The Integration of Genetic Technologies Into Health Care and Public Health

A Progress Report and Future Directions of the Secretary's Advisory Committee on Genetics, Health, and Society

January 2009

Preface

To the Secretary of Health and Human Services:

This report will acquaint you with the contributions and active concerns of the Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS). Established in September 2002 and rechartered in 2004 and 2008, the Committee is a source of advice to the Department of Health and Human Services (HHS) and, if requested, to other departments and agencies of the Executive Branch. It serves as a public forum for deliberations on a broad range of human health and societal issues as a public forum for deliberations on a broad range of human health and societal issues raised by the development and use, as well as potential misuse, of genetic technologies.

During its tenure, the Committee has issued four major reports and has communicated with the HHS Secretary on several issues of critical importance, including the importance of the Genetic Information Nondiscrimination Act, the need for enhanced oversight of genetic testing, and the promise of pharmacogenomics. In this progress report, we provide you with a summary of past SACGHS activities, suggestions for several immediate action steps, and future directions.

The Committee has recently developed its strategic priorities for the next phase of its work, including (1) addressing issues relevant to reform of the health care delivery system (e.g., ensuring clinical utility of genetic tests, appropriate coverage and reimbursement policies, an adequately trained health care workforce); (2) evaluating ways to optimize the use of genetics to improve public health and deploy population-based disease prevention efforts; (3) suggesting means to foster productive consumer and patient engagement with genetics and personalized medicine (e.g., addressing issues of informed consent, privacy, direct-to-consumer services); and (4) assessing approaches to ensure that genomic technologies enhance equity in health outcomes. Our central concern is ensuring that the rapid progress in genetics and related science will best serve the requirements of public health and health care reform, and we believe that it is in these four areas where our contributions may be most useful.

We would welcome the opportunity to discuss with you and/or a member of your staff these and other issues of concern. Such feedback would help us ensure that our work will be as relevant as possible to you as you begin to address the Nation's significant health and human services needs.

We have greatly appreciated the opportunity to provide advice about the challenges and opportunities for health and society arising from genetic technologies, and we look forward to continuing to be of service to you as you take the helm of the Department of Health and Human Services.

Introduction

Advances in genetics and genomics promise to improve human health and, in addition, may have far-reaching implications for society in nonhealth arenas, including education, employment, and the law. The Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS) was first chartered in 2002 by the Secretary of the Department of Health and Human Services (HHS) as a public forum for deliberation on a broad range of policy issues raised by the development and use of genetic technologies and, as warranted, for the provision of advice on these issues. Its mandate includes the following areas of study:

- Integration of genetic and genomic technologies into health care and public health
- Clinical, public health, ethical, economic, legal, and societal implications of genetic and genomic technologies and applications
- Opportunities and gaps in research and data collection and analysis efforts
- Impact of current patent policy and licensing practices on access to genetic and genomic technologies
- Uses of genetic information in education, employment, insurance, and the law

SACGHS is composed of 17 individuals from around the Nation with expertise in disciplines relevant to genetics and genetic technologies, including biomedical sciences, human genetics, health care delivery, evidence-based practice, public health, behavioral sciences, social sciences, health services research, health policy, health disparities, ethics, economics, law, health care financing, consumer issues, and other relevant fields (see Appendix A). At least two of the members are specifically selected for their knowledge of consumer issues and concerns and of the views and perspectives of the general public.

Representatives of at least 19 Federal departments or agencies also have seats on SACGHS in an ex officio (nonvoting) capacity. The departments and agencies are the Department of Commerce, Department of Defense, Department of Education, Department of Energy, Department of Justice, Department of Labor, Department of Veterans Affairs, Equal Employment Opportunity Commission, Federal Trade Commission (FTC), and the following HHS Offices and agencies: Administration for Children and Families, Agency for Healthcare Research and Quality, Centers for Disease Control and Prevention, Centers for Medicare & Medicaid Services (CMS), Food and Drug Administration (FDA), Health Resources and Services Administration, National Institutes of Health, Office for Civil Rights, Office for Human Research Protections, and Office of Public Health and Science.

This report provides a summary of the Committee's prior work, a description of projects under way, and issues identified for future study and for immediate action.

Appendix B provides a list of SACGHS reports, letters, and other products as of December 2008. Appendix C provides a list of SACGHS recommendations from four SACGHS reports.

Priority Issues and Accomplishments: 2004-2008

Since its inception, SACGHS has explored, analyzed, and deliberated on a broad range of human health and societal issues raised by the development and use of genetic technologies. In considering the depth and breadth of the issues before it, the Committee devised an iterative prioritization process to help identify areas designated in the SACGHS charter whereby it might make recommendations to enhance the responsible integration of genetics into health care. In 2004 the Committee created a Roadmap[1] for its study priorities and identified three overarching issues to be considered in all aspects of its work—access to genetic technologies, public awareness and understanding of genetic technologies, and genetic exceptionalism (i.e., whether genetic information is different from other personal health information). Areas identified for study and possible recommendations included:

- Genetic discrimination
- Genetics education and training of health professionals
- Coverage and reimbursement of genetic technologies
- Oversight of genetic technologies
- Large population-based genomic studies
- Pharmacogenomics
- Gene patents and licensing practices and patient access to genetic tests
- Direct-to-consumer marketing of genetic technologies

SACGHS activities in these areas are summarized below. It is important to note that all Committee reports are disseminated for an extensive public comment process before completion. Requests for comments are posted in the *Federal Register*.[2]

Genetic Discrimination

From its first meeting, public concern about the potential misuse of genetic information in health insurance and employment was the highest priority issue for the Committee's study, and successful passage of Federal genetic nondiscrimination legislation was a major goal of the Committee. The Committee also commissioned an analysis of the adequacy of current law, and the results of these evidence-gathering activities were regularly communicated to the Secretary. The Genetic Information Nondiscrimination Act (GINA) was signed into law on May 21, 2008, to protect U.S. citizens against discrimination on the basis of their genetic information as it relates to health insurance and employment. The Committee plans to monitor the rulemaking and implementation process.

---

[1] *A Roadmap for the Integration of Genetics and Genomics into Health and Society: The Study Priorities of the Secretary's Advisory Committee on Genetics, Health, and Society*, June 2004. Available at: http://oba.od.nih.gov/oba/sacghs/reports/SACGHSPriorities.pdf.

[2] *Federal Register.* Available at: http://www.gpoaccess.gov/fr/index.html.

Genetics Education and Training of Health Professionals

In June 2004 the Committee issued a resolution[3] on genetics education and training of health professionals, encouraging the Secretary to pursue a series of activities to improve opportunities for professional and public education, particularly promoting sensitive and culturally appropriate public education to equip consumers with the knowledge and skills they need to participate effectively in health care decisions that are informed by genetic and genomic perspectives.

Coverage and Reimbursement of Genetic Technologies

In February 2006 the Committee completed its report *Coverage and Reimbursement of Genetic Tests and Services*[4] and concluded that although advances in genetics and genomics are driving the development of new genetic tests and services, problems with coverage and reimbursement are limiting their accessibility and integration into the health care system. The Committee made nine recommendations to alleviate the barriers and improve current mechanisms for coverage and reimbursement of genetic tests and services.

Oversight of Genetic Technologies

In its review of the oversight system for genetic technologies, the Committee identified five key gaps in existing policy: (1) regulations governing clinical laboratory quality; (2) oversight of the clinical validity of genetic tests; (3) transparency of genetic testing; (4) the level of current knowledge about the clinical usefulness of genetic tests; and (5) the ability of health professionals, the public health community, patients, and consumers to use these new tests effectively. In its April 2008 report *U.S. System of Oversight of Genetic Testing: A Response to the Charge of the Secretary of Health and Human Services,*[5] the Committee highlighted critical steps for addressing these gaps.

Large Population-Based Genomic Studies

A large-scale project in the United States to enhance the understanding of common diseases and improve treatments and therapies is considered by some scientists to be a logical next step that would build on the complete sequencing of the human genome. In June 2005 National Institutes of Health Director Dr. Elias Zerhouni asked the Committee to focus on preliminary questions that need to be addressed before considering whether the United States should undertake such a study. The resulting March 2007 report *Policy Issues Associated with Undertaking a New Large U.S. Population Cohort Study of Genes, Environment, and Disease*[6] presents issues for consideration by the Secretary in the areas of research policy; research logistics; regulations and ethics; public health, social, and economic implications; and public engagement.

---

[3] *Resolution of the Secretary's Advisory Committee on Genetics, Health, and Society on Genetics Education and Training of Health Professionals*, June 2004. Available at: http://oba.od.nih.gov/oba/sacghs/reports/EducationResolutionJune04.pdf.
[4] *Coverage and Reimbursement of Genetic Tests and Services*, February 2006. Available at: http://oba.od.nih.gov/oba/sacghs/reports/CR_report.pdf.
[5] *U.S. System of Oversight of Genetic Testing: A Response to the Charge of the Secretary of Health and Human Services*, April 2008. Available at: http://oba.od.nih.gov/oba/SACGHS/reports/SACGHS_oversight_report.pdf.
[6] *Policy Issues Associated with Undertaking a New Large U.S. Population Cohort Study of Genes, Environment, and Disease*, March 2007. Available at: http://oba.od.nih.gov/oba/sacghs/reports/SACGHS_LPS_report.pdf.

