DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Secretary's Advisory Committee on
Genetics, Health, and Society
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The Honorable Kathleen Sebelius
Secretary of Health and Human Services
200 Independence Avenue, S.W.
Washington, DC 20201

Dear Secretary Sebelius:

On October 5-6, 2010, the Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS) held its 23rd and final meeting to complete work on a report on genetics education and training and to continue its deliberations on three topics the Committee began to explore over the last year—affordable genome sequencing, genomic data sharing, and comparative effectiveness research. In light of the decision to end the SACGHS charter, the Committee endeavored to bring its final deliberations to a productive close by identifying the most salient concerns in these three areas and recommending a specific course of action that the Department of Health and Human Services (HHS) could take to understand the issues further and develop appropriate policy solutions. In addition, to summing up its conclusions on those three topics, the Committee also wishes to recognize the need for public policy deliberations around the integration of genetics and genomics in public health efforts, a topic of importance that SACGHS had planned to explore in the near future. SACGHS approved the genetics education and training report; the final, copy-edited version will soon be sent to you.

On behalf of all the members of the Committee, it has been our privilege to be of service to the HHS. We would like to conclude with an articulation of guiding principles that we think may be of lasting value to HHS as the integration of genetics and genomics in health care proceeds.

Implications of Affordable Whole Genome Sequencing

Genetic and genomic tests—along with other innovations in diagnostics and therapeutics—will likely play a significant role in defining a new approach to health care. The promise of these innovations is to enable a more precise prediction of patient risk for common diseases, more accurate diagnosis of disease, and improved use of existing drugs and the development of targeted therapeutics.

Advanced sequencing methods have brought the clinical use of whole genome sequence (WGS) data to reality. Although these technologies provide exciting, even paradigm-shifting, opportunities to improve health care, there are many challenges that will need to be addressed. Based on preliminary exploration of data quality and management issues; associated ethical, legal, and social issues; and informed clinical practice and economic impacts, SACGHS identified the issues below as particularly salient challenges of WGS.

- An inadequate understanding of genotype-phenotype associations impedes the interpretation of the many variants revealed through WGS. There is often limited information about the clinical validity and clinical utility of tests for variants in single genes and even less information about the clinical utility of testing the genome as whole, which is a major barrier to its appropriate use.
- Most health professionals currently do not have the expertise necessary to interpret and skillfully communicate findings of genetic tests. This reality will prove to be an even greater challenge for assuring the appropriate use and clinical interpretation of WGS testing, which includes large numbers of variants of unknown significance, incidental findings, and findings of a potentially sensitive nature.
- The current coverage and reimbursement system is ill-suited for WGS testing; it does not adequately cover or reimburse informatics costs or the cognitive services required to interpret WGS data.
- There is insufficient capacity to store and analyze WGS data and, as research reveals new, actionable findings, to effect timely and appropriate reassessment of the data by clinicians and patients. It is not clear who will be responsible for accessing, reevaluating, interpreting, and communicating these findings in "real time" to the patients and providers.
- The acceptable threshold of analytical validity and accuracy for WGS has not been defined nor do reliable tools and materials exist to evaluate the analytical validity of WGS tests.
- The current regulatory paradigm will require novel and creative approaches to mange WGS.
- The economic impact that WGS will have on the health care system is uncertain, and it may be significant.

SACGHS Recommendation: In light of these considerable challenges, experts and stakeholders should be convened on a regular basis to advise policy makers on the efficient adoption and clinical use of whole genome sequencing technologies to improve health outcomes.

<u>Genomic Data Sharing</u>

Genomic research and broad sharing of genomic data from individual research subjects is underway to advance the understanding of the genetic basis of common diseases. SACGHS explored the implications of such broad sharing by examining current data sharing models and governance structures and by gathering perspectives about the risks and benefits of genomic data sharing to ethnic, racial, and indigenous groups. Based on the insights gained through this work, SACGHS identified the following central issues that will require further deliberation and action:

- The importance of considering cultural perspectives and historical experiences in the design and implementation of genomic studies, including groups' expectations and motivations for participating in genomic research (the benefits);
- Existing data on group perspectives are being underutilized in policy development;
- The need for additional research on group perspectives, particularly groups that traditionally have not been surveyed;
- The need for guidance for researchers on best practices for engaging communities;
- The adequacy of funding, training opportunities, and other resources necessary for building genomic research capacity within underrepresented groups and communities;

- Lack of clarity about the role of IRBs, which typically focus on the protection of individual research subjects rather than risks to communities or groups, and other oversight bodies in ensuring that risks and potential benefits to groups are carefully considered in the design and conduct of genomic research and data sharing;
- The adequacy and effectiveness of existing U.S. policies to protect groups in genomic research and data sharing, including, for Native American groups, the relevance of Executive Order 13175, which establishes regular and meaningful consultation and collaboration with tribal officials in the development of Federal policies that have tribal implications, to genomic research and data sharing policy development; and
- The applicability of policies from other countries to policy development in the United States.

