Secretary's Advisory Committee on Genetics, Health, and Society
Summary of Sixteenth Meeting
July 7-8, 2008
Bethesda, Maryland

Committee Members Present

Steven Teutsch, M.D., M.P.H., Chair
Mara Aspinall, M.B.A.
Sylvia Mann Au, M.S., C.G.C.
Paul Billings, M.D., Ph.D., FACP, FACMG (appointment pending)
Rochelle Dreyfuss, M.A., J.D.
James P. Evans, M.D., Ph.D.
Kevin FitzGerald, S.J., Ph.D., Ph.D.
Julio Licinio, M.D.
Barbara Burns McGrath, R.N., Ph.D.
Paul Steven Miller, J.D. (appointment pending)
Joseph Telfair, Dr.P.H., M.S.W., M.P.H.
Marc S. Williams, M.D., FAAP, FACMG
Paul Wise, M.D., M.P.H.

***Ex Officios*/Alternates Present**

Gurvaneet Randhawa, M.D., M.P.H. (HHS/Agency for Healthcare Research and Quality)
Muin J. Khoury, M.D., Ph.D. (HHS/Centers for Disease Control and Prevention)
Jeffrey Roche, M.D. (HHS/Centers for Medicare & Medicaid Services)
Steven Gutman, M.D., M.B.A. (HHS/Food and Drug Administration)
Denise Geolot, Ph.D., R.N., FAAN (HHS/Health Resources and Services Administration)
Francis S. Collins, M.D., Ph.D. (HHS/National Institutes of Health)
Alan E. Guttmacher, M.D. (HHS/National Institutes of Health)
Robinsue Frohboese, J.D., Ph.D. (HHS/Office for Civil Rights)
Michael Carome, M.D. (HHS/Office for Human Research Protections)
John Cusey (Administration for Children and Families)
Charles N.W. Keckler, M.A., J.D. (Administration for Children and Families)
Michael Amos, Ph.D. (Department of Commerce)
Col. Scott McLean, Medical Corps, U.S. Army (Department of Defense)
Peter T. Kirchner, M.D. (Department of Energy)
Amy Turner, J.D. (Department of Labor)
Sherrie Hans, M.D. (Department of Veterans Affairs)
Peter Gray, J.D. (Equal Employment Opportunity Commission)
Matthew Daynard, J.D. (Federal Trade Commission)

Executive Secretary

Sarah Carr, NIH Office of Biotechnology Activities

JULY 7, 2008

Opening Remarks

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

Dr. Steven Teutsch, Chair of the Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS), welcomed those in attendance and stated that the public was made aware of the meeting through notices in the Federal Register and announcements on the SACGHS website and listserv. He stated that a public comment session would be held the following day and encouraged members of the public who wished to address the Committee to sign up at the registration desk.

Dr. Teutsch welcomed Ms. Rochelle Cooper Dreyfuss, a new member of the Committee who was attending her first meeting. Professor Dreyfuss is the Pauline Newman Professor of Law at the New York University School of Law and served as a member of two National Academy of Sciences committees investigating intellectual property issues. She is a past chair of the American Association of Law Schools' Intellectual Property Committee. Professor Dreyfuss earned a law degree from Columbia University, as well as a degree in chemistry, and has worked as a research chemist. Dr. Teutsch also welcomed Charles Keckler, Deputy Assistant Secretary for Policy in the Administration for Children and Families (ACF) as the new ACF *ex officio*. Dr. Teutsch explained that Mr. Martin Dannenfelser left ACF to become Staff Director of the U.S. Commission on Civil Rights. Dr. Teutsch also noted a change in representation from the Office of Public Health and Science (OPHS). Dr. Inyang Isong left OPHS to pursue postdoctoral training in genomics and primary care through a pediatric health services research fellowship at Harvard. Until a new *ex officio* was named, Dr. Michael Carome was serving as the *ex officio* from OPHS, as well as from the Office for Human Research Protection (OHRP). Dr. Teutsch also noted two staff changes. Ms. Suzanne Goodwin left the SACGHS staff in May 2008 to complete her doctoral studies, and Mr. David Slade was serving as a summer intern.

Dr. Teutsch saluted the enactment of the Genetic Information Nondiscrimination Act (GINA) on May 21, 2008. GINA is a Federal law that protects consumers from discrimination in health insurance and employment on the basis of genetic information. Dr. Teutsch stated that much work lay ahead to implement the protections afforded by the law, which would take effect in June 2009 for health insurance provisions and December 2009 for employment provisions. He stated that, as important as the passage and enactment of GINA was, it did not cover life, disability, or long-term care insurance; or prevent all possible misuses. He commended the many advocates who brought the law to fruition and noted the role of SACGHS in supporting this legislation.

Dr. Teutsch reported that in April and May of 2008, the SACGHS reports on the oversight of genetic testing and the promise of pharmacogenomics (PGx) were formally transmitted to Secretary of Health and Human Services (HHS) Michael Leavitt. The Office of the Secretary (OS) was carefully assessing the recommendations in both reports.

Dr. Teutsch said the Committee would focus on three main agenda items during the meeting: deliberation about new study priorities, the marketing of personal genome information and services directly to consumers, and a proposed charge and action plan for Genetics Education and Training Task Force. He noted that in the afternoon, the Committee would attend a workshop on personal genome services sponsored by the Office of the Assistant Secretary for Planning and Evaluation (ASPE) and the

Secretary's Initiative on Personalized Health Care. The workshop would focus on understanding the needs of consumers in the use of genomic-based health information services.

Executive Secretary Sarah Carr reviewed the Committee's ethical responsibilities, and Dr. Teutsch turned the floor over to Dr. Paul Wise, Chair of the Priority-Setting Task Force.

Overview of Priority-Setting Process and Outcomes to Date

Paul Wise, M.D., M.P.H.
Chair, SACGHS Priority-Setting Task Force

Dr. Wise stated that the Priority-Setting Task Force was established at the February 2008 SACGHS meeting with the primary goal of identifying new priority topics for the Committee. He presented a timeline of Task Force activities, stating that between February and May 2008, 73 issues were identified for consideration by the Task Force. In June, issue statements on these topics were sent to SACGHS members and *ex officios* for scoring, and the results were tabulated. Dr. Wise said he would present these results with the goal of reaching Committee consensus on issues that merited further exploration. Following the meeting, during the period from July through November, additional background information and issue briefs will be developed on the issues (or categories of issues) considered of highest priority by SACGHS. This information would be sent to the Committee and *ex officios* for review. At the December meeting, final decisions will be made on new study priorities.

Several processes were used to identify issues for consideration. The first was a brainstorming session at the February 2008 SACGHS meeting. Additional ideas were solicited from the full Committee via email. A conference call was held with the *ex officios* to explore other potential issues for consideration. A request for public comment generated a large number of helpful suggestions. The request was disseminated through the usual mechanisms, including the Federal Register and the SACGHS website and listserv. These mechanisms were supplemented with outreach efforts to a variety of consumer organizations, medical associations, groups focused on health care disparities, and business groups and payers. In addition, telephone interviews were held with "horizon scanners," that is, experts who are studying the future of genetics and its impact on health care and society.