Pharmacogenomics

The emerging field of pharmacogenomics (PGx) arises from the convergence of advances in pharmacology, genetics, and, more recently, human genomics. Greater understanding of the role of certain drug-metabolizing enzymes has the potential to improve the health of large populations and subgroups by providing clinicians with tools to select therapies appropriate for their patients. In May 2008 the Committee issued its report *Realizing the Potential of Pharmacogenomics: Opportunities and Challenges*,[7] which identifies untapped opportunities and critical barriers associated with PGx research and makes policy recommendations to enhance the development of PGx applications and their integration into clinical practice and public health.

Gene Patents and Licensing Practices and Patient Access to Genetic Tests

Patent and licensing practices may affect access to genetic technologies and services by limiting the number of providers and increasing the costs of these technologies and services. In 2006 SACGHS initiated a study to assess the positive and negative effects of gene patenting and licensing practices on patient and clinical access to genetic tests and on the public's health and quality of life. A draft report is in preparation and is anticipated to be released for public comment in early 2009.

Direct-to-Consumer Marketing of Genetic Technologies

When they are based on science and are properly administered, analyses of an individual's genetic and molecular profiles can be used to predict predisposition to certain diseases, guide disease prevention strategies, and facilitate more effective use of therapies—that is, select treatments that are more likely to be effective and less likely to be dangerous based on an individual's genetic characteristics. The Committee, however, has been concerned about claims made by some companies that market genetic tests directly to consumers (DTC) or physicians. It communicated concerns about the role of FTC in the oversight of advertising claims of genetic testing companies to the Secretary in 2004 and 2006. The Committee has also identified DTC genetic testing as a high-priority topic because of concerns that consumer-initiated testing has the potential for adverse patient outcome, social stigmatization, privacy violations, and cost implications for the health care system.

[7] *Realizing the Potential of Pharmacogenomics: Opportunities and Challenges,* May 2008. Available at: http://oba.od.nih.gov/oba/SACGHS/reports/SACGHS_PGx_report.pdf.

Priority-Setting Process: Looking Ahead

During 2008 the Committee engaged in its second round of priority setting, which included public comments. The following issues have been identified as areas of possible future study.

Genetics and the Future of the Health Care System

Genetic/genomic tests—along with other innovations in diagnostics and therapeutic technology development—will likely play a significant role in defining a new health care approach. The hope is that new research will advance the development of genetic/genomic tests that can more precisely predict patient risk for common diseases, that can more accurately diagnose disease, and that will lead to more accurate use of existing drugs and the development of targeted therapeutics. Nonetheless, there are many questions about which changes and benchmarks would be needed to realize the benefits of this new approach. Which sustainable business models would provide adequate and sustainable financial incentives for the development of innovations? What systematic steps are necessary to support an affordable, accessible health care system that best uses advances in genetics and genomics? How will the Federal Government help ensure that the appropriate resources and infrastructure are available to learn about differences in genetic and epigenetic variations among various geographic and ethnic U.S. subpopulations?

Ensuring the Clinical Utility of Genetic Information

Clinical utility and comparative effectiveness determinations help guide clinical care, establish clinical guidelines, and inform coverage decisions. Given the growing role that genetic testing is expected to play in the future of health care, assessing the clinical utility and comparative effectiveness of various genetic tests will be a constructive way to ensure high-quality health care and potentially control future health care costs. Methods for conducting comparative effectiveness research, which include randomized trials, observational studies, systematic evidence reviews, and modeling, are the subject of considerable policy debate, and evidentiary standards for assessing the clinical utility of genetic tests have not yet been firmly established. In addition to the lack of underlying utility studies (and the lack of standards for judging those studies), there is no existing government or private-sector system capable of efficiently conducting utility assessments for the large number of emerging genetic tests. The practical effect of this series of problems is that public and private insurers and health care providers are unsure of the value of these tests and their appropriate use. Thus, problems in assessing the clinical utility of genetic tests are impeding the appropriate integration of genetic tests into health care.

Public Health Applications of Genomics With Attention to Health Disparities

Public health genomics is a multidisciplinary field concerned with the effective and responsible translation of genome-based knowledge and technology to improve population health. Risks for almost all human diseases result from interactions among genetic, behavioral, and environmental factors, which raise the possibility of targeting disease prevention and health promotion efforts to individuals at high risk because of their genetic makeup. Although the emerging field of genomics offers the promise of improved health for individuals and populations, the benefits may not be realized uniformly across all groups. For example, research suggests that there are racial differences in attitudes toward genetic screening for Alzheimer's disease and cancer predispositions. In addition, information is lacking about the distribution of genotypes in different populations, the benefits and risks of genetic testing, and the efficacy of early interventions. This priority area will focus on health disparities and population-level topics such as the distribution of genetic variants in the U.S. population and its subgroups and the interplay of genes, environment, and behaviors in determining population-level risk for disease and how this information can be appropriately used to improve health outcomes.

Implications of Consumer-Initiated Use of Genomic Services

The number of personal genomics services marketed directly to the general public has increased over the past few years as costs have decreased and data showing associations between genetic variants and disease susceptibility have become more widely available. Clinically, these new services focus more on detecting the possible risks for common chronic diseases than on single-gene disorders. Several companies also offer pharmacogenetic tests for drug metabolism profiles. Attempts to integrate the results of such tests into clinical practice are in the early stages, and concerns exist about whether knowing the results of such tests will actually improve health. Concerns include (1) the relative value of the information being provided, (2) the level of consumer understanding of the meaning and significance of test results, (3) the provider community's ability to understand the test results and translate such information for patients, and (4) the potential risks of misuse of information by consumers or third parties (e.g., insurers, employers).

Informed Consent, Privacy, and Discrimination Issues Relating to Genomic Data Sharing

Informed consent is a critical ethical requirement for individuals who volunteer for either clinical testing or participation in research. The issues associated with informed consent in the area of genetic and genomic tests are not necessarily different from informed consent issues related to other medical testing. However, the distinction between clinical practice and research is growing less clear, a trend that may be more pronounced with respect to genetic information. For example, in the clinical setting, outcome data can be used to assess the clinical utility of a genetic test (e.g., PGx testing), which may be considered research. In the research setting, large-scale, population-based, genome-wide association studies may uncover clinically meaningful information about individuals or groups of individuals, which has implications for the consent process. A particular concern is that whole-genome scans will provide a unique DNA identifier that could potentially be linked with data obtained or stored in other contexts, which has implications for consent and privacy. Thus, the issue of informed consent should be revisited to determine whether the evolving research paradigm using large databases of genomic information and the growth of personalized medicine challenges long-held assumptions about informed consent.

Coverage and Reimbursement for Genetic Services

Although advances in genetics and genomics are driving the development of new genetic tests and services, problems with coverage and reimbursement limit their accessibility and integration into the health care system. The Committee continues to pursue the issues identified in the February 2006 SACGHS report *Coverage and Reimbursement of Genetic Tests and Services* that remain unresolved—including identifying strategies to address obstacles to implementation—as well as any new issues that have emerged since the report was released. Public comments during the SACGHS priority-setting process highlighted the importance of addressing (1) problems within Medicare coding, billing, and payment and (2) reimbursement policies that serve as barriers to appropriate coverage and reimbursement of innovative genetic tests and, thereby, to patient access to these tests.

Genetics Education and Training

Advances in genetics and genomics are leading to better insights into disease processes and improved applications of genetic testing to inform health decisions, such as PGx testing to guide cancer treatment. The health community and the general public, however, are challenged to keep pace with these advances. Adequate and appropriate education is needed to ensure that all people have the tools necessary to aid their decisionmaking regarding genetic testing and screening, to know how to interpret results, and then to understand and follow subsequent guidelines. Underserved populations may benefit from research, such as variations in drug response, which holds promise as one way to address health disparities. Cultural and language barriers affect health care access and utilization. Cultural competence among health providers is needed to improve quality of care and patient outcomes. Efforts are also needed to increase the diversity of the health care workforce, including recruitment of genetic professionals from underrepresented groups. The SACGHS Education and Training Task Force was established in November 2007 to identify current strengths and deficiencies in the genetic and genomic education and training of health professionals, the public health workforce, and the general public. In assessing the workforce of health care providers and public health professionals, this Task Force will examine the needs of those with and without training or expertise in genetics. It will also examine the educational needs of patients and consumers to make informed decisions about the use of genetic and genomic services. In addition, the Task Force will assess the use of evaluative research methods to determine the efficacy of genetics and genomics education and training efforts.

Opportunities for Immediate Action

SACGHS has made many recommendations that address the integration of genetics and genomics into health care practice and public health. Although all of the identified issues warrant attention, there are four issues from the Committee's standpoint that need immediate action.

1. Create a national registry of genetic tests and testing facilities
2. Issue FDA guidance on the co-development of pharmacogenomic drugs and diagnostics
3. Incorporate family history in Medicare coverage policy and clarify Medicare billing options now available to genetic counselors
4. Enhance the oversight of genetic tests, especially those marketed directly to consumers

The first issue relates to a recommendation in the April 2008 report *U.S. System of Oversight of Genetic Testing: A Response to the Charge of the Secretary of Health and Human Services.* Currently, there is no authoritative source for information about genetic tests or their quality, validity, and utility. **Creating a national registry of genetic tests and testing facilities** would address a significant gap in the availability of information about genetic tests and the laboratories performing them.

