Association for Molecular Pathology
Promoting Clinical Practice, Basic Research, and Education in Molecular Pathology
9650 Rockville Pike, Bethesda, Maryland 20814
Tel: 301-634-7939 ▪ Fax: 301-634-7990 ▪ Email: amp@asip.org ▪ *www.amp.org*

July 8, 2008

Steven Teutsch, MD, MPH
Chair, Secretary's Advisory Committee on Genetics, Health and Society
NIH Office of Biotechnology Activities
6705 Rockledge Drive, Suite 750
Bethesda, MD, 20892

Dear Doctor Teutsch:

The Association for Molecular Pathology is pleased to have the opportunity to remain engaged with the Secretary's Advisory Committee on Genetics, Health and Society (SACGHS) and share our recommendations on priority areas to focus on in the future. 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.

We list below our suggestions for the committee's ongoing efforts.

Research Funding for Genetic Testing Clinical Outcomes Research
Discussion of clinical laboratory oversight always includes a requirement for clinical utility as there is a perception that genetic tests are being implemented for clinical use before any clinical utility is definitively established. However, little funding is available for the requisite clinical studies that would establish this utility to the rigorously defendable degree associated with more traditional diagnostic markers or pharmaceuticals. Biomarker discovery research is well funded, but this can lead to the discovery new biomarker – disease state relationships, yet no subsequent translational funding to move the discovery to clinical practice. As evidence to the need in this area, The Centers for Disease Control and Prevention (CDC) recently made a Request for Proposals for this type of clinical outcomes research, with a total of only $1.5M, for which they received approximately 35 applications.

We would like to see SACGHS investigate the current mechanisms for funding outcomes research for clinical diagnostics tests. Moreover, we would like to see research focus on the implementation and performance of tests in real clinical practice settings; incorporating the steps of test ordering by the physician, patient influence on whether or not to have a test, the interpretation of the test result and use of the test result for patient management/family decision making. SACGHS should also investigate whether there is a research funding gap, and if so, provide recommendations on how to meet this crucial need.

Role of Genomics in Comparative Effectiveness Research
An area of outcomes research garnishing more attention in Congress and among other policy makers is examining the comparative effectiveness of treatments, including how it relates 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. With the failure to adequately assess the value of diagnostics in the past, examining the role of genomics in comparative effectiveness research and ultimately policy decisions will be critical. We encourage SACGHS to join the dialogue on comparative effectiveness research and strive to encourage cooperation and collaboration among the HHS agencies.

Clinical Decision Support Tools

The inclusion of genetic/genomic information in the health care information pipeline will provide important information that could have an impact in the determination of disease risk, appropriate drug dosing to avoid adverse events, and the selection of effective treatment. For example, single nucleotide polymorphisms in the cytochromes P450 enzymes, which are determinants of the metabolism and activity of many prescribed pharmaceutical agents, contribute to unanticipated adverse events or therapeutic failures. It has been long known that an individual P450 "SNP profile" can influence clinical response but the clinical impact of genotype remains uncertain. Yet, tests to determine such SNP profiles are commercially availability and their use is growing.

As the effective clinical applications of genomic information become more prevalent, genomic technologies and bioinformatics tools will increasingly impact the Electronic Health Record. The application of Health Information Technology to support the effective integration of genomic information in routine clinical care will require broad access and data transmission capabilities to connect the patient, laboratory, clinician, and researcher and to optimize the exchange of clinical information and data that will be pivotal to clinical decision support. This information exchange relies upon the development of standards, best practices, and accepted protocols for efficient test ordering, performance, reporting, and interpretation of genetic information. Clinical Decision Support (CDS) tools could be used to drive the widespread adoption of these genetic technologies in clinical practice by providing education at the point-of-care. While the FDA provides general guidance on the validation of clinical software, there are no guidelines describing a formal process for the adoption and validation of local CDS configurations and the current regulatory framework for these tools.

In this context, we recommend that SACGHS survey the areas under development and explore future needs for the formation of standards, services, and resources for the integration of genomic information and clinical decision support. In addition, the committee should evaluate current oversight and policy needs to overcome systematic barriers and challenges for the integration of these tools in the care of patients.

Genetic Testing in a Non-Traditional Framework

The evolution of genetic testing and personalized medicine is moving in two parallel tracks. In addition to the well established traditional medical track that relies on clinical trials to establish clinical validity and utility, an alternate framework for genetic testing and utilization is apparent outside the usual mechanisms of medicine. This is driven by a number of factors including widespread availability of information to the public through the internet, the availability of testing services outside the traditional clinical laboratory, including whole genome testing information, the ability of genetic and genomic testing to have predictive value in the absence of active disease (and hence outside the realm of traditional medicine), and a fear of genetic discrimination if traditional routes are followed. While regulatory efforts may seek to restrain these non-traditional avenues of genetic testing, it is likely that they will persist and even flourish.

Acknowledging that seeking genetic information by the lay public will continue to grow, it is important that SACGHS examine the consequences of this non-traditional genetic testing track. Important aspects include an understanding of how non-traditional genetic testing will be used by the lay public and an understanding of how non-traditional genetic test results will be interfaced with traditional medical practice. The development of appropriate QA measures and practices to validate the quality of non-

traditional laboratory test results or integration of these laboratories into current regulatory oversight is critical to the utilization of this information in conventional clinical evaluations and treatment decisions.

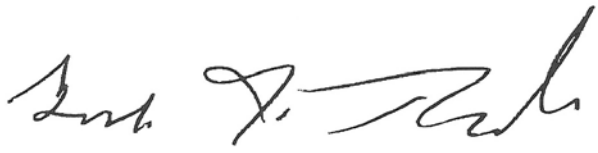
The consumer genomics industry has hastened the delivery of genetic information derived from genome wide association studies to the patient. SACGHS should explore the range of clinical applications and the appropriateness of providing this information to the patient population. Also, SACGHS should explore privacy concerns related to databases containing both phenotype and genotype information, as even without identifiers, there could be enough sequence data available to break confidentiality.

Previously, SACGHS focused and worked with the Federal Trade Commission on concerns about the advertising associated with "snake-oil" or fraudulent tests. SACGHS should take the next step to focus on legitimate diagnostics and the manner in which they are marketed to the consumer, which is inevitably an expanding market. SACGHS should identify areas in which standards should be created to define how tests can be appropriately marketed to the consumer and work with stakeholders on developing those standards.

Continued Monitoring of Oversight efforts and Reimbursement and Coverage Policy
SACGHS has released influential and important reports on both the oversight of genetic testing and the reimbursement and coverage of those tests. We encourage SACGHS to continue to build upon those efforts, work with stakeholders within and outside of HHS to revise and implement recommendations, and strive to improve the quality of genetic tests and appropriate determination of their value.

In closing, we reiterate AMP's commitment to the support of SACGHS, not only in pursuing the next phase of deliberations, but in translating the results of this effort for the improvement of the public's health and well being. Please contact Jean Amos Wilson, AMP Professional Relations Committee Chair at jamoswilson@sequenom.com if we can provide further information.

Sincerely,



Gregory J. Tsongalis, PhD
President