Of 73 issues submitted for consideration as priority topics, 33 were from public comments; 16 from horizon scanners; 18 from Committee members, staff, and *ex officios*; 5 from OS; and 1 topic was suggested from a journal article. These 73 items were sent to members and *ex officios* for scoring based on a 1-through-5 Likert scale, with 1 indicating "not important" and 5 indicating "very important." The criteria for scoring included the urgency and national importance of the issue; the extent to which the Federal Government has jurisdiction and authority over the issue; the need for Federal guidance or regulation on the issue; whether the issue raises concerns that only the Federal Government can address; whether the issue raises ethical, legal, or social concerns that warrant Federal Government involvement or leadership; whether the Committee's policy and advice on this issue would significantly benefit society; whether the failure to address the issue would prolong any negative impact the issue may be having on society; whether there is sufficient data about the issue for the Committee to develop informed policy advice; whether another body is already addressing the issue or is better equipped to address it; and whether the issue falls within the charter of the Committee.

Dr. Wise presented the 20 highest scoring issues, noting patterns in the voting created by clustering issues into categories that might be worthy of further development. He displayed a heat map that was generated as a mechanism to look at the profile of voting patterns. Dr. Wise stated that clustering voting

patterns could inform the way the issues could be grouped for further consideration. The categories that emerged based on these patterns were:

- Genetics and Health Care Reform
- Ensuring the Clinical Utility of Genetic Information
- Public Health Applications of Genomic Research
- Consumer Access to Genomic Information
- Informed Consent for Genomic Data Sharing
- Coverage and Reimbursement for Genetic Services
- Genetics Education and Training, and
- Genetics, Minorities, and Health Disparities.

Dr. Wise explained that the clusters were a starting point for the discussion, not an endpoint, and served only as guidance to the process. He said the Committee was free to rearrange the categories or create new ones. He said the next step was to reach consensus on the process used by the Task Force so that issue briefs could be developed on potential priority topics. He noted that the Priority-Setting Task Force would coordinate closely with the Evaluation Task Force and Genetics Education and Training Task Force, because many of the issues identified as high priority would likely fall under the their purview. Dr. Teutsch reminded the Committee that the Evaluation Task Force had been created more than a year ago to address translation, evaluation, and economics issues, but their activities had been deferred until the oversight report was completed. Ms. Mara Aspinall had been appointed Chair and the members identified. He said their efforts were just beginning, in contrast with the Education Task Force, whose efforts were well underway.

Dr. Wise stated that once issue briefs were developed, they would be distributed to the Committee for review, and the topics would be voted on at the next SACGHS meeting. This process would result in new priority issues for the Committee.

Discussion and Determination of High-Priority Issues

Dr. Evans reiterated that the impact of personalized medicine on health care was very different from the issue of clinical utility, and suggested that the two topics be teased apart into two categories. Dr. Wise said that sorting through these issues and recategorizing them would be an important focus of the Evaluation Task Force as the issue briefs were developed.

Dr. Paul Miller asked Dr. Wise to describe differences in SACGHS member scoring versus *ex officio* scoring. Dr. Wise said the *ex officios* generally conformed to the same hierarchy of priorities as the members, although they focused somewhat on areas that represented the activities of their agencies. Dr. Kevin FitzGerald asked if the Committee planned to address topics from a high-level vantage point or from a more detailed, fine-grained level. Dr. Evans said that some topics could be looked at from a broad view and others could be looked at narrowly. Dr. Joseph Telfair suggested the use of a grid map for the final priorities, such as those used in social statistics to demonstrate interrelationships.

Dr. Gurvaneet Randhawa asked about the types of products the Committee would develop for the new topics. For example, would they all require exhaustive fact-finding and result in large reports, or could there be white papers with a shorter turnaround time? Dr. Wise replied that different action steps might be appropriate for different issues and Ms. Aspinall agreed. Dr. Barbara Burns McGrath was concerned that some of the issues that ranked from 11 through 20 might not receive enough attention. She said the topic

on increased communication and coordination with bodies similar to SACGHS in Europe and Asia could cut across several other issues, such as informed consent. Dr. Wise said that although the international issue was not ranked highly by either *ex officios* or members, the Committee could choose to address it.

Dr. Sherrie Hans noted that *ex officios* in the Executive Branch were updating their presidential transition briefing books in preparation for the November election because new leadership was expected in all Departments. She stated that the Committee could take the opportunity to communicate three to five high priorities to the incoming administration during the transition. Dr. Teutsch agreed that it would be important to engage the new administration concerning new and previously addressed issues. He said PGx, oversight, and reimbursement issues would not be easily resolved and would require ongoing attention.

Dr. Teutsch asked the Committee to discuss the categories of issues presented by Dr. Wise. Dr. Wise suggested that they begin with the category titled, Consumer Access to Genomic Information. He stated that the elements of personalized medicine and genetics and personalized and direct-to-consumer (DTC) provision of genetic testing clustered together in the February brainstorming session and in the cluster analysis of the voting patterns. Dr. Hans stated that she was not aware of specific work in this area by HHS, in the public forum, or through committee work by other groups, and considered this an important opportunity for SACGHS. Dr. Evans said the first topic in the category, concerning the affordable genome sequence, would be difficult to distill, since it would have significant effects in many different areas. He did not believe it fit with the other topics in the category. He suggested that the remaining issues be subsumed under one category called, Impact On and Access by Consumers. Dr. Miller agreed that the affordable genome topic was more global than the others in the category and that the remaining issues fit well together and could lead to specific products or activities. Dr. Telfair added that the issue, Comprehensive Consumer Protection Strategies was driving the other three consumer issues in the group. He also suggested defining “access.” Dr. FitzGerald and Dr. Telfair agreed that the concept of “protection strategies” should be dropped, and Dr. Evans suggested substituting the phrase “implications of genetics as a consumer product.”

The Committee moved to a discussion of the category, Ensuring the Clinical Utility of Genetic Information. Dr. Telfair said he saw two groupings within the category on different aspects of outcomes. Dr. Dreyfuss asked about the difference between the terms "consumer" and "patient" and questioned whether the topic, Clinical Validity and Clinical Utility of DTC Genetic Tests for Common Disorders belonged in the category. Dr. Telfair and Dr. Evans agreed that it did not. Dr. Evans stated that only three of the topics in the category belonged together, as they addressed efforts to apply evidence-based medicine in the genomic field. However, he said the second and third issues—Impact of Personalized Medicine on Health Care and Clinical Validity and Clinical Utility of DTC Genetic Tests for Common Disorders—should be taken out and placed in different categories. Dr. Teutsch noted that these issues were addressed in part in the PGx and oversight reports in the sections on clinical utility guidelines and outcomes research. He said it was important to determine which areas had not yet been addressed in SACGHS reports.