Not only would a registry empower consumers and providers by arming them with reliable information about what is known and not known about the quality and validity of tests, but also it would provide a foundation for fulfilling other critical needs in the oversight of genetic tests. Specifically, such a registry would support the conduct of research on the clinical utility of genetic tests, the collection of postmarket outcome data, and the development of decision support tools for the electronic health record.

In the long term, the Committee recommends that HHS appoint and fund a lead agency to develop and maintain a mandatory, publicly available, Web-based registry for laboratory tests. However, there are practical and legal questions that require further analysis before a final decision can be made about how and where to implement the registry and require stakeholder input to determine the associated data elements that should be included in the test registry as well as the cost and burden of collecting them. In the interim, the Committee urges that the Secretary take steps to create incentives for laboratories to make their test menus and analytical and clinical validity data for these tests publicly available through GeneTests[8] or, at least, post them on their own Web sites. Access to high-quality, reliable information is imperative in an increasingly consumer-driven testing market. The growing availability of personal genomic information only heightens the importance of such information.

[8] The GeneTests Web site (http://www.geneclinics.org/) is a publicly funded medical genetics information resource developed for physicians and other health care providers and researchers and is available at no cost to all interested persons.

The second issue is found in the Committee's report *Realizing the Potential of Pharmacogenomics: Opportunities and Challenges*, which highlights the need for further progress in (1) the development and implementation of guidance on the co-development of PGx drugs and diagnostics and (2) the coordination of review of such products within FDA. **This critical and emerging area of personalized medicine requires FDA guidance on the co-development of PGx drugs and diagnostics.**

FDA can significantly encourage the development of PGx by providing a coordinated review process that promotes collaboration between drug and diagnostic developers. FDA recently published a table of biomarkers and associated drugs with guidance about how PGx tests should be used. However, additional guidance from FDA is a critical policy tool to promote co-development. Drug and test developers need additional incentives and a greater understanding of regulatory requirements to assume the additional economic costs associated with development of a PGx test.

The co-development guidance document and coordinated review process would provide a transparent and predictable pathway for both small and large diagnostic and drug developers as well as a clear signal that they will not be disadvantaged in the product review process. In the longer run, it is also important for FDA to promote more research and partnerships—as it has through the Critical Path Initiative and The Biomarkers Consortium.

The third issue, a recommendation in the Committee's 2006 report *Coverage and Reimbursement of Genetic Tests and Services,* deserves renewed attention. The Medicare program's current coverage policy impedes the integration of genetic technologies for the care of patients with a family history of disease. One way to address this problem is to **direct CMS to develop criteria defining when a family history should be considered a personal history of disease**. Such a change would make it possible for a Medicare beneficiary with a family history of disease to meet the "reasonable and necessary" standard for Medicare coverage of a genetic test or other indicated course of treatment. If the test showed that the patient was at high risk of developing the disease, steps could be taken to try to prevent or delay its onset. Family history is a key element of personalized medicine, and the Medicare program should embrace it.

As the importance of genomics in health care accelerates, ensuring an adequate genetics workforce and an informed public becomes an even more daunting challenge. One way to begin to address this challenge is to **clarify the billing options available to certified genetic counselors**. Currently, there is no clear guidance from CMS about which Current Procedural Terminology (CPT) code(s) genetic counselors are allowed to use when billing for services. Enabling genetic counselors to use the full range of CPT evaluation and management codes can enhance patient accessibility to genetic counseling services and informed decisionmaking before and after genetic testing. If it becomes clear that genetic counselors are allowed to use only one CPT code, the Medicare statute should be amended. Addressing this issue is one clear and straightforward step that could help the Nation meet the urgent and growing need for an adequate genetics workforce and enhance patient accessibility to genetic counseling services and informed decisionmaking before and after genetic testing.

The fourth issue highlights the Committee's remaining concern about certain types of DTC genetic tests that may fall outside the scope of Federal oversight. Some laboratory tests, such as nutrigenomic tests (e.g., a test for caffeine metabolism) and tests that determine the gender of a fetus, are examples of health-related tests that skirt the boundaries of the authority of the Clinical Laboratory Improvement Amendments

Act (CLIA). There is insufficient oversight of laboratories offering such tests, and their potential impact on public health is an increasing concern. In its report *U.S. System of Oversight of Genetic Testing: A Response to the Charge of the Secretary of Health and Human Services,* SACGHS recommends that **CLIA regulations and, if necessary, CLIA's statutory authority, along with FDA's risk-based regulatory authority and regulatory processes, should be expanded to encompass the full range of health-related tests, including those offered directly to consumers. Relevant Federal agencies should collaborate to develop an appropriate definition of health-related tests that FDA and CMS could use as a basis for expanding their scope**. Additionally, these Federal agencies, including the HHS Office for Civil Rights, along with State agencies and consumer groups, should propose strategies to protect consumers from potential harm and from unanticipated and unwanted compromises in privacy that may lead to harm. Additional oversight strategies that might be established should be balanced against the benefits that consumers may gain from wider access to genetic tests and potential cost savings.

Conclusion

This brief report provides a summary of the Committee's prior work, a description of projects under way, issues identified for future study, and recommended options for immediate action. The Committee hopes that its prior work has provided policy analyses and recommendations that are of use to the Department in addressing critical issues raised by the development and use of genetic technologies. In keeping with its charter, the Committee looks forward to being of continuing service to HHS and the other departments and agencies represented on SACGHS in the years ahead and to working with the Secretary to address important policy issues to ensure that genetic technologies provide real value to the U.S. population.

Appendix A

Committee Roster

Chair

Steven Teutsch, M.D., M.P.H.
(as of February 1, 2009)
Chief Science Officer
Los Angeles County Department of Public Health
Los Angeles, CA

Members

Mara Aspinall, M.B.A.
Senior Advisor
Genzyme Corporation
Cambridge, MA

Sylvia Mann Au, M.S., CGC
Hawaii State Genetics Coordinator
Genetics Program
Hawaii Department of Health
Honolulu, HI

Paul Billings, M.D., Ph.D., FACP, FACMG
President and Chief Executive Officer
CELLective Dx
Mountain View, CA
Chairman
Signature Genomics Laboratories, LLC
Spokane, WA

Rochelle Dreyfuss, M.A., J.D.
Pauline Newman Professor of Law
New York University School of Law
New York, NY

James P. Evans, M.D., Ph.D.
Professor of Genetics and Medicine
Director of Clinical Cancer Genetics and the
Bryson Program in Human Genetics
Departments of Medicine and Genetics
University of North Carolina at Chapel Hill
Chapel Hill, NC

Andrea Ferreira-Gonzalez, Ph.D.
Professor of Pathology and
Director of Molecular Diagnostics Laboratory
Virginia Commonwealth University
Richmond, VA

Kevin T. FitzGerald, S.J., Ph.D., Ph.D.
Dr. David P. Lauler Chair in Catholic Health Care
Ethics
Research Associate Professor
Department of Oncology
Georgetown University Medical Center
Washington, DC

Julio Licinio, M.D.
Professor and Chairman
Department of Psychiatry & Behavioral Sciences
Miller School of Medicine University of Miami
Miami, FL

Barbara Burns McGrath, R.N., Ph.D.
Research Associate Professor
University of Washington School of Nursing
Seattle, WA

Paul Steven Miller, J.D
Director, UW Disability Studies Program
Henry M. Jackson Professor of Law
University of Washington School of Law
Seattle, WA

Joseph Telfair, Dr.P.H., M.P.H., M.S.W.
Professor
Public Health Research and Practice
Department of Public Health Education
University of North Carolina at Greensboro
Greensboro, NC

Marc S. Williams, M.D., FAAP, FACMG
Director Intermountain Healthcare
Clinical Genetics Institute
Salt Lake City, UT

Paul Wise, M.D., M.P.H.
Richard E. Behrman Professor of Child Health and Society
Center for Health Policy
Center for Primary Care and Outcome Research
Stanford University
Stanford, CA

Ex Officio Members

Michael Amos, Ph.D.
Department of Commerce

(To be appointed)
Department of Defense

Daniel Drell, Ph.D.
Department of Energy

Department of Health and Human Services

Charles N.W. Keckler, M.A., J.D.
Administration for Children and Families

Gurvaneet Randhawa, M.D., M.P.H
Agency for Healthcare Research and Quality

Muin J. Khoury, M.D., Ph.D.
Centers for Disease Control & Prevention

Barry M. Straube, M.D.
Centers for Medicare & Medicaid Services

(To be appointed)
Food and Drug Administration

Denise Geolot, Ph.D., R.N.
Health Resources and Services Administration

Alan Guttmacher, M.D. (Acting Ex Officio Member)
National Institutes of Health

Robinsue Frohboese, J.D., Ph.D.
Office for Civil Rights

Michael A. Carome, M.D.
Office for Human Research Protections

Michael A. Carome, M.D. (Acting Ex Officio Member)
Office of Public Health and Science