SACGHS Recommendation: A mechanism(s) is needed to address the issues surrounding the risks and benefits to indigenous, racial, and ethnic groups that participate in genetic and genomic research and data sharing. A federal entity or entities should be charged with the ongoing consideration of the unresolved issues identified here. For example, advisory bodies, such as The Presidential Commission for the Study of Bioethics Issues and the Secretary's Advisory Committee on Human Research Protections, or federal agencies, such as the Office for Human Research Protections and the National Institutes of Health (NIH) and its individual institutes, could be assigned to take up these important matters.

Comparative Effectiveness of Genetic Testing Information

In light of the major effort under way to advance the appropriate use of health care technologies through comparative effectiveness research (CER), focused attention is needed on clinical utility and comparative effectiveness research in genomic and personalized medicine. SACGHS has identified the following gaps in this area:

- The lack of evidence-based recommendations and guidelines for the use of genomic tests to assure their appropriate introduction in clinical practice;
- Defined thresholds of evidence that reflect the context of the specific test/intervention such as the rarity of disorder, clinical situation (e.g., severity of condition, alternative management strategies); economic impact, population likely to be affected, and type of test (e.g., screening, diagnostic, prognostic) do not exist;
- The value of a given test/intervention (i.e., impact on patient outcomes and economic impact on the health system) needs to be determined; and
- The current infrastructure, particularly information systems/electronic health records, is incapable of supporting implementation or capturing postmarket data.

SACGHS Recommendations: Based on these gaps and a review of the priorities defined by the Institute of Medicine (IOM) and Federal Coordinating Council for Comparative Effectiveness Research (FCCCER) and an analysis of CER projects funded through September 30, 2010, the steps below should be taken.

- **In order to achieve the goals of health care reform, the administration and Congress have invested significant resources in CER. Family history (FH), genetic, and genomic information are critically important factors to consider if the results of CER studies are to yield fully valid information. Further research is needed to ensure the appropriate translation of genomics into health care. Necessary programmatic direction is needed to ensure that:**

    - **The initiative "Identification of New and Emerging Issues for CER (AHRQ-10-10003)" includes a focus on FH, genetic, and genomic issues;**
    - **At least one of the eight Centers charged with identifying evidence gaps focuses on issues relating to CER and clinical utility of FH, genetic, and genomics in health care;**
    - **The inventory of CER that will be carried out (Solicitation Number: 10OS32990) explicitly collects and includes information related to the use of FH, genetics, and genomics in all inventoried projects;**
    - **The evaluation of CER studies to be carried out under the initiative "Evaluation and Impact Assessment of ARRA CER (Solicitation Number: 10-233-SOL-00191)" describes the extent, if any, to which the funded studies included FH, genetic, genomic information and assesses the impact of the decision to include or exclude such information;**
    - **The Comprehensive Informatics Framework for CER Dissemination supports the use of FH, genetics, and genomics; and**
    - **FH, genetic, and genomic issues are given priority consideration as funds become available (e.g., through the Agency for Healthcare Research and Quality's Unfunded Meritorious Applications program), particularly studies of the translation of personalized medicine into clinical practice.**

- **The development and use of fully functional EHRs is another key element to health care reform. Current informatics systems and EHRs are not capable of capturing FH, genetic, and genomic information in a coded computable fashion. This deficiency will impede CER studies and postmarket data collection for conditions where these data are critical. It will also affect the inclusion of point-of-care educational resources for clinical decision support. As such, the Office of the National Coordinator of Health Information Technology should be directed to explore options to facilitate the development of EHRs capable of handling FH, genetic, and genomic information and clinical decision support systems.**

- **The reform of the health care system is dependent on the development of evidence of best practices. While HHS agencies are supporting some efforts to develop evidence-based recommendations for genetics and genomics (e.g., the Evaluation of Genomic Applications in Practice and Prevention at the Centers for Disease Control and Prevention), HHS should be dedicating additional resources to expand the development of systematic evidence-based recommendations.**