Dr. Randhawa asked the Committee to consider adding some related topics, even though they did not receive the highest numbers of votes. He stated that the topic, Research Priorities for PGx overlapped with this category and was not addressed in the PGx Report. He also wanted to add the topic that addressed the use of PGx for improving the safety and efficacy of existing medicine. Dr. Evans pointed out that many of the implications of PGx fall into the realm of public health and would fit in that category. Dr. Khoury agreed, and stated that many of the other issues fell under the umbrella of public health, including those that relate to health disparities, screening, consumer awareness, education of

providers, policy, and oversight. Concerning other public health issues, Col. Scott McClean and Dr. Teutsch noted that the concepts of environmental and occupational genomics were relatively novel and might require attention by the Committee at some point.

Dr. Michael Amos suggested that the Committee create a list of short-term priorities that would coincide with the timing of the changing administration and result in some immediate products, with other products to be developed over a longer time period. Dr. Amos noted that the National Institute of Standards and Technology (NIST) is preparing the Executive Summary of a strategic plan that would be available the first week of December 2008. He said the times of greatest opportunity for Federal agencies would take place immediately after the election. Dr. Wise noted that the creation of short-term priorities would require a change in the timeframe of the current priority-setting process, which called for identification of priorities at the December meeting. However, he said the Task Forces could act quickly in areas that merited immediate attention. Ms. Aspinall suggested identifying one or two time-sensitive, priority issues the following day, for which position papers could be written quickly. Dr. Wise stated that the Committee could discuss this suggestion the next day. Dr. Teutsch pointed out that HHS had received several sets of recommendations for PGx, oversight, and reimbursement and coverage, which still required action. He said these issues could inform the processes in each of the HHS agencies and were important to move forward. Ms. Aspinall stated that re-articulating those issues for the new administration could be useful. Dr. FitzGerald suggested writing a letter to the Secretary describing the recommendations that had already been submitted to HHS. Dr. Wise suggested using this idea as a framing principle for the rest of the discussion.

Dr. Wise introduced the category titled, Genetics and Health Care Reform. Dr. Telfair noted that health care reform would entail a very large structural activity that would require much more thought and effort than the Committee could provide, although a contribution could be made in terms of recommendations. He noted that many other groups were working together on this issue. Dr. Keckler emphasized the importance of the issues in the category that related to the incorporation of genetics into electronic health records (EHRs), particularly since there was a vast increase in the amount of data generated on individual genomes that needed to be standardized or integrated. Dr. FitzGerald added that this category should include issues of privacy and confidentiality in EHRs.

Concerning the category titled, Coverage and Reimbursement for Genetic Services, the Committee agreed that it was important to follow up on the actions recommended in the report on this topic submitted to HHS. Dr. Marc Williams noted that several Committee members had met with representatives of the Secretary earlier in the year to discuss the Coverage and Reimbursement Report. He suggested that the Committee develop a process to maintain engagement around each report or other product generated for the Secretary to ensure forward movement. Dr. Teutsch and Dr. FitzGerald agreed. Ms. Au noted that the lack of adequate coverage and reimbursement for genetic tests created a stumbling block for other recommendations of the Committee, including those on education, access, and health disparities. She suggested emphasizing this point to the new administration and urging them to work on reimbursement issues.

Dr. Wise displayed the category of issues under, Education of Health Professionals on Genetics and Genomics, stating that it fell into the domain of the Education Task Force. He displayed the category, Genetics, Minorities, and Health Disparities; noting that the issues displayed did not rank in the top 20, but were very close. The Committee discussed whether these issues should be cross-cutting and they noted the work already done by SACGHS in this area. Dr. Wise said the issue brief for this category would attempt to make a case for this cluster of issues and would provide the Committee with more information with which to make judgments on whether work in this area was a priority.

Dr. Wise brought the discussion of the categories to a close and led the Committee in a discussion of next steps.

Next Steps

Ms. Aspinall reiterated her support for 1) summarizing the work already completed by the Committee to ensure that it would be a priority with the next administration, and 2) fast-tracking one or two new issues for additional work prior to the December SACGHS meeting. Dr. FitzGerald said it would be helpful for the Committee to identify barriers to their previous recommendations, with specific advice for moving forward. Dr. Evans and Dr. Teutsch agreed.

The Committee had a final discussion of the specifics of the categories, and Dr. Miller recommended that the title for Informed Consent for Genomic Data Sharing be broadened to include privacy and discrimination. Dr. Evans agreed, and added that the two issues in the top 20 regarding electronic medical records should be moved to the category on informed consent. He also suggested changing Consumer Access to Genomic Information to Implications of Genetic Information as a Consumer Commodity. Ms. Aspinall suggested Consumer Issues with Future Access to Genomic Information as an alternative.

Dr. Julio Licinio questioned whether SACGHS was the appropriate body to take on the political topic of health care reform. Dr. Evans said it was reasonable for the Committee to weigh in on the effects of the rise of genetic medicine on health care delivery and the structure of health care. Dr. Licinio and Dr. Miller suggested using the phrase “health care delivery” in the title of the category. Ms. Aspinall agreed that the word "reform" had political implications, but suggested the word “system” instead of “delivery.”

Dr. Williams raised the issue of how Medicare would apply the preventive medicine exclusion, which is relevant to genetics and health care reform and under the purview of the Secretary. He recommended working to gain an understanding of how the Center for Medicare and Medicaid Services (CMS) would interpret genetic tests as they relate to the preventive medicine exclusion, and he said this could be done in a relatively short time frame.

Dr. FitzGerald noted that there was not enough evidence on the potential exacerbations or positive contributions of genetics and genomics concerning minorities and health care disparities. He said that SACGHS could recommend to the Secretary that someone produce this data.

Dr. Teutsch verified that there was agreement by the Committee on the categories, including the recommended changes. He stated that the following day, the Committee would address whether some issues should be dropped, some should be addressed by an existing Task Force, or some should be taken up with a sense of urgency over the next 5 months prior to the vote on new priorities. Dr. Teutsch thanked Dr. Wise for his work and asked the Committee to depart for the Reagan Trade Center to attend the workshop *Understanding the Needs of Consumers in the Use of Genomic-Based Health Information Services*, sponsored by ASPE and the Secretary’s Initiative on Personalized Health Care.

JULY 8, 2008

Welcome and Opening Remarks

Opening Remarks
Steven Teutsch, M.D., M.P.H, Chair

Dr. Teutsch opened the meeting and turned the floor over to Mr. Rick Campanelli, Counselor for Science and Health Policy at OS.

Presentation of Award to Dr. Francis Collins
Richard Campanelli, J.D.
Counselor for Science and Health Policy, OS

Mr. Campanelli addressed the departure of Dr. Francis Collins from the National Human Genome Research Institute (NHGRI) and from SACGHS. He thanked Dr. Collins for his many years of service on behalf of the Secretary and the Department, stating that he had shaped the vision for the Human Genome Project and had fostered scientific achievements that would unlock the potential for improving human health. He noted that, as new scientific endeavors were pursued, Dr. Collins would continue to be a voice that placed ethical issues at the forefront. Dr. Teutsch added that Dr. Collins had made many significant contributions to SACGHS through his work on numerous Task Forces. He presented Dr. Collins with a gift from the Committee, which the members hoped would be a fitting symbol of his extraordinary leadership and vision. Dr. Collins thanked Mr. Campanelli and Dr. Teutsch for their remarks and said the American public needed those present to take the opportunity to transform the practice of medicine in a manner that benefits people and does not expose them to unnecessary risks. He stated that it was a great honor and privilege to serve as the NIH liaison to SACGHS.