Thomas Alexander, J.D.
Department of Labor

Ellen Fox, M.D.
Department of Veterans Affairs

Naomi Earp, J.D.
Equal Employment Opportunity Commission

Sarah Botha, J.D.
Federal Trade Commission

Appendix B

SACGHS Products as of December 2008

Reports and Resolutions

- Realizing the Potential of Pharmacogenomics: Opportunities and Challenges (May 2008)
  http://oba.od.nih.gov/oba/SACGHS/reports/SACGHS_PGx_report.pdf

- U.S. System of Oversight of Genetic Testing: A Response to the Charge of the Secretary of Health and Human Services (April 2008)
  http://oba.od.nih.gov/oba/SACGHS/reports/SACGHS_oversight_report.pdf

- Policy Issues Associated with Undertaking a New Large U.S. Population Cohort Study of Genes, Environment, and Disease (March 2007)
  http://oba.od.nih.gov/oba/sacghs/reports/SACGHS_LPS_report.pdf

- Coverage and Reimbursement of Genetic Tests and Services (February 2006)
  http://oba.od.nih.gov/oba/sacghs/reports/CR_report.pdf

- A Roadmap for the Integration of Genetics and Genomics into Health and Society: The Study Priorities of the Secretary's Advisory Committee on Genetics, Health, and Society (June 2004)
  http://oba.od.nih.gov/oba/sacghs/reports/SACGHSPriorities.pdf

- Resolution of the Secretary's Advisory Committee on Genetics, Health, and Society on Genetics Education and Training of Health Professionals (June 2004)
  http://oba.od.nih.gov/oba/sacghs/reports/EducationResolutionJune04.pdf

Letters

- Letter to the Secretary of Health and Human Services on the Need for Urgent Action on a Laboratory-Developed Test Registry, FDA Guidance for the Co-Development of Pharmacogenomics Drugs and Diagnostics, and Medicare Coverage and Billing Policies (August 18, 2008)
  http://oba.od.nih.gov/oba/SACGHS/reports/letter_to_Sec_08-18-08.pdf

- Letter to the Secretary of Health and Human Services on the Oversight of Genetic Technologies (April 27, 2007)
  http://oba.od.nih.gov/oba/SACGHS/reports/GenTest_letter_to_Sec_042707.pdf

- Letter to the Secretary of Health and Human Services on Direct-to-Consumer Marketing of Genetic Tests (February 8, 2006)
  http://oba.od.nih.gov/oba/sacghs/reports/DTC_letter_to_Sec_02_08_2006.pdf

- Letter to the Secretary of Health and Human Services on the Surgeon General's Family History Initiative (June 7, 2005)
  http://oba.od.nih.gov/oba/sacghs/reports/letter_to_Sec_06_07_2005.pdf

- Letter to the Secretary of Health and Human Services on Genetic Discrimination (May 3, 2005)
  http://oba.od.nih.gov/oba/sacghs/reports/letter_to_Sec_05_03_2005.pdf

- Letter to the Secretary of Health and Human Services on Direct-to-Consumer Marketing of Genetic Tests (December 8, 2004)
  http://oba.od.nih.gov/oba/sacghs/reports/DTCletter.pdf

- Letter to the Secretary of Health and Human Services on Genetic Discrimination (March 29, 2004)
  http://oba.od.nih.gov/oba/sacghs/reports/letter_to_Sec_03_29_2004.pdf

- Letter to the Secretary of Health and Human Services on Genetic Discrimination (June 27, 2003)
  http://oba.od.nih.gov/oba/sacghs/reports/letter%20to%20Sec_06-27-2003.pdf

Appendix C

Recommendations From SACGHS Reports

Realizing the Potential of Pharmacogenomics: Opportunities and Challenges, May 2008

1. Basic Research

The National Institutes of Health (NIH) should receive and put more resources into (1) basic research on the biochemical pathways associated with drug metabolism and drug action, the genes and gene variations involved in these pathways, and the functions of these genes related to the safety and effectiveness of drug treatments and diagnostics and (2) nonhypothesis-based approaches to understanding the relationship between genetic variations and individual responses to drugs.

2. Translational Research

As knowledge of the underlying biology accrues, further research will be needed to translate this knowledge into the development of clinically useful pharmacogenomics (PGx) products and to assess their clinical validity and clinical utility. HHS agencies should facilitate the development of clinically useful PGx products by investing more resources in all components of translational research (including translating basic research findings into clinical trials and translating clinical research findings into clinical practice, public health, insurance coverage, and health policy).

3. Clinical Research

A. Where study results will be used to demonstrate safety and efficacy to support a premarket review application, sponsors and researchers should be encouraged to consult with the Food and Drug Administration (FDA) and the Centers for Medicare & Medicaid Services (CMS) early in the study design phases. This approach will help ensure that these studies have adequate clinical study designs (e.g., sufficient statistical power) and quality controls in place should the study later be submitted for regulatory review.

B. As appropriate, NIH should consider making FDA's existing quality-of-evidence standards a component of its assessments of the scientific merits of grant and contract submissions.

C. In situations where PGx tests are essential to clinical drug use, HHS should require its grantees and contractors to participate in FDA's Voluntary Genomic Data Submission Program during the exploratory phase of drug development and/or the review process for preinvestigational device exemption.

D. To enable the investigation of biomarkers associated with drug response, HHS should encourage sponsors of federally funded clinical drug trials to obtain appropriate biological samples from research participants. HHS also should develop guidance and standards on how these samples and other participant data will be collected, stored, shared, and used (see also Recommendation 4 in the Research Logistics section of the SACGHS report *Policy Issues Associated with Undertaking a New Large U.S. Population Cohort Study of Genes, Environment, and Disease,* March 2007).

4. Development of PGx Products

A. FDA should develop and implement guidance on the co-development of PGx drugs and diagnostics. The guidance should clarify the review process for co-developed PGx products and promote collaboration between drug and diagnostics developers.

B. FDA's Office of Combination Products should coordinate FDA's review of co-developed PGx products to minimize delay in approvals and ensure timely access to them.

C. HHS should engage all stakeholders in identifying and providing incentives to encourage the development of PGx products, especially for smaller patient populations and/or markets.

5. Establishing an Evidence Base

The adoption of PGx technologies will hinge on the availability of evidence of their analytical and clinical validity, clinical utility, cost-effectiveness, and value of PGx. The following steps should be taken to facilitate the establishment of the evidence base and support the integration of PGx technologies into clinical practice and public health:

A. HHS should identify and address evidence gaps in the analytical and clinical validity, clinical utility, cost-effectiveness, and value of PGx technologies. Progress will require high-quality data resources; improved methodologies in the design, conduct, and analysis of observational studies; and empirical research on the evidence and standards necessary for making decisions for various purposes (e.g., coverage, clinical guidelines, performance metrics, value-driven health care) in various clinical contexts.

B. HHS should initiate and facilitate collaborations between public (e.g., Agency for Healthcare Research and Quality [AHRQ], Department of Veterans Affairs [VA], Centers for Disease Control and Prevention [CDC], CMS, FDA, NIH, National Institute of Standards and Technology) and private entities (e.g., private health insurance plans, pharmacy benefits managers, health care facilities with electronic medical records, clinical research databases, genetic repositories) to advance the generation and sharing of knowledge on the analytical and clinical validity, clinical utility, cost-effectiveness, and value of PGx technologies.

C. HHS should encourage and facilitate studies on the clinical validity and clinical utility of PGx technologies and the dissemination of study findings, including negative findings, through publications, meetings, and an information clearinghouse.

D. HHS should provide mechanisms that promote interactions among basic, translational, clinical, and outcomes researchers for the identification of endpoints and data elements to be measured. The goal of these interactions is to maximize the value and utility of basic and translational research data for downstream assessments of the clinical validity and clinical utility of PGx technologies.

6. Data Sharing and Database Interoperability

A. HHS should encourage private sector entities (including academic institutions) to share proprietary data voluntarily to advance the development and co-development of PGx products. Manufacturers should be encouraged to make their data publicly available to allow others to conduct research and publish such studies.

B. HHS should work with the private sector to identify obstacles to data sharing and develop solutions to overcome these obstacles (e.g., legal and data confidentiality assurances, intellectual property protections, funding of databases, and health information technology).

C. HHS should work with other relevant Federal Departments (e.g., VA, Department of Defense [DOD], Department of Commerce) and the private sector to improve data sharing and interoperability among databases. Specifically, HHS should work with existing organizations to create uniform genomic data standards, explore ways to harmonize data analysis methodologies, and develop an infrastructure to enable data exchange. Data sharing and interoperability of research, regulatory, medical record, and claims databases will facilitate the study of the molecular pathogenesis of disease, identification of targets for drug development, validation of PGx technologies, assessment of health outcomes associated with use of PGx technologies, and determination of the cost-effectiveness and economic impact of using these technologies.

D. FDA should identify, initiate, and facilitate research opportunities and public-private partnerships to encourage the development and co-development of PGx products (e.g., through the Critical Path Initiative, The Biomarkers Consortium).

7. Protection of Personal Information

Stronger data security measures will be needed as more PGx researchers access patient data. HHS, through mechanisms such as the American Health Information Community's (AHIC) Confidentiality, Privacy, and Security Workgroup, should develop guidance on how to balance the protection of privacy and confidentiality of personal data with access to these data for PGx research.