- **Evidence-based genomics is critically important in ensuring that CER studies develop and achieve meaningful comparative effectiveness data. As such, individuals with specific expertise in evidence-based genomics should be nominated for membership on the methodology committee of the Patient-Centered Outcomes Research Institute.**

Public Health Implications of Genomics

While the translation of genomics into public health practice and mechanisms for addressing health disparities have been considered in all SACGHS reports, the Committee's primary focus has been on the integration of genomics into clinical practice, rather than on public health. There are wide-ranging implications of genetics and genomics for population health that should also be explored systematically to ensure the effective and responsible translation of genome-based knowledge and technology to improve health for all members of society. These issues include:

- The role of genomics in infectious disease control, occupational, and environmental health;
- The need for a better understanding of how genetic and environmental (both physical and social) factors interact to cause disease and public health programs that can assess those risk factors at the population level as well as the policy and programmatic implications of those risk factors; The lack of evidentiary standards and guidelines for population-based genetic screening, particularly using new genomic technologies;
- The capacity of public health systems to accelerate widespread implementation of evidence-based genomic recommendations;
- The need for policy development to lower barriers and assure cost-effective use of genomic information and technologies at the population level; and
- The need for public health tracking systems to monitor population use of genetic tests and services to determine safety, effectiveness and impact.

SACGHS Recommendation: Federal, state, and local health agencies as well as other public health stakeholders need guidance about all of these issues, and we encourage HHS to undertake a systematic examination of these challenges and opportunities.

Guiding Principles

During its tenure, the Committee produced in-depth reports, letters, and commentaries on topics central to the appropriate introduction and use of genetic technologies and information. Our studies have focused on coverage and reimbursement of genetic technologies, direct-to-consumer genetic testing, electronic health records, gene patents and access to genetic tests, genetic discrimination, genetic education and training, policy implications of large population studies, oversight of genetic testing, and pharmacogenomics. The sum total of the Committee's work, and the more than 60 recommendations contained in it, could provide a roadmap to help the Nation realize the benefits of genetics and genomics while avoiding potential harms and pitfalls. In addition, SACGHS's work reflects the guiding principles outlined below that may serve HHS well as new issues related to the integration of genetics and genomics in clinical care and public health arise.

- Genetic information resulting from the application of genetic technologies should never be used for discriminatory purposes, for example, to limit or exclude individuals or populations from health insurance benefits, employment, or participation in social activities.

- Historically, our society has regarded genetics and genetic information as having special characteristics. Increasingly, the public is beginning to appreciate that genetic information is not fundamentally different from other medical information. As the integration of genetics and genomics in clinical care and public health proceeds, the rationale for genetic exceptionalism should continue to diminish. This shift will be a welcome development since genetic information and test results should be treated like other complex laboratory tests that are expected to meet high standards of accuracy, validity, and utility.
- Genetic tests and technologies offered to the public should be subject to oversight of their safety and utility. The public should have access to complete, accurate, and balanced information describing the benefits, risks, and limitations of genetic technologies and genetic and genomic information to maximize the benefits and minimize the risks to health and welfare.
- To translate genetics and genomics fully into health care delivery requires evidence of the clinical benefit and economic value of those technologies and information systems that are capable of incorporating the information and, as appropriate, enabling the responsible sharing of the information.
- The application of genetics and genetic technologies should aim to enhance equity in health outcomes and reduce health disparities, and access to genetic technologies should be equitable and fair. Coverage and reimbursement policies also play an important role in patient access, and a number of adjustments are needed before such policies can bring about equity and fairness.
- To ensure that the benefits of emerging genetic and genomic technologies and knowledge are accessible to all Americans, public health professionals should receive adequate and appropriate genetics and genomics education and training.
- Research in genetics and genomics is essential and should be conducted responsibly, with consideration and attention directed toward protecting the rights and welfare of research participants (i.e., individuals and groups), protecting and appropriately sharing data, and conscientiously reporting and disseminating research results.
- The government, industry, academia, nonprofit organizations, communities, patients, and consumers must work collaboratively to address the principles enumerated above, particularly with regard to oversight, education, and responsible development and use of genetic technologies.

On behalf of the entire Committee, it has been an honor to be part of SACGHS, and we thank you for the opportunity to be of service. We hope that our work will be of lasting value to the Department in the years ahead as the integration of genetics in health care, public health, and society continues.

Sincerely,

Steven Teutsch, M.D., M.P.H.
SACGHS Chair