Dr. Teutsch turned the floor over to Ms. Sylvia Au to lead the discussion on personal genome services.

Session on Personal Genome Services

Overview of Session and Introductions
Sylvia Mann Au, M.S., CGC

Ms. Au noted that the previous day, the Committee had attended a workshop sponsored by ASPE and the Secretary's Initiative on Personalized Health Care, which explored consumer interest in understanding personal genome services offered directly to consumers. The Committee would continue to focus on personal genome services in this session, including the state of the science, consumer perspectives, and public policy considerations. Representatives from several companies agreed to present on their information about their services and participate in a roundtable that would explore the genetic information they provide and how they help consumers interpret and use test results in health care decisionmaking. Ms. Au introduced Dr. Teri Manolio, who spoke to the Committee about the state of the science of genetic associations and genetic markers of disease. Dr. Manolio is the Director of the Office of Population Genomics at NHGRI and Senior Advisor to the Director of NHGRI for Population Genomics.

The Science of Genomic Associations: Current Status and Future Directions
Teri Manolio, M.D., Ph.D.

Dr. Manolio stated that few genomic associations with complex diseases were known until the 2005

genome-wide association findings for age-related macular degeneration. In 2006, three more associations were added, and in 2007, so many breakthroughs were made that 2007 was called the Year of Genome-Wide Association Studies (GWAS) by the journal *Science*. This work was based on the Human Genome Project and a haplotype map (HapMap) that showed relationships among 10 million single nucleotide polymorphisms (SNPs) based on individuals from four different geographic populations. A second generation HapMap was published in 2007, which expanded the number of known SNPs and provided a higher resolution map. The HapMap allows researchers to use a subset of the 10 million SNPs to infer genetic variation-disease relationships across the genome. The goals of using the HapMap for efficient association studies are: (1) to use a subset of SNPs with the proper density to find associations between polymorphisms and disease, (2) to identify chromosomal regions associated with disease, and (3) to develop a tool to assist in the discovery of genes affecting health and disease status.

In parallel with the development and expansion of the HapMap, the cost of genotyping has fallen dramatically—from about a dollar per SNP genotype in 2001 to about a penny in 2005, and the cost continues to decline. The combination of decreased cost and increased number of SNPs per analysis led to the discovery of genome-wide associations for many diseases and traits. Dr. Manolio said there were few, if any, similar bursts of discovery in the history of medical research. NHGRI maintains a website (http://www.genome.gov/gwastudies) that serves as a catalog of published GWAS.

A functional classification of 284 SNPs associated with complex traits revealed that less than 10 percent of the polymorphisms occurred in regions of the DNA that codes for proteins. About 40 percent of the SNPS occurred in intronic regions with no known role, and about half were in unknown regions of the DNA.

Several lessons were learned from the initial association studies, including the discovery of novel candidate genes that are associated with disease. For example, macular degeneration was thought to be an ischemic disease, but is actually very strongly related to complement factor H (CFH), an inflammatory disease-related factor. A cell cycle variant, previously known to be related to melanoma, was found associated with coronary disease. Childhood asthma, type II diabetes, and QT interval prolongation are also related to previously unsuspected genes. Initial studies also revealed that “gene deserts”—sections of DNA with no known gene-coding regions—are associated with disease. For example, prostate cancer is associated with variations with 8q24, and Crohn's Disease is associated with multiple gene deserts (5p13.1, 1q31.2, and 10p21). Additionally, GWAS have revealed common associations across seemingly unrelated diseases. For example, genetic variations in the CDKN2A and CDKN2B genes are associated with coronary heart disease and melanoma; variations in the PTPN22 gene are associated with rheumatoid arthritis and type 1 diabetes.

Dr. Manolio addressed the question: What are the recent advances in genomics research and how have these facilitated the emergence of personal genomic services? She stated that low-cost, high-throughput genotyping have been used for large-scale population research studies. Approximately 170 such studies have been completed, with more than 180 well-replicated loci associated with nearly 60 diseases and traits. She also noted that genotyping costs are now also within the reach of some consumers. She stated that valuable information about genetic associations will be learned from copy number variants, next-generation sequencing, DNA methylation, and gene expression.

Concerning the question: For which diseases are strong genetic associations and/or markers established?, Dr. Manolio said that “strong” could be defined in different ways, such as a large odds ratio, a very small P value, a risk allele occurring in the more than half the population, a large proportion of disease attributable to the risk allele, or the risk allele explains a large proportion of the genetic variance.

Dr. Manolio addressed the criteria that should be used to determine whether associations between a particular genetic marker and a phenotype are strong enough for that marker to be included in genetic testing. She noted again that the answer to this question depended on the definition of “strong," but stated that it also depended to a large degree on the purpose of the testing. Possible purposes of genetic testing are to improve health and prevent disease; provide targeted, proven risk reduction strategies to those at greatest risk; identify persons at high risk for a disease and who would be candidates for later rapid implementation of newly proven interventions; improve the cost efficiency of nongenetic risk reduction strategies; facilitate reproductive choices; or provide information that may be of personal value to individuals.

Dr. Manolio listed the following criteria to consider when selecting genetic variants for testing: the strength of the evidence for an association with risk; availability and acceptability of proven risk reduction interventions; the validity, availability, and cost of the test; the potential anxiety, stigma, cost, additional testing, or other harms caused by receiving the results; and the confusion that it may cause for the individual’s physician. Lastly, she listed the limitations in risk assessment for disease, which include that most genetic markers are not deterministic, that is, many people who do not have the markers will develop the disease, and many people who do have the markers will not develop the disease. Much of the genetic risk remains unexplained. At best, about 10 percent of the variance is explained for complex diseases. There is also little or no evidence that interventions based on genotype will improve outcomes.

Dr. Manolio stated that much research was still needed. One example is the multiplex genetic susceptibility initiative at NHGRI, which is designed to test approximately 15 risk variants for common, complex diseases in healthy people and provide that risk information back to participants to note what changes they made in their lifestyle and health behaviors. This initiative is also one step in creating an infrastructure to facilitate public health research.

Question-and-Answer Session

Dr. Licinio noted that most people have difficulty understanding risk information. A person could have a 1 percent risk of developing a condition and develop it, or a person could have a 99 percent risk of developing a disorder and not have it. He asked how this information is communicated to patients and doctors. Dr. Manolio agreed with Dr. Licinio’s concern and said that others present might be better qualified to comment.

Dr. Khoury queried how we should balance the implementation of genetic testing so that it is neither premature nor delayed unnecessarily. He also asked Dr. Manolio where, in her estimation, does the field of genetic association and its clinical utility lie compared to more traditional ways of stratifying risks such as using traditional risk factors and/or family history. What is the added value of genetic information? Dr. Manolio replied that no one had examined these questions very well and that additional research is needed to prove that genetic information adds to what we currently know based on family history or traditional risk factors.