8. Population Stratification in Drug Response

A. FDA should develop guidance that encourages the collection and analysis of genetic and other biological factors that may be better biological predictors of individual differences in drug response than broad categories such as race, ethnicity, and gender.

B. When drugs are shown to be more or less effective in certain racial and ethnic subpopulations, FDA should encourage manufacturers to conduct additional postmarket studies to identify genetic and

other biological, social, behavioral, and environmental markers that may underlie the differential drug effects.

9. Coverage and Reimbursement for PGx Products

A. CMS should develop a guidance document detailing current Medicare, Medicaid, and State Children's Health Insurance Program coverage and reimbursement of PGx products. CMS also should survey public and private health plans about their decisionmaking processes and coverage policies to help inform its future PGx coverage and reimbursement decisions.

B. Because the issues identified in the SACGHS report *Coverage and Reimbursement of Genetic Tests and Services* (February 2006) are relevant to issues in this report, SACGHS urges HHS to act on the Coverage and Reimbursement report's recommendations.

10. Use of PGx Technologies in Clinical Practice and Public Health

Health care providers need guidance on how to use PGx information when making clinical decisions. The following steps will help ensure that PGx technologies are integrated effectively into clinical practice:

A. HHS should assist other Federal agencies, State agencies, and private sector organizations in the development, cataloging, and dissemination of case studies and practice models relating to the use of PGx technologies.

B. HHS should assist professional organizations in their efforts to help their members achieve competence in the appropriate use of PGx technologies. HHS also should encourage and facilitate collaborations between these organizations and the Federal Government around these activities.

C. As evidence of clinical validity and clinical utility for a PGx technology accrues, HHS should support the conduct of systematic reviews and technology assessments to summarize the evidence base. These systematic reviews and technology assessments should be disseminated to facilitate the development of clinical practice guidelines.

D. HHS should facilitate the development of evidence-based clinical practice guidelines and dosing guidelines by supporting consensus-building efforts among guidelines developers. These consensus-building efforts should include development of standards that define the minimal levels of evidence required to support guidelines decisions. These standards should take into account the clinical contexts (e.g., prevention, diagnosis, treatment) in which the PGx test may be offered.

E. To inform the development of PGx tests and dosing guidelines, HHS should fund clinical studies that provide evidence on whether PGx information is clinically useful.

F. The HHS Secretary should encourage organizations to submit clinical practice guidelines on PGx testing to AHRQ's National Guideline Clearinghouse™ to facilitate dissemination and encourage their implementation and use.

G. FDA should work with manufacturers to ensure that all relevant PGx information is included in drug labels in a timely manner. When a PGx test is mentioned in a drug label, information should be included about the test's analytical validity, clinical validity, clinical utility, dosing, adverse events, and/or drug selection for clinicians to use when making treatment decisions based on PGx test results. FDA should provide guidance on the standards of evidence that must be met for PGx information to be included in the label.

H. NIH and FDA should continue expanding the Internet-based DailyMed project, which provides up-to-date, real-time prescription drug label/package insert information to individuals who have Internet access. To ensure that all sectors of the public have access to this information, NIH and FDA should develop additional ways to disseminate this information.

11. Public Education and Engagement

A. To inform the public about the availability, benefits, risks, and limitations of PGx technologies, HHS should ensure that credible educational resources are widely available through Federal Web sites and other media.

B. HHS should use existing public consultation mechanisms to stimulate dialog on the potential benefits, risks, and limitations of PGx technologies. This dialog should include an assessment of the public's perceptions of and receptiveness to PGx and the public's willingness to use these technologies and participate in PGx studies.

12. Health Information Technology

The Office of the National Coordinator for Health Information Technology, through the activities of AHIC, should study how clinically validated PGx test results are being incorporated into electronic health records. HHS, in consultation with VA and DOD, also should take steps to ensure that the necessary infrastructure is in place to support the representation of PGx data in electronic health records for use in decision support systems and tools. HHS should explore the development of pilot studies that examine the impact of clinical decision support systems for PGx technologies on clinical practice at the point of care to maximize evidence-based best practices.

13. Enhancing Access to PGx Technologies

HHS should support policies that afford access to PGx technologies in ways that reduce health and health care disparities, improve health care quality, and prevent genetic discrimination. To this end, HHS should continue to encourage and fund research in support of this goal.

14. Consideration and Implementation of Recommendations

The HHS Secretary should take all necessary steps to review and prioritize these recommendations, assess whether and how to implement them, monitor HHS progress, and report back to SACGHS.

U.S. System of Oversight of Genetic Testing: A Response to the Charge of the Secretary of Health and Human Services, April 2008

Overarching Recommendation

In keeping with the HHS Secretary's responsibility and commitment to protect and improve public health and as part of an effort to support the advancement of personalized health care, the HHS Secretary charged SACGHS to assess the adequacy of the U.S. system of oversight of genetic testing. After extensive factfinding, consultation, and analysis, the Committee found significant gaps in the U.S. system of oversight of genetic testing that can lead to harms. The Committee also identified novel opportunities that would enhance oversight. The Committee formulated recommendations that, if implemented and sufficiently supported, would close major gaps, enhance future oversight, help ensure public safety and health, and facilitate the realization of personalized health care. These steps are extraordinarily challenging, and they will require both swift action and sustained leadership by the HHS Secretary and coordinated efforts at the highest level within the administration of HHS.

Analytical Validity, Proficiency Testing, and Clinical Validity

1. For a number of years, CMS had been planning to address gaps in the oversight of laboratories that conduct genetic tests by adding a genetic testing specialty under the Clinical Laboratory Improvement Amendments (CLIA). Recently, CMS changed direction and is now addressing these gaps with a multifaceted action plan. SACGHS considered the CMS rationale and reviewed the CMS action plan. SACGHS also carefully considered the recommendations of prior groups as well as the perspectives of stakeholders that support the specialty. In the end, the Committee concluded that identified gaps can be addressed without the creation of a genetic testing specialty. SACGHS proposes the following recommendations to support and/or augment the CMS action plan:

    A. Currently, CLIA requires all nonwaived tests to undergo some form of performance assessment, but only 83 specific analytes, none of which are genetic tests per se, are required to undergo the type of assessment called proficiency testing (PT). PT is currently considered to be the most rigorous form of performance assessment. In principle, genetic tests and all other nonwaived laboratory tests should be required to undergo PT. However, such a goal cannot be achieved immediately. Consequently, the following actions should be taken:

    - CMS should require PT of all nonwaived laboratory tests for which PT products are available. For tests without PT products, laboratories must use alternative assessment methods, as required under current CLIA regulations.
    - To promote the development of new PT products and facilitate performance assessment efforts, HHS should fund studies of the effectiveness of other types of performance assessment methods to determine whether they are as robust as PT and should support innovations in the way PT is performed, such as through methodology-based processes.

    B. CMS should consult or contract with experts in the field to train inspectors of genetic testing laboratories. Training by such experts will enhance inspectors' understanding of the technologies, processes, and procedures utilized by genetic testing laboratories and equip them to assess

compliance with CLIA requirements. In addition, CMS should identify and evaluate innovative, alternative mechanisms to inspect genetic testing laboratories.

C. As recommended in a 2006 Government Accountability Office report on clinical laboratory quality, CMS should use revenues generated by the CLIA program to hire sufficient staff to fulfill CLIA's statutory responsibilities, and the program should be exempt from any hiring constraints imposed by or on CMS.

2. Currently, there are gaps in the extent to which analytical validity and clinical validity data can be generated and evaluated for genetic tests. To address these gaps, SACGHS recommends devoting public resources for genetic testing through the following actions:

   A. In consultation with relevant agencies, HHS should ensure funding for the development and characterization of reference materials, methods, and samples (e.g., positive and negative controls and samples from different ethnic/geographic populations) for assay, analyte, and platform validation; for quality control and performance assessment; and for standardization.

   B. HHS should ensure funding for the development of a mechanism to establish and support a laboratory-oriented consortium to provide a forum for sharing information regarding method validation, quality control, and performance issues.

   C. HHS agencies, including NIH and CDC, should continue to work with public and private partners to support, develop, and enhance public reference databases to enable more effective and efficient collection of mutation and polymorphism data, expand clinical reference sequence databases, and provide summary data on gene-disease associations to inform clinical validity assessments (e.g., RefSeqGene, HuGENet). Such initiatives should be structured to encourage robust participation; for example, there is a need to consider mechanisms for anonymous reporting and/or protections from liability to encourage information sharing among members.

   D. HHS should provide the necessary support for professional organizations to develop and disseminate additional standards and guidelines for applying genetic tests in clinical practice. CMS should work with professional organizations to develop interpretative guidelines to enhance inspector training and laboratory compliance.

3. The Committee is concerned by the gap in oversight related to clinical validity and believes that it is imperative to close this gap as expeditiously as possible. To this end, the Committee makes the following recommendations:

   A. FDA should address all laboratory tests in a manner that takes advantage of its current experience in evaluating laboratory tests.

   B. This step by FDA will require the commitment of significance resources to optimize the time and cost of review without compromising the quality of assessment.

