Association for Molecular Pathology
Promoting Clinical Practice, Basic Research, and Education in Molecular Pathology
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March 27, 2009

Harold C. Sox, MD, Chair
Committee on Comparative Effectiveness Research Priorities
Institute of Medicine
500 Fifth Street NW
Washington DC 20001

Dear Dr. Sox:

The Association for Molecular Pathology is pleased to have the opportunity to provide comments to the Institute of Medicine on the subject of comparative effectiveness research (CER) and share our recommendations on priority areas on which to focus CER activities.

AMP is an international medical professional association representing approximately 1,500 physicians, doctoral scientists, and medical technologists who perform laboratory testing based on knowledge derived from molecular biology, genetics, and genomics. Since the beginning of our organization we have dedicated ourselves to the development and implementation of molecular diagnostic testing, which includes genetic testing in all its definitions, in a manner consistent with the highest standards established by CLIA, the College of American Pathologists (CAP), the American College of Medical Genetics (ACMG), and FDA. Our members populate the majority of clinical molecular diagnostic laboratories in the United States. They are frequently involved in the origination of novel molecular tests, whether these are laboratory developed or commercially developed. Our members proudly accept their responsibilities in assessing the analytical validity, clinical validity, clinical utility, and the clinical utilization of these tests for each specific patient.

CER is garnering more attention in Congress and among other policy makers who see it as a method to examine the comparative effectiveness of treatments, including how they relate to coverage and reimbursement decisions. Diagnostic tests will most definitely be viewed under this paradigm, especially when the effectiveness of treatments will vary among different population subgroups. Unfortunately, the value of diagnostics has not been appreciated adequately in the past; therefore, examining the role of genomics under CER will be critical.

Accordingly, AMP identifies the following areas as recommended priorities for CER research:

Clinical Outcomes in Genetic Testing. As information becomes available that relates clinical outcomes to genetic variations, the regulatory, medical and lay communities expect that it will be immediately incorporated into routine clinical care. FDA labeling that relates pharmacogenomic response to maintenance dose, for example, has created demand for both testing and reimbursement in the absence of large clinical trials that demonstrate the efficacy of such laboratory testing by comparison with either “usual care” or alternative approaches, such as use of daily home prothrombin time testing under medical supervision during the first few weeks of anticoagulation. Funding for large, carefully designed comparative efficacy trials for genetic tests should be coupled

with funding for observational comparative effectiveness studies that complement randomized controlled trials by including patients who may be tested, but do not meet the inclusion criteria for prospective trials.

Evaluating the Proficiency of Genomic Tests and the Laboratories that Perform Them. For the public to reap the benefits of effective genetic tests, it is critical that "ordinary" laboratories meet the same high performance standards that typically characterize those of academic participants in comparative effectiveness research. Towards this end, the laboratory community supports and participates in a variety of proficiency testing activities sponsored by professional organizations or organized informally by members of the laboratory community in an effort to guarantee the quality of testing. AMP members have been particularly active in extending these rigorous proficiency testing practices to include molecular and genetic testing. Nevertheless, AMP believes that there may be opportunities to significantly improve the effectiveness of proficiency testing and other quality assurance activities such that the full potential of molecular medicine and personalized health care can be realized:

- *The development of suitable test materials*. To further facilitate the advancement of personalized medicine, AMP recommends funding for a program to develop reference materials, exploiting traditional and innovative methodologies, to aid the continued advancement of quality measures in the field of laboratory medicine.
- *Novel ways to evaluate laboratory proficiency*. AMP supports the development of proficiency testing methods as alternatives to distributing surrogate test specimens. As is evident in cytogenetics, it is impossible to send out surrogate specimens for every known translocation and rearrangement. Categorical methodologic proficiency testing should be evaluated as one such alternative.
- *Methods to evaluate novel and emerging types of genomic testing.* AMP believes efforts should be taken to develop appropriate quality assurance for new technologies such as whole genome sequencing, using carefully designed methods to determine the relative effectiveness of various quality assurance methods in improving laboratory testing and ultimate clinical outcomes.

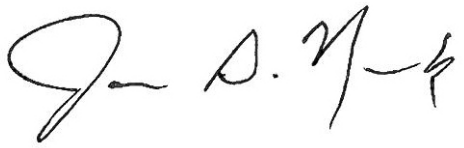
Interpretation and Reporting of Genetic and Genomic Test Results. The data collected by AMP's Clinical Practice Committee in recent years indicates that the transmission of genetic test information is not optimal. The influence of this information on ultimate clinical outcomes cannot be overstated and could be an important area for CER given this influence.

Valuation, Reimbursement and CPT Coding. Current methods for determining reimbursement for laboratory tests limit the incentive and ability of clinical laboratories to improve patient outcomes through improvements in quality assurance, testing, or communication with clinicians and patients. It may be useful to explore the effectiveness of both alternative testing and alternative reimbursement strategies in improving clinical outcomes. It is possible that changes in reimbursement strategy could significantly improve the use of laboratory tests, and thus clinical outcomes, with potential savings of thousands of dollars per patient. Such research could also include approaches to "coding" of clinical activities; AMP believes that it is possible that the use of new approaches to coding and reimbursement that can accurately describe the types of "evaluation" and "management" practices that are emerging with regard to molecular and genomic testing can improve resource utilization by focusing on clinical outcomes rather than on "procedure counts." This can only be possible if the approach to coding and reimbursement is itself subjected to rigorous scientific scrutiny,

Comparative Methodology Research. Many different technical approaches are available for generating the same genetic test result. Relating testing approach to health outcomes is a neglected area of comparative effectiveness research. AMP supports the evaluation of a multiplicity of platforms in the evaluation of companion diagnostics. For example, studies that relate therapeutic outcomes to the test used to select patients for targeted therapeutics may result in more cost effective testing methods. As an example, had careful randomized trials and observational studies compared outcomes in patients who received Herceptin therapy on the basis of immunochemical testing with outcomes of those who were selected based on DNA tests, which correlate imperfectly with immunohistochemical tests, later breast cancer patients might have had better outcomes at lower cost.

Thank you for your attention and consideration of our comments. AMP hopes to continue to be a valuable resource to you as the Institute considers CER and other policy affecting molecular medicine. Please contact us if you need any clarification or further information.

Sincerely,



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