Dr. Billings asked what kind of study would have to be done to undo a relatively well evidence-based standard such as mammographic screening of all women above the age of 50. Dr. Manolio responded that it would likely require a large randomized trial, in which some women are screened and others are not based on their genetic variants. Observational data would probably not be sufficient, as in the United States mammography is not universally applied. She clarified that using genetic variants as a basis for screening was only one possible use of risk information.

Dr. Collins noted that although GWAS have provided insights for disease pathways and new directions for therapeutics, researchers are not yet in a position to account for more than a small percentage of the heritability for a disease, even when several genetic loci have been identified for it. It could be that rare alleles—which are not identified through GWAS but can be detected by sequencing—have large heritable effects. He stated that much effort is being exerted to explore copy number variants and to apply sequencing techniques to identify genetic factors with large heritable effects. There are likely to be twists and turns in the path of discovery but potentially, in a few more years, we'll be in a more powerful position to make risk predictions.

Dr. Amos asked whether whole genome analysis studies were still worth doing. Dr. Manolio replied that genome-wide association is today's technology and that tomorrow's technology would probably be whole-genome sequencing. She predicted that genome-wide association would probably not be the tool of choice for research and discovery within the next few years. However, she said it might be of great value in assessing an individual's risk for a number of diseases. That type of information could probably be captured by GWAS without doing whole genome sequencing.

Ms. Au thanked Dr. Manolio and introduced Mr. David Ewing Duncan, Director of the Center for Life Science Policy and a visiting researcher at the University of California at Berkeley. He is an award-winning, best-selling author of six books and numerous essays, articles, and short stories; and a television, radio, and film producer and correspondent. Mr. Duncan presented his experience utilizing multiple personal genome services.

Personal Genomic Information: A Consumer's Perspective
David Ewing Duncan

Mr. Duncan said that as a journalist covering biotechnology and as an author writing a book called, *Experimental Man: What One Man's Body Reveals about His Future, Your Health, and Our Toxic World*. The experiment involves using a wide array of new tests that aim to forecast the future health outcomes of a healthy individual. For this experiment, he has been tested by all the major genomic testing services and used additional tests that analyzed environmental impacts and his microbiome, proteome, and other –omes.

The Committee had suggested that he address several questions, the first of which was, "What were your reasons for pursuing personal genome services?" He said that his primary purpose was as a journalist, but he was also interested in gaining insight concerning his future health. He stated that he was a healthy white male from a mostly healthy family with several members living into their nineties and beyond.

In response to the question "What sort of information did you anticipate receiving from these services?," he said he had fairly low expectations of receiving useful information given the early phase of the science but also hoped to confirm his health. He was also interested in the health of his family, and the following family members agreed to be tested: his mother and father, who were in their mid-70s at the time of testing and very healthy; his brother, who was 48; and his daughter, who was 19.

The next set of questions addressed the tests and their results: "What tests did you take? What were your results? Were there differences or overlapping results?" Mr. Duncan said he had been tested on most of the major SNP array chips and also received some information on insertions, deletions, and copy number variants. He was also tested for several dozen individual genes and is planning to have his entire genome sequenced. He was tested by many commercial companies, academic laboratories, and nonprofit

organizations. The cost of his tests, so far, is about $16,000; however, many of the companies and laboratories performed the work pro bono, and some of the costs were covered by the publications for which he was writing.

Mr. Duncan spoke primarily about three genomic-testing companies—Navigenics, deCODEme, and 23andMe. He explained that Navigenics focuses on diseases and does not analyze ancestry traits. It tested for 17 diseases. This company offers genetic counseling and is more expensive than the other two services, at $2,500. The deCODEme service, offered by the Icelandic company deCODE, provided him with information on 25 diseases and six traits and tested for ancestry and other attributes. deCODE is a publicly traded company that was founded more than a decade ago. It is involved in drug discovery, and its scientists have conducted some of the major studies that are used by many genomic testing services. The deCODEme service offers no genetic counseling and costs about $1,000. Testing by 23andMe also costs $1,000, and the company tested for 78 traits and provided ancestry information. It also rates whether the genetic associations are preliminary or established.

Mr. Duncan also had one test done by DNA Direct, which is a more established, online direct-to-consumer company that offers only individual genetic tests, primarily for those who have a predisposition in the family. He noted that his experience with DNA Direct was different than with the other companies because of the strong emphasis on genetic counseling. He added that DNA Direct provides a rich site of information that includes the pros and cons of genetic testing. Mr. Duncan recommended that the Committee look into the nonprofit company called The Coriell Institute. Over the next several years, it will use grant money to test 10,000 to 100,000 individuals for risk of about 15 diseases. Initial testing will begin with physicians in the Philadelphia area.

Mr. Duncan briefly described his results from the three major companies. He had low to high risk factors for age-related macular degeneration and type II diabetes. He observed that the genotyping results were very consistent across the three companies. The risk factor results provided from SNP analysis were generally consistent when the companies used the same SNPs. However, the lifetime risk factors presented by disease were not always consistent. Mr. Duncan explained that he received inconsistent and confusing results for his lifetime risk for heart attack. He noted that he had no family history of heart disease. From deCODEme, he received a low risk of heart attack, a high risk from Navigenics, and an intermediate risk from 23andMe. Some of the reasons for the lack of consistency include the fact that the companies used different SNPs in their analyses, different methods to determine risk, different methods for determining combined SNPs to produce a lifetime risk, and reliance on correlative SNPs, which consider linkage disequilibrium. In the end, the results for risk of heart attack left me confused.

Mr. Duncan said that the three-generation study of his family led to one surprising result. His father and brother were heterozygous for a risk variant for Alzheimer disease. There is no history of this disease in his family. His father noted that he had made it to age 76 without getting the disease and was not worried by the results. His brother also was not concerned.

Mr. Duncan remarked that there is a difference between common and rare diseases and questioned whether rare disease should be part of DTC testing. He shared that he brother has osteogenesis imperfecta and preferred to learn about this disorder through a medical professional, not through a DTC process. Mr. Duncan noted that the three genomic testing companies did not test for rare disorders.

The final question Mr. Duncan addressed was: "Did you alter your behavior in light of the test results?" He emphasized that he was atypical, both as a journalist and because of his deeper knowledge after being tested on many sites. His answer was that he did not significantly alter his behavior. Mr. Duncan also

noted that he did have some follow-up tests that are not yet available to consumers. Through these tests he learned that he has a higher than normal risk for heart attack and has altered his diet.

Mr. Duncan discussed the pluses and minuses of DTC testing. He noted that he received a great deal of information that would have been difficult to organize and understand on his own. Other minuses include high cost (which is likely to decrease), testing based on new technology that is a work in progress, genomic association studies are not always applicable to individuals, disease and nondisease results are sometimes mixed together, there are no standards for the validity of these tests or for how risk factors are determined, many physicians are not yet trained in genetics, and there is the potential that this information might frighten some people. However, he stated that the pluses of DTC testing include insight into personal and societal health and a sense of personal empowerment. The DTC companies are also nudging researchers and the health care industry to commit time and resources toward making genetic testing more relevant for individuals. DTC testing is also opening new avenues for genomic research and drug development.