C. The Committee recommends that HHS convene a multistakeholder public and private sector group to determine the criteria for risk stratification and a process for systematically applying these criteria. This group should consider new and existing regulatory models and data sources (e.g., New York State Department of Health Clinical Laboratory Evaluation Program). The multistakeholder group should also explicitly address and eliminate duplicative oversight procedures.

D. To expedite and facilitate the review process, the Committee recommends the establishment of a mandatory test registry as noted in the following recommendation.

4. There are considerable information gaps about the number and identity of laboratories performing genetic tests and the specific genetic tests being performed. To gain a better understanding of the genetic tests being offered as laboratory-developed tests and to enhance the transparency in this field, SACGHS reviewed proposals for a voluntary or mandatory test registry and considered the benefits and burdens of each type of system. The Committee decided that a mandatory, publicly available, Web-based registry that is well staffed to maintain an accurate and current database would offer the best approach to addressing these information gaps in the availability of tests and their analytical and clinical validity. Since genetic tests are not different from other laboratory tests for oversight purposes, the registry should include all laboratory tests. The Committee also discussed whether such a database should reside at CDC, CMS, or FDA, but recognized that unresolved issues, including practical and legal questions, require further analysis before a final decision can be made about how and where to implement the registry. In concluding that a mandatory registry should be established, SACGHS recommends the following course of action:

   A. HHS should appoint and fund a lead agency to develop and maintain the mandatory registry for laboratory tests. The lead agency should work collaboratively with its sister agencies to create a comprehensive registry and minimize duplicative collection of registry information. For this purpose, the lead agency should be staffed with qualified personnel who are experienced in developing and updating large databases in a timely and accurate manner.

   B. The lead agency, in collaboration with its sister agencies, should convene a stakeholder meeting by September 2008 to determine the data elements associated with analytical validity, clinical validity, clinical utility, and accessibility that should be included in the test registry. The lead agency should cast a wide net for broad stakeholder representation, including individuals from the private sector who can represent a role for public-private partnerships in developing a registry. The lead agency, through this stakeholder effort, should assess the level of effort, as well as the burden on the laboratory and the impact on other key stakeholders such as patients, physicians, and payers, necessary to obtain each data element, including linking to reliable sources of existing information.

   C. While awaiting completion of the above processes, HHS should use short-term voluntary approaches such as incentivizing laboratories to register with GeneTests and encouraging laboratories to make their test menus and analytical and clinical validity data for these tests publicly available on laboratory Web sites.

5. Factfinding by SACGHS also identified gaps in the enforcement of existing regulations. For example, the CLIA program has an array of enforcement actions available, but those actions cannot be directly imposed on uncertified laboratories. Instead, CMS must report the laboratory to the HHS Inspector General for action. Neither Medicare nor Medicaid can reimburse laboratories without CLIA certificates, but this restriction has no consequence for laboratories that perform direct-to-consumer (DTC) testing. To address enforcement gaps, SACGHS recommends the following actions:

   A. To prevent laboratories from performing tests without appropriate CLIA certification, CMS should establish and exercise its regulatory authority to take direct enforcement actions against laboratories that perform tests for clinical purposes without proper CLIA certification. CMS should step up its efforts to make publicly available a list of laboratories that have been cited by CLIA for condition-level deficiencies.

   B. Appropriate Federal agencies, including CDC, CMS, FDA, and the Federal Trade Commission (FTC), should strengthen monitoring and enforcement efforts against laboratories and companies that make false and misleading claims about laboratory tests, including DTC tests.

6. SACGHS is concerned about certain types of health-related tests that are marketed directly to consumers and apparently fall outside the scope of CLIA. Some nutrigenomic tests (e.g., a test for caffeine metabolism) and tests that determine the gender of a fetus are examples of health-related tests that skirt the boundaries of CLIA's authority. There is insufficient oversight of laboratories offering such tests, and their potential impact on the public health is an increasing concern. DTC marketing of laboratory tests and consumer-initiated testing have the potential for adverse patient outcomes, social stigmatization, privacy concerns, and cost implications for the health care system. SACGHS recommends that:

   CLIA regulations and, if necessary, CLIA's statutory authority, along with FDA's risk-based regulatory authority and regulatory processes, should be expanded to encompass the full range of health-related tests, including those offered directly to consumers. Relevant Federal agencies (e.g., CMS, CDC, FDA, FTC) should collaborate to develop an appropriate definition of health-related tests that FDA and CMS could use as a basis for expanding their scope. Additionally, these Federal agencies, including the HHS Office for Civil Rights, along with State agencies and consumer groups should propose strategies to protect consumers from potential harm and from unanticipated and unwanted compromises in privacy that may lead to harm. Additional oversight strategies that might be established should be balanced against the benefits that consumers may gain from wider access to genetic tests and potential cost savings.

Clinical Utility

1. Information on clinical utility is critical for managing patients, developing professional guidelines, and making coverage decisions. SACGHS found a paucity of information on the clinical utility of genetic testing. There are inadequate data on which to base utility assessments, and only a few studies have been done of the clinical utility of specific genetic tests. More fundamentally, there has been insufficient analysis of the standard of evidence on which the clinical utility of genetic tests should be evaluated and on which evidence-based methods applicable to genetic testing should be developed.

Further policy analysis is also needed to define the process by which clinical utility assessments will be applied. To fill these needs, SACGHS recommends the following:

A. HHS should create and fund a sustainable public-private entity of stakeholders to assess the clinical utility of genetic tests (e.g., building on CDC's Evaluation of Genomic Applications in Practice and Prevention [EGAPP] initiative). This entity would:

- Identify major evidentiary needs
- Establish evidentiary standards and level of certainty required for different situations such as coverage, reimbursement, quality improvement, and clinical management
- Establish priorities for research and development
- Augment existing methods for assessing clinical utility as well as analytical and clinical validity, such as those used by EGAPP and the U.S. Preventive Services Task Force, with relevant modeling tools
- Identify sources of data and mechanisms for making them usable for research, including the use of data from electronic medical records
- Recommend additional studies to assess clinical effectiveness
- Achieve consensus on minimal evidence criteria to facilitate the conduct of focused, quick-turnaround systematic reviews
- Increase the number of systematic evidence reviews and make recommendations based on their results
- Facilitate the development and dissemination of evidence-based clinical practice guidelines and clinical decision support tools for genetic/genomic tests
- Establish priorities for implementation in routine clinical practice
- Publish the results of these assessments or otherwise make them available to the public via a designated HHS or other publicly supported Web site (e.g., GeneTests)

B. To fill gaps in the knowledge of the analytical validity, clinical validity, clinical utility, utilization, economic value, and population health impact of genetic tests, a Federal or public-private initiative should:

- Develop and fund a research agenda to fill those gaps, including the initial development and thorough evaluation of genetic tests and the development of evidence-based clinical practice guidelines for the use of those tests
- Disseminate these findings to the public via a designated HHS or other publicly supported Web site (e.g., GeneTests)

2. Health care payers are increasingly requiring evidence of clinical utility before they will pay for genetic tests. Therefore, coverage and reimbursement decisions play a critical role in stimulating innovation and facilitating access to genetic testing. In February 2006 SACGHS issued a report that made recommendations for developing evidence of clinical utility and addressing other barriers to the coverage and reimbursement of genetic tests and services in the public and private sectors. SACGHS offers the following recommendation concerning the development of clinical utility evidence:

Because the issues identified by SACGHS in the Coverage and Reimbursement report are still current, the Committee urges HHS to act on the report's recommendations. In addition, public and private health care payers, in collaboration with relevant groups such as test developers and clinical laboratorians, should develop mechanisms, such as coverage with evidence development or phased reimbursement, to facilitate the collection of clinical utility evidence for high-priority tests and applications. Implementation of innovative approaches should be accompanied by careful evaluation to assess whether they enhance or hinder innovation, the understanding of effectiveness, and appropriate utilization.

3. The value of genetic tests to patients is realized only when they are used appropriately. Quality improvement processes are needed to ensure that genetic tests are delivered consistently to appropriate patients. Furthermore, an ongoing process is needed to identify opportunities for improving the use of genetic testing, including the collection of postmarket outcome data. SACGHS, therefore, makes the following recommendation:

   HHS should conduct public health surveillance to assess health outcomes (or appropriate surrogate outcomes), practice measures (including appropriate utilization), and the public health impact of genetic testing. Information should be linked to quality improvement practices that affect patient outcomes and the provision of health care services. Data on specific genetic testing results would be required to permit understanding of the significance of genetic variants and new detection methods to improve the utility of genetic testing.

4. The clinical utility and value of genetic testing is inextricably linked to methods to improve health care processes and decision support. Interoperable electronic health records will play a central role in the translation of guidelines into health care practices through their decision support and educational functions. These records will serve as a critical resource for assessing clinical utility and quality of health care. SACGHS therefore makes the following recommendation:

   HHS should ensure the coordination and implementation of efforts—including the deliberations of SACGHS; AHIC and/or its successors; and other workgroups addressing personalized health care, population health and clinical care connections, and confidentiality, privacy, and security—to advance the appropriate use of interoperable patient-level data for research and enhance the quality of decisionmaking.

