not all of our members perform genomic/genetic testing (terms used interchangeably); thus, ACLA has a significant interest in this issue.

According to the announcement for this meeting, the Centers for Medicare and Medicaid Services (CMS) has asked MEDCAC to make recommendations “regarding the desirable characteristics of evidence that could be used by the Medicare program to determine whether genetic testing as a laboratory diagnostic service improves health outcomes.” ACLA recognizes the importance of this issue, especially given the growth in genetic testing since the completion of the Human Genome Project. Knowledge gained from the Human Genome Project has resulted in meaningful discoveries in our understanding of disease and its care. It has led to a new era of “personalized medicine” replacing a trial and error approach. Genetic tests are powerful – their results assist in the selection of the specific medication, or optimal dosage, that can lead to the best treatment outcome; predict the risk of disease before symptoms occur, and provide information that helps physicians and patients manage disease or condition effectively.

ACLA believes it will help MEDCAC, in responding to this request from CMS, to recognize several key points.

- According to the National Institutes of Health GeneTests on line web site (<http://www.genetests.org/>), there are over 1,600 different diseases for which genetic tests are available. These tests are performed using various methodologies and are done for different purposes. Tests may be done to make a medical decision, confirm a diagnosis while others may be used to predict the possibility that a condition will develop or recur. Some tests are used in connection with pharmaceuticals to determine whether a particular drug will be effective or what dosage is necessary. The variety of tests and the differing circumstances under which they are ordered makes it difficult to determine a single answer to the questions raised by CMS, one that will be applicable to all tests and circumstances. ACLA believes these tests should be considered on a case-by-case basis, rather than a one size fits all approach applicable to all genetic tests. MEDCAC, and CMS, should look at a variety of factors in determining what level of evidence is appropriate for any given test.

- In addition, the level of evidence required also can vary depending on the applications of the particular diagnostic test. For example, where a test is being used to confirm a diagnosis, less rigorous evidence may be sufficient to demonstrate the utility of the test. Where significant therapeutic decisions may be made based on the test results, a higher level of evidence may be required. However, we note that there already are well accepted standards for judging most clinical, diagnostic testing. For the most part, these standards focus on two necessary and complementary requirements (1) the analytical validity of the test - does it consistently and accurately measure the analyte for which it is testing - and (2) the clinical validity - does it consistently identify the clinical condition associated with the analyte in the patient population for whom the test is intended. Beyond analytical and clinical validity, an assessment of the utility of a diagnostic test should be informed by evidence of the extent to which the results of the test can influence patient management. Because this is dependent upon treatment and other diagnostic options evidence requirements should be tailored to the condition for which the test is designed. Since diagnostic tests necessarily have a less direct effect on health outcomes than therapeutics, diagnostic tests should not be subjected to the same degree of evidentiary rigor as therapeutics. The perceived benefits gained from lengthy, comprehensive evidentiary methodologies must be balanced against the significant opportunity costs such methodologies often can impose, including disincentives to medical innovation and delayed or denied access to diagnostics that could have avoided negative health outcomes and their associated costs.
- There is a broad spectrum of evidence that could be considered in evaluating diagnostic tests. While randomized clinical trials (RCT) may be the “gold” standard for some procedures and therapies, they may have significant limitations when applied to many diagnostic situations. For example, to determine whether a given test can predict recurrence of a condition, the only way to perform a RCT would be to track patients prospectively over a long period of time to determine whether the condition returned prior to some set endpoint. It could be many years before the results of such a study would be known, thus delaying unnecessarily the availability of an important diagnostic tool and important information for patients. Alternative scientific methods exist for estimating the penetrance of genetic conditions. RCTs may be too narrowly constructed to apply to broader populations at risk. Carefully constructed retrospective studies involving germline or somatic analysis can yield scientifically valid clinically meaningful data. Finally, the economic difficulties of constructing RCTs over the long term are complicated by rapid changes in therapeutic approaches where the drug regimens used to treat patients are in constant states of revision. In these cases, scientifically sound alternative approaches must be considered, to avoid costly, time consuming, and impractical requirements that unnecessarily may risk the health and well being of patients.
- Genetic testing is often performed and validated using archived specimens that have been stored and catalogued. It is often possible to use such samples, consistent with principles of informed consent and appropriate treatment of patients and patient specimens, to determine whether an individual with a given genetic profile ultimately had a recurrence, or responded to a particular drug or therapy. It is possible to analyze such findings to determine whether it adequately supports the conclusions being drawn. Utilizing such retrospective reviews of archived specimens, in lieu of prospective clinical trials, can result in more rapid determination of the utility of a diagnostic procedure, without adversely affecting incentives to develop beneficial new tests.

- Differences in the types and uses of tests strongly suggest that it would be both difficult and inappropriate to develop a single National Coverage Decision that can apply to all genetic testing. The current approach allows the local carriers, or Medicare Administrative Contractors, to make coverage determinations at least initially. The Medical Directors are able, in most instances, to review the documented research and to make a determination about the value of the test based on that information. While it may be useful to develop an approach by which CMS can be consulted, when necessary, the current approach appears to be the best one for the time being. Given the variety of genetic testing, the differing uses of tests and the relative newness of the technology, it seems inappropriate, and possibly counterproductive, to try to develop a single set of standards at this time.

We thank you for the opportunity to submit these comments. We are happy to answer any questions that may arise in connection with this testimony.

Sincerely,

David Mongillo  
Vice President, Science and Policy