Mr. Duncan concluded by stating that consumers should be free to buy these services and access their genomic information. He encouraged discussions among all stakeholders and said that guidelines and standards for tests should be established to ensure that consumers receive accurate information. He added that it would be helpful to have a program to set validation standards. Mr. Duncan stated that disease markers should be handled differently than nondisease markers such as those to determine ancestry and that counseling should be offered for markers that might impact a person's health. Physicians working with DTC companies should review disease markers and alert customers of serious findings. DTC companies should also provide customers with lists of local physicians and counselors trained in genetics.

Mr. Duncan invited the Committee to visit the Experimental Man website at experimentalman.com, which will eventually have all his test results.

Question-and-Answer Session

Dr. Khoury asked how to reconcile the need for guidelines with individual freedom. Even if guidelines recommend against the use of particular tests, Mr. Duncan would have used them anyway out of curiosity or to validate information he already had. Mr. Duncan replied that he engaged in the testing as a journalist to write a story. He said that data and information are becoming more accessible, and there are independent ways to analyze the data, such as through the Prometheus program. He added that we need to establish some guidelines but perhaps they could be voluntary. Consumers want accuracy, so standards would follow naturally.

Col. McLean asked whether Mr. Duncan had planned to share the test results with his physician from the beginning. He also questioned whether Mr. Duncan had consulted with experts, and if so, how he identified these experts. Mr. Duncan explained that he started the project with his personal physician, who had since retired. He also consulted with experts who he knew as a journalist.

Mr. Miller stated that human variation is a natural part of the human experience. Technologies can identify genetic anomalies, but what is the expectation from having this information? To eliminate differences? To create better health? Mr. Miller stated that he has achondroplasia but considered himself in good health. He asked if Mr. Duncan's brother with osteogenesis imperfecta (OI) was in good health, and if today's technologies had been available 40 years ago would his parents have screened their embryos for OI? Mr. Duncan answered that his brother cannot work because of his health and is taking drugs to slow his bone loss. Mr. Duncan said it would have helped the family dynamic to know his

brother's diagnosis when he first began having health problems. He added that many words need to be defined such as "health," "valid," and "usefulness." Mr. Miller stated that he was concerned about what genomic technologies are doing to assumptions about health and unhealthy and how that is related to disability and non-disability. Mr. Duncan responded that we all have different ways of viewing health and that Mr. Miller helped him with deep-felt sensibilities about who we are.

Dr. Billings asked Mr. Duncan whether he thought the error rate of the services he utilized was high or low. Mr. Duncan felt that the tests were very accurate because they were performed in laboratories certified through the Clinical Laboratory Improvement Amendments (CLIA). He emphasized that consumers should understand that risk information from test results can change as more is learned through research. Dr. Billing inquired if Mr. Duncan will monitor the traits that put him at increased risk. Mr. Duncan replied that he is monitoring his increased risk for heart problems. Dr. Billings asked if Mr. Duncan would disclose his increased risk for heart attack to his insurance company. Mr. Duncan said he contacted his insurance company but did not get a response. He also spoke to a major national actuarial group and asked them about their position on such test results. They said that association studies do not yet have the predictive power than an actuary would need to apply them, however, that could change in the future.

Dr. Telfair asked about the outcomes Mr. Duncan expected from the testing and what he recommended related to prevention. Mr. Duncan explained that we are in an interim phase. In the future, perhaps there will be ihealth programs that will provide measurements from the environment. He repeated the need to accelerate the validation of new technologies.

Dr. Evans asked to what extent the information from these tests could be personally empowering, since there was not yet enough evidence that the information could be applied and make a difference in health outcomes. Mr. Duncan said the information was not particularly personally empowering, but he believed that it would be useful to consumers in the future. He encouraged the development of standards and guidelines, as well as an educational process to explain to the public that DTC testing is in a transition period.

Ms. Aspinall asked about the role of genetic counseling. Mr. Duncan said he thought it was important to have access to a counselor if needed. He thought all the companies should have genetic counselors available. He suggested that physicians hired by the companies, or perhaps working independently, should review results to ensure that the consumer does not overlook or misunderstand any information.

Ms. Au thanked Mr. Duncan and began the session on personal genome service providers. She introduced Dr. Dietrich Stephan, Co-founder and Chief Science Officer at Navigenics.

Personal Genome Service Providers

Dietrich Stephan, Ph.D.
Co-founder, Chief Science Officer, Navigenics

Dr. Stephan said the original vision of Navigenics was to articulate an individual's entire germline genetic risk for all human diseases early in life and unmask useful portions of that information across the life span. The data could be used in conjunction with a physical assessment to allow an individual to avoid environmental stimuli that might trigger a complex genetic disease and to begin a focused biomarker monitoring program.

Dr. Stephan explained that genomic testing is not that different from medical genetic testing. Mutations are identified, and a penetrance metric is associated with it. As we use whole genome sequencing in unaffected people, we are discovering compound heterozygotes for mutations that do not have a disease phenotype. The concept of penetrance will be modified as we move forward. Primary prevention therapy or early treatment could reduce the burden of disease for individuals and on a public health level. He posited that alleles of "low effect size" (i.e., odds ratios between 1 and 10) are not very different from monogenic mutations that have penetrance variables associated with them.

Dr. Stephan stated that we are facing a health care crisis in this generation and indicated that a key driver in mitigating this crisis was early detection and prevention. Therefore, all presymptomatic risk information should be used to maximize the ability to focus prevention efforts and improve outcomes across the population. He said genetic risk factors could be used to refine risk in a clinical setting, but a new delivery vehicle was needed for these risk factors as the traditional monogenic testing environment was not geared to take them into account. Dr. Stephan said Navigenics was building the necessary infrastructure to take genomic samples early in life; fully sequence the genome for common, rare, and de novo variants; conduct holistic copy number analysis; sift through the epigenetic modifications; sequence the mitochondrial genome; and assemble all of the information together into a report?. The data would be entered in a computer, resulting in a rank-ordered list of predispositions for which preventive medicine could be practiced.

Dr. Stephan stated that Navigenics was building a new industry, and they understood the need for a gold standard team that could deal with ethical concerns, clinical paradigm shifts, and new ways to interact with the medical community. He said a scientific advisory board was guiding the company through the complex science and methods for providing genetic counseling, and they hired risk communication experts and an in-house team of genetic epidemiologists.

Navigenics decided that quality control (QC) and quality assurance (QA) were of utmost concern. The first year and a half of the company's existence was spent trying to understand the regulatory environment. As a result, they decided they needed a CLIA-certified laboratory with extremely stringent QC and QA parameters. Dr. Stephan said they also expended a great deal of effort understanding how to use retrospective case control data.

Dr. Stephan addressed the argument that the effect size of genetic variations was too low to be meaningful. He said that odds ratios or relative risks of between 1 and 5 were on the same scale and order of magnitude as the environmental risk factors the public health community had commonly messaged.