Communication and Decision Support

1. There are documented deficiencies in genetic knowledge in all relevant stakeholder groups. In addition to the creation of the SACGHS education task force, SACGHS recommends the following strategies to address these deficiencies:

   A. HHS should work with all relevant government agencies and interested private parties to identify and address deficiencies in knowledge about appropriate genetic and genomic test applications in practice and to educate key groups such as health care practitioners, public health workers, public and private payers, and consumers of health care. These educational efforts should take into account differences in language, culture, ethnicity, and perspectives on health and disability as well as issues of medical literacy, access to electronic information sources such as the Internet,

and deficiencies in public infrastructures (e.g., libraries) that can affect the use and understanding of genetic information.

B. Based on increased research regarding analytical validity, clinical validity, and clinical utility, sufficient resources should be provided to translate this knowledge into evidence-based clinical practice guidelines that enhance the quality of clinical health care and public health care outcomes.

2. Although FDA has asserted its authority over clinical decision support systems, the extent to which the Agency intends to regulate such systems is not clear. Given that clinical decision support systems will be necessary to communicate information appropriately in the preanalytical and postanalytical periods and given that these systems contain elements that involve the practice of medicine, clarification of the nature and scope of FDA oversight of such support systems is critical. SACGHS recommends that:

   FDA should engage with other relevant Federal agencies, advisory committees to the HHS Secretary (e.g., AHIC, Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children), and stakeholders to gather perspectives on the appropriate regulatory framework for clinical decision support systems in light of changing health care delivery and health care data collection systems. As part of this process, FDA should prepare a guidance document articulating the basis of its authority to regulate clinical decision support systems as well as its rationale for and approach to such regulation, explaining in particular which features of the system constitute a device.

3. The need for genetic expertise to support best genetic testing practices has been identified as an essential element for the provision and interpretation of appropriate genetic tests. Access to genetic expertise could be addressed in part by solving problems in the reimbursement of genetic tests and services. SACGHS recommends that:

   HHS should act on the recommendations in the 2006 SACGHS report Coverage and Reimbursement of Genetic Tests and Services.

4. There are extensive gaps in knowledge about genetic tests and their impact on patient care. Prioritizing activities under the authority of HHS would help close these gaps and enhance the quality of patient care. SACGHS recommends that:

   HHS should allocate resources to AHRQ, CDC, NIH, and the Health Resources and Services Administration to design and support programmatic and research efforts to encourage the development and assist in the evaluation and dissemination of tools, particularly computerized tools, for clinical decision support in the ordering, interpretation, and application of genetic tests. HHS also should address current inadequacies in the clinical information needed for test interpretation. These efforts will require engaging health care providers and payers as well as providing incentives and protections to ensure their participation in the design and dissemination of tools, the implementation of clinical decision support, and the contribution of necessary data.

Policy Issues Associated with Undertaking a New Large U.S. Population Cohort Study of Genes, Environment, and Disease, March 2007

Overarching Recommendation

As part of the process for determining whether to undertake such a large-scale research project, the HHS Secretary should initiate a thorough consideration of the full range of policy issues outlined in this report. The HHS Secretary should consult and engage the full range of potential partners for such a project during this decisionmaking process, including the public at large, the full scientific community, a wide spectrum of Government agencies and policymakers, and the private sector.

Recommendations: Research Policy

If a new large population cohort study is conducted:

1. The HHS Secretary should continue to promote and facilitate ongoing consultation with the public, the private sector, and the international community to explore opportunities for collaboration on a large population study.

2. The HHS Secretary, in consultation with relevant HHS agencies and appropriate congressional committees, should assess support for sustaining a long-term and stable investment in a large population study.

3. Given the interdisciplinary nature of its scope, the HHS Secretary should establish a highly collaborative model of project leadership and management in multiple HHS and non-HHS agencies (e.g., NIH Institutes and Centers, CDC, the Environmental Protection Agency, and VA) and with other stakeholders. This includes the public and private sectors; biological, behavioral, social, public health, and population science disciplines; and basic biological scientists and epidemiologists.

4. The HHS Secretary, in consultation with relevant HHS agencies, should ensure that there are opportunities available to the general scientific community to (a) be informed about the potential for such a project; (b) present its views about the scientific validity and feasibility of such a project; (c) present its views on the commitment of resources to such an effort, including whether there are benefits to leveraging existing efforts; and (d) provide input on issues related to fair access by scientists to the project resources and the sharing of data and samples collected within it.

5. To ensure public benefits, the HHS Secretary should require that there are clear intellectual property policies in place for discoveries made using the data and samples collected.

Recommendations: Research Logistics

If a new large population cohort study is conducted:

1. The HHS Secretary should encourage the project leadership and the scientific community to develop clear, consistent definitions and parameters for the stratification and classification of the projected sample population to ensure diversity and appropriate representation in the population to be studied.

2. The HHS Secretary should seek input from the public, as well as from researchers and clinicians, on the best approaches for identifying, recruiting, educating, and enrolling various subpopulations. Project organizers should be encouraged to consult with community-based organizations as part of their recruitment, assessment, and enrollment strategies.

3. The HHS Secretary, in consultation with both HHS and non-HHS agencies, should refine methods for collecting and analyzing environmental (i.e., physical, behavioral, social) factors influencing health and ensure that resources are devoted to developing new tools to validate existing methods and improve assessments of the environment.

4. The HHS Secretary should encourage the project leadership to consult with health care providers and organizations to develop uniform and secure approaches for collecting, storing, tracking, and centralizing clinical information to be gathered over the course of the project, including the use of electronic health records.

Recommendations: Regulations and Ethics

If a new large population cohort study is conducted:

1. The HHS Secretary should convene a working group of representatives from the Office for Human Research Protections, FDA, Office for Civil Rights, and other relevant HHS and non-HHS agencies to address issues and questions raised by the public and to provide technical assistance and guidance to research sites on legal requirements regarding the protection of research subjects, health information privacy, and patient safety.

2. The HHS Secretary should establish an independent ethics committee to serve in an advisory capacity to the institutional review boards and the project leadership.

3. The project leadership should systematically and regularly seek the input of study subjects regarding their experiences, concerns, and recommendations for enhancing protections to ensure that the appropriate protections are in place and are being consistently implemented.

4. The project leadership should develop a policy regarding the use of data and samples to ensure the legal and ethical use of clinical and epidemiological data and specimens. This policy should be made available to study subjects.

Recommendations: Public Health, Social, and Economic Implications

If a new large population cohort study is conducted:

1. The HHS Secretary and the project leadership should systematically and regularly integrate project findings with other emerging data from other types of studies and regularly disseminate the accumulated knowledge base in a manner to benefit the population's health. This information should be tailored to meet the information needs of the public, health care providers, and the public health community to use integrated information for the benefit of the population's health. Project resources should be sufficient for the integration, dissemination, and translation activities necessary to maximize the public health impact.

2. The HHS Secretary, in consultation with the project leadership, should establish an independent standing committee for the duration of the project to periodically assess the persistent and emerging social and economic implications of this initiative, with special attention to health disparities. The committee could consist of individuals with expertise in the relevant sciences, medicine, law, ethics, and patient and community advocacy. The committee would routinely seek input from the public on the implications of project results and report its findings.

Recommendations: Need for Public Engagement

1. Before embarking on such a large population study and in advance of any funding decision, the HHS Secretary should assess the public's willingness to participate in such an extensive endeavor.

2. If a decision is made to proceed with a large population study, it will be important for the HHS Secretary to ensure that public engagement occurs throughout all aspects and stages of the research process, from conceptualization through design, planning, implementation, conduct, and data analysis and reporting. Public engagement also will be important in applying the knowledge gained by the research and in addressing its implications. The HHS Secretary should ensure that sufficient project resources are dedicated to public consultation activities before and throughout the duration of the project.

Coverage and Reimbursement of Genetic Tests and Services, February 2006

Evidence-Based Coverage Decisionmaking

Health care cost constraints, demands to improve health outcomes, a greater emphasis on quality, and the introduction of new technologies and procedures available for clinical use all are driving health care payers to reassess how they make decisions about which tests and services to cover and under what conditions they will reimburse them. Health insurance plans have emphasized evidence-based coverage decisionmaking as a way to determine which technologies and services are appropriate to cover. However, the evidence needed to make informed coverage decisions is lacking for many genetic tests and services. In addition, many genetic diseases are rare and/or currently lack therapeutic and preventive options, and rationalizing coverage for genetic tests and services can be more difficult when short-run costs cannot be recouped in short timeframe.

1. The HHS Secretary should task an appropriate group to develop a set of principles to guide coverage decisionmaking for genetic tests and services. The guiding principles should address the issues identified in this report, including economic evaluation/cost-effectiveness, prevention, rare disease tests, therapeutic benefit, and informational utility. The group also should assess the type, quality, and quantity of existing evidence for specific genetic tests to determine whether the evidence is adequate to establish a test's analytical validity, clinical validity, and clinical utility. If not, the group should identify any evidentiary gaps.

   This group should consist of experts from both the public (i.e., HHS agencies) and private sectors and make use of resources and models from both sectors. A workgroup organized by the Centers for Disease Control and Prevention, called the Evaluation of Genomic Applications in Practice and Prevention Working Group, is an example of such a group. It is made up of a diverse range of experts from both sectors and is performing related work, and thus could be tasked to develop these principles.

   In addition, a mechanism should be established to promote and fund studies to address evidentiary gaps identified by the group.