Dr. Stephan stated that Navigenics was increasing access to counselors and physicians, particularly since the passage of GINA reduced the risk of discrimination in health insurance and life insurance. He concluded by stating that Navigenics was trying to use genetic information to motivate behavior change. Published studies indicate that genetic testing promotes behavior change. For example, a prospective study of 59 individuals at high risk of melanoma based on family history examined screening behavior. Those who had genetic testing went for screening more often than those who had only family history information.

Ms. Au thanked Dr. Stephan and introduced Ms. Linda Avey, a Co-founder of 23andMe.

Linda Avey
Co-founder, 23andMe

Ms. Avey stated that 23andMe offered a new way to engage with consumers in a large-scale, Web-based effort to conduct genetics research. 23andMe was attempting to allow individuals access to their genomes in a very broad way, but Ms. Avey acknowledged that the company was in the early stages. 23andMe's services are available to individuals who send in a saliva sample, from which DNA is extracted at a CLIA-certified laboratory, and a set of about 600,000 data points are generated.

23andMe has created an interface called the Gene Journal to communicate risk information to its customers. The company's scientists review the literature and developwhite papers that explain the criteria they use to rate the research confidence for studies of specific diseases or traits as established or preliminary. The company began with 14 categories, but it has expanded because users have requested more information. The Gene Journals are kept current based on new studies. Ms. Avey said 23andMe was working with others in the industry to develop standards for risk information. The Personalized Medicine Coalition t is helping to organize these efforts.

Ms. Avey stated that data security was taken very seriously. Regular security audits were conducted and all sensitive data were encrypted. All account, genotype, and phenotype date are stored separately and are de-identified.

The company recently introduced the ability to conduct customer surveys that were validated by epidemiologists. This effort started with surveys on simple traits, such as eye color and handedness, to help 23andMe assess the accuracy of its model to conduct web-based research. Ms. Avey noted that people who participated in the surveys wanted immediate feedback and comparisons with others in the database.

Ms. Avey said 23andMe has funded the Michael J. Fox Foundation to conduct an in-depth Parkinson's disease study. The Parkinson's Institute in Sunnydale, California, had developed many tools for diagnosis and was interested in attempting to validate instruments online. The Institute also wanted to develop tools for measuring aspects of movement disorders on the Web using new technologies. Ms. Avey said the Michael J. Fox Foundation was interested in funding innovative research, such as the work by the Stanford Research Institute (SRI), which was devising ways to use the Nintendo Wii game to measure motor skills. 23andMe met with SRI and with Qualcomm, which was developing mobile technologies for understanding, measuring, and monitoring disease.

Ms. Avey stated that one of the company's goals is to let consumers be active participants in research and provide them with individual data. The overall goal is to work together to improve health care.

Ms. Au thanked Ms. Avey and introduced Dr. Jeff Gulcher, who was filling in for Dr. Kari Stefansson from deCODE Genetics.

Jeff Gulcher, M.D., Ph.D.
Co-founder, deCODE Genetics

Dr. Gulcher said that he and Dr. Stefansson co-founded deCODE Genetics 12 years previously to find genes for common disease that might help in predictive diagnostics and in targeting novel drug pathways. They set up operations in Iceland to focus on one population and had collected data on about 140,000 Icelanders. They also collected data on about 230,000 non-Icelandic samples from Europe, the United States, and Asia to help them rapidly replicate and determine whether these findings are valid in populations outside of Iceland.

Scientists at deCODE Genetics conducted linkage studies using their genealogy database and discovered associations with the TCF7L2 gene for type II diabetes and the 8q chromosomal region for prostate cancer. They expanded their analyses using the Illumina platform and added genome-wide association data from 370,000 to 1 million SNPs per individual. They have genotyped about 45,000 Icelanders and performed a combination of linkage family-based studies and genetic association studies. The goal of deCODE Genetics, from a risk diagnostic point of view, was to make available some of its discoveries for common diseases, picking diseases for which the relative risk, compared to the general population, might be high enough to have an impact on prevention and early detection. The company has launched disease risk tests for individual diseases such as myocardial infarction, type II diabetes, glaucoma, prostate cancer, atrial fibrillation, and stroke. Dr. Gulcher said physicians were already using some of this information in their practices to help risk stratify certain patients. For example, prospective studies indicate that TCF7L2 testing can help identify pre-diabetics at high risk for developing diabetes.

Dr. Gulcher said there was there a role for consumers to access their genetic information directly, with or without their physicians. He said they offered such access, as well as genetic counseling, which they had recently begun to provide at no cost. They also encouraged people to work with their physicians.

The deCODEme personalized genome analysis offers information on 30 diseases. Dr. Gulcher stated that analytical validation for genetics is much simpler than analytical validation for C-reactive protein (CRP) or low-density lipoprotein (LDL) cholesterol measurements, because the accuracy of the genotyping can be documented, whether it is individual SNP genotyping or an Illumina array. The company is required to be compliant with CLIA, including quarterly proficiency testing (PT), and with Food and Drug Administration (FDA) standards. It also documents clinical validations the same way FDA defines them(i.e., replicating the markers and demonstrating that those markers are consistent across populations). In addition to analytical validation reports, deCODEme sends clinical validation reports to CMS as part of its demonstration that the results are reliable. Dr. Gulcher said the genetic markers that are annotated at deCODEme (or the individual disease tests offered by deCODE), are well validated. Thecompany does not use preliminary data or disease markers for which there are only one or two studies. Genetic markers must be replicated widely before they are included in deCODEme's risk classification. Most of these variants are based on data sets that include up to 10,000 patients and controls. In some cases, there are 5,000 patients and 30,000 controls, in other cases 12,000 or 17,000 patients and 30,000 controls. The bases for assessments of relative risk are based on data sets that are much larger than those used for FDA approval or for diagnostic tests approved by the FDA.

To derive a customer's risk profile, deCODEme combines genetic risk information in a reliable and consistent manner by converting odds ratios for each variation into a relative risk compared to the general population. These relative risks are multiplied together, because for the vast majority of diseases there are no significant redundant or synergistic interactions.

Dr. Gulcher said deCODEme communicates results in a clear and consistent manner. Results are described in terms of relative risk, because patients and physicians can understand relative risk better than a table of odds ratios. Risk scores can incorporate environmental factors and also be converted to a lifetime risk. Dr. Gulcher said the tests are useful in identifying those at highest risk, such as those with genetic variations that place them at risk for a heart attack.

Dr. Gulcher used himself as a case study, stating that he had a prostate-specific antigen test (PSA) at the age of 42. When his prostate cancer test results were returned, his relative risk was 1.88 compared to the general population for white males, and his calculated lifetime risk was 30 percent. He expressed additional markers that suggested he was 1.3-fold more likely to have an aggressive form of cancer. These

results prompted his primary care physician to order another PSA. Dr. Gulcher's high normal test result (2.5 ng/mL), coupled with his genetic risk factors led to his referral to a urologist. The doctor performed a biopsy and found that Dr. Gulcher had prostate cancer with a Gleason score of 6(i.e., intermediate grade) for which he was seeking treatment.

Dr. Gulcher closed by stating that deCODEme is trying to improve the sensitivity and specificity of the its biomarkers t. He hoped that the improvements, used in conjunction with family history information, would result in better health care outcomes.