Medicare's Influence on the Private Insurance Market

Because Medicare is the largest provider of health insurance in the United States, its coverage decisions are closely monitored by private health insurance plans. Because genetic tests often are used for preventive, reproductive, or life planning purposes and because most hereditary diseases will manifest prior to age 65, it may not be appropriate for private health insurance plans to follow Medicare's lead in making coverage decisions for predictive and predispositional genetic tests and services.

2. Although standardization of coverage decisions using the best scientific evidence across public and private payers is ideal (see Recommendation 1 above), private health insurance plans are encouraged to make their own coverage determinations about genetic tests and services relative to the populations they serve. The group described in Recommendation 1 should make available the scientific evidence needed to make these decisions.

Medicare Coverage Decisionmaking Process

Medicare coverage decisions are made at both the national and local levels. Although national decisions apply to all beneficiaries, local decisions apply only to those beneficiaries living in the particular region (28 regions in all), which can lead to inconsistencies in coverage from one region to another. This dual system impedes rapid and widespread coverage of genetic tests and services.

3. The HHS Secretary should encourage CMS to move forward with the development of a plan to evaluate new local coverage decisions to determine which ones should be adopted nationally and to what extent greater consistency in Medicare coverage policy can be achieved (such a plan is mandated in Section 731 of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003). As part of its implementation of Section 731, CMS should consider a mechanism that would automatically initiate a national coverage review process for any test or service approved for coverage by a certain number of local Medicare administrative contractors.

Medicare Screening Exclusion

Federal statute prevents Medicare from covering preventive services unless explicitly authorized by Congress. The screening exclusion is embodied in a CMS policy that states, "Tests for screening purposes that are performed in the absence of signs, symptoms, complaints, or personal history of disease or injury are not covered except as explicitly authorized by statute." Since CMS considers predictive and predispositional genetic tests to be screening tests and since coverage of such tests has not been explicitly authorized by Congress, they are not covered by Medicare. The screening exclusion also limits Medicare coverage for genetic counseling.

4. Predictive and predispositional genetic tests can be clinically beneficial even when there are no current signs, symptoms, or personal history of illness. As such, predictive and predispositional genetic tests and their accompanying services that meet evidence standards should be covered under Medicare.

   The HHS Secretary should urge Congress to add a benefit category for preventive services that would enable CMS to use its national coverage decisionmaking process, which includes an assessment of existing evidence, to determine whether a test or service is reasonable and necessary for the prevention or early detection of an illness or disability in asymptomatic individuals and, thus, ought to be covered. A statutory change would allow CMS to consider covering many more genetic tests and services used for preventive purposes.

   More immediately, the HHS Secretary should direct CMS to clarify that, in certain cases as scientific evidence warrants, a "personal history" of disease can include having a family history of a disease. This change would make it possible for a beneficiary with a family history of a disease to meet the "reasonable and necessary" standard for Medicare coverage. CMS will need to develop criteria that define when a family history should be considered a personal history of disease.

Medicaid Coverage of Genetic Tests and Services

With the exception of newborn screening, genetic tests and services are optional Medicaid benefits. As a result, coverage for genetic tests and services can be affected by State budget cuts. Changes in States' Medicaid funding can create instability in access to genetic tests and services for the Medicaid population. Also, variation in Medicaid coverage across States can result in disparate access to genetic tests and services. Information and resources for making informed Medicaid coverage decisions can help minimize State variation in access to genetic tests and services.

5. The HHS Secretary should ensure that States receive information about the existing evidence base and other supporting information about genetic tests and services, such as guiding principles that serve as the basis for coverage decisionmaking (see Recommendation 1 above). This information should be used by States to inform their Medicaid coverage decisions.

   Through the provision of grant funding, HHS should continue to encourage States to cover, adopt, and provide genetic tests and services with a sound evidence base.

Medicare Clinical Laboratory Fee Schedule

Many providers who bill Medicare contend that Medicare's payment rates for clinical laboratory tests have not kept pace with inflation or with economic and technological changes in laboratory practices. As a result, Medicare laboratory fees often do not reflect a genetic test's true cost. In addition, Congress imposed a freeze on payment rates for clinical laboratory tests, locking rates at the 2003 level until 2009. HHS does have authority (known as the "inherently reasonableness" authority) to revise payment levels when they threaten beneficiary access to care or represent a misappropriation of taxpayer dollars.

6. When the congressional freeze on laboratory payment rates ends in 2009, the HHS Secretary should be prepared to revise payment rates to reflect the true cost of a genetic test. In the meantime, the HHS Secretary should direct CMS to invoke its inherent reasonableness authority to address variations in payment rates for the genetic test Current Procedural Terminology (CPT) codes.

Billing and Reimbursement for Genetic Counseling Services

Although genetic counseling is often critical to ensuring the appropriate use of genetic tests, counseling services are not being adequately reimbursed, a situation that can lead to access problems for patients in need of such services. The reimbursement problem has at least three sources. First, current CPT codes for billing are inadequate. Genetic counseling sessions can last for 2 to 3 hours, but the highest available CPT code accounts for a significantly shorter timeframe. There is a way to augment the CPT code, but such prolonged service codes are rarely reimbursed. Second, not all genetic counseling providers are eligible to bill Medicare directly. Currently, nurse practitioners, physician assistants, certified nurse specialists, certified nurse midwives, clinical psychologists, and clinical social workers are statutorily eligible to bill Medicare directly. Other nonphysician counseling providers must bill "incident to" a physician and, when billing Medicare for their services, they may use only certain CPT codes. Third, State licensure is an important credential for being recognized by payers as a qualified provider, yet only three States have authorized the licensing of genetic counselors.

7.

A. To ensure full access to genetic counseling services for all Americans, the HHS Secretary should expeditiously identify an appropriate entity to determine (1) which health professions are qualified to provide genetic counseling services (see page 49 of the Coverage and Reimbursement report for discussion of genetic counseling services and providers), and of those determined to be qualified, (2) which should be able to practice without physician supervision and, thereby, bill payers directly for their services. The entity selected to make these determinations should be guided by the professions' credentials, licensure status, scope of practice, and any other criteria deemed appropriate. The credentialing standards of a number of professional societies, such as the American Board of Genetic Counseling and the Genetic Nursing Credentialing Commission, could be used as reference points. A description of existing credentialing programs is provided in Appendix B of the Coverage and Reimbursement report.

   If this review process results in the determination that a health profession should be allowed to practice independently, the HHS Secretary should urge Congress to add this health profession to the list of nonphysician practitioners eligible to bill Medicare directly for its services.

B. HHS should assess the adequacy of existing CPT Evaluation & Management (E&M) codes and their associated relative values with respect to genetic counseling services. This assessment should be carried out with input from genetic counseling service providers. HHS should address any inadequacies as deemed appropriate.

C. The HHS Secretary should direct CMS to allow nonphysician health care providers who are deemed qualified to provide genetic counseling services and who currently bill incident to a physician to use the full range of CPT E&M codes available for genetic counseling services.

D. The HHS Secretary should ensure that all HHS programs are reimbursing prolonged service codes when they are determined to be reasonable and necessary.

E. The HHS Secretary should direct CMS to deem all nonphysician health care providers permitted to bill a health plan directly as eligible for a National Provider Identifier.

Provider Education and Training

Genetic tests are being marketed to health care providers and directly to consumers. If providers are not adequately trained in the use and interpretation of genetic tests, they may provide inappropriate services to their patients and expect to be reimbursed for them. Providers need adequate genetics education and training to know when genetic tests are appropriate and to help their patients make decisions about when to be tested. A working knowledge of genetics also is important for health payers because it will help them make informed and appropriate coverage decisions.

8. Since genetic tests and services are being integrated into all areas of health care and since providers have an important role in ensuring appropriate use of and access to genetic tests and services among diverse populations, there is a critical need for programs to educate and train health care providers and payers in genetics and genomics. Health care providers should be able to meet established genetic competencies and, thereby, integrate genetics effectively into their practices. The HHS Secretary should develop a plan for HHS agencies to work collaboratively with Federal, State, and private organizations to develop, catalog, and disseminate case studies and practice models that demonstrate the relevance of genetics and genomics.

   The HHS Secretary should provide financial support to assess the impact of genetics education and training on health outcomes.

   The HHS Secretary should strive to incorporate genetics and genomics into relevant initiatives of HHS, including the National Health Information Infrastructure.

Public Awareness

Public awareness of new health care tests and treatments can create consumer demand. Although greater public awareness and demand can facilitate coverage for new, safe, efficacious, and appropriate genetic tests and services, because of the complexity of genetic tests, they also can result in misinformation and inappropriate demand for genetic tests and services.

9. For patients and consumers to evaluate health plan benefits and health care providers and to make the most appropriate decisions for themselves and their families, they need reliable and trustworthy information about family history, genetics, and genetic technologies. The HHS Secretary should ensure that educational resources are widely available through Federal Government Web sites and other appropriate public information mechanisms to inform decisions about genetic tests and services.

Implementation of these recommendations should help improve appropriate access to and utilization of genetic tests and services by ensuring appropriate coverage and reimbursement throughout the health care system. Although the recommendations are primarily directed at HHS, the Committee hopes that private health insurance plans also will address the identified barriers that are relevant to them.