Ms. Au thanked Mr. Gulcher and introduced Dr. George Church, founder of Knome and the Director of the Personal Genomes Project.

George Church, Ph.D.
Knome, Inc.

Dr. Church stated that many people are interested in learning about the risks they face even if they are at risk for diseases with no cure. They are embracing genetics and becoming activists. They are saying we can do something for our families by doing research on ourselves. Examples of this personal activism are Nancy Wexler's research of Huntington disease and Michael J. Fox's support of research efforts in Parkinson disease.

Dr. Church asked if privacy in genomics is realistic. He said there are many ways privacy could be compromised such as the theft of a laptop computer with patient data, re-identification after "de-identification" using public data, hackers gaining access to to confidential medical information, inferring phenotype from genotype data, and unauthorized access to DNA from samples such as hair. Dr. Church said it is unrealistic to overpromise privacy for genetic information, however, within the research landscape genomic data are kept de-identified and as safe as possible.

Dr. Church described the Personal Genomes Project, which is scalable up to 100,000 research subjects. The project received Institutional Review Board (IRB) approval in 2005. Some of its goals are to connect DNA sequences with traits, reduce the costs of DNA sequencing and obtaining data on RNA regulation, attain full subject participation, and provide open access to data. Participants in the project take an exam to assure informed consent and the privacy of genetic sequence data is not overpromised.

Dr. Church explained that the project's researchers are focusing on next-generation sequencing, which has the potential to reduce the cost of DNA sequencing by a factor of 1,000. He explained that they are trying to produce a platform that would support multiplex chemistries based on DNA polymerase or DNA ligase. In addition to commercial instruments, the project's researchers are using an instrument at the juncture between academic and commercial activity, which they call a "polonator." He said it uses completely open-source hardware, software, and wetware and was intended to be easily modular. The cost of the polonator was $155,000, about four times less than the previous device used. Dr. Church said this technology resulted in plummeting costs, which increased the likelihood of the $1,000 genome in the near future. Dr. Church said Knome was the only company that offered full genome sequencing, which includes coding regions, regulatory sequences, and the microbiome. The current cost per individual is $350,000but is likely to decrease very soon.

Dr. Church said that in addition to genome sequence, environmental components were very important for determining disease risk. He stated that the phrase, "personal genomics" should include regulatory elements, which might be less expensive and more interpretable if analyzed at the RNA level. He stated

that some of the environmental components could be factored in either by measuring microbiological components, allergens, microbes, and viruses; or by measuring their impact on the immune system. To learn about RNA regulatory interactions with the environment, the Personal Genomes Project included multiple cell types from adults, whether healthy or diseased. Project researchers are taking one biopsy from the skin to establish stem cell lines and reprogramming them to create other types of tissue. Dr. Church said they had studied the resistance settlement for 18 major classes of antibiotics over 140 days in some Project volunteers. They were able to determine which isolates were resistant to multiple antibiotics.

In closing, Dr. Church suggested several questions for the Committee to consider: How do we fund association studies and education? Is there a role for DTC companies? How do we celebrate and incentivize the best protocols? What about do-it-yourself genetics and research? What are the risks of not educating people in the face of radical change?

Ms. Au turned the floor over to Dr. Teutsch to introduce the Secretary of HHS, Mr. Michael Leavitt. Dr. Teutsch stated that the Committee was fortunate to be joined by Secretary Leavitt, who was showing enormous initiative in the area of personalized health care. He said the Committee greatly appreciated his leadership.

Remarks by the Secretary
Secretary of HHS, Michael O. Leavitt

Secretary Leavitt thanked Dr. Teutsch and Dr. Tuckson for their leadership of SACGHS and thanked the Committee members for their service. He said that many of the issues SACGHS was addressing were on the leading edge of personalized medicine. He noted his appreciation of the Committee's support for GINA and acknowledged his great admiration for Dr. Collins. Secretary Leavitt emphasized the importance of staying ahead of policy issues related to the rapid pace of discoveries in genomics. He said the Nation needed the ability to manage health care information in a standardized way, while also protecting privacy.

Question-and-Answer Session

Dr. Lucinio noted the advancement of DTC genetic information by the private sector and the hesitation of academic health centers and the traditional side of medicine to embrace this approach. He asked Secretary Levitt how we should move ahead with the DTC and traditional medical approaches. The Secretary replied that innovation should move forward but that consumers should be assured of the security of new technologies. He said if people were given high-quality information they will use it in a way that will drive their own interest and, in doing so, would continue to drive up the quality of information and reduce cost. The tension between the two approaches will lead to improvements to each approach. He added that the capacity of consumers to sort through the issues is often underestimated. Well-intended protection can sometimes constrain progress but must be balanced against not pushing the envelope too far.

Dr. Collins mentioned the SACGHS report on coverage and reimbursement of genetic tests and the potential for personalizing prevention. He noted that the medical care system was directed more toward reimbursement for addressing disease than for covering prevention services. He asked Secretary Leavitt about opportunities for improving prevention efforts using an economic framework that would enable implementation across the board (i.e., as a public health strategy). Secretary Leavitt replied that it was important to move in that direction, and that it was a function of confidence in the science and an economic model that could demonstrate the capacity for long-term savings. He acknowledged that the

Federal Government did not score prevention very favorably in its budget process and that scoring models need to change.

Dr. Billings inquired how the Committee could be optimally useful to the Secretary in his remaining tenure and how it might be useful to the incoming Secretary. Secretary Leavitt responded that the report on the oversight of genetic testing is a very useful tool. He noted that it is very helpful for the HHS Secretary to have a Committee to answer difficult questions. He expected that the work of the Committee would increase because he and future Secretaries will need to address thorny and difficult policy issues.

Dr. Muin Khoury agreed with the Secretary's earlier comment that we need to balance innovation of genetic technologies with providing high-quality information to consumers and finding the right balance in oversight. He asked if there would be any movement on the SACGHS oversight report during the next several months. Secretary Leavitt said the report was very useful and was in the process of being analyzed.

Dr. FitzGerald asked if the Secretary would be interested in receiving brief papers on priority issues, rather than the large reports the Committee had been developing. Secretary Leavitt responded that the Executive Summaries of the reports were the most important sections for his use. However, at times, he also reviewed other sections of the reports to gain a more thorough understanding of complex problems and respond to policy issues. He noted that the reports were not just a response to OS, but were creating a body of information that would help connect many different parts of the health care system in the future. Mr. Campanelli stated that OS might sometimes come to the Committee with specific questions that would require brief responses.

Dr. Teutsch thanked Secretary Leavitt for his visit and turned the floor over to Ms. Au.

Personal Genome Service Providers (Continued)

Ms. Au thanked Dr. Church for his presentation and introduced Ms. Ryan Phelan, the Founder and CEO of DNA Direct. Ms. Phelan had also worked as a consumer health advocate for the previous 25 years.

Ryan Phelan
Founder and CEO, DNA Direct

Ms. Phelan started DNA Direct in 2004 to bring the power of personalized medicine to patients, consumers, and providers. The company's scientific advisors helped to innovate a delivery medium that Web-enabled standard clinical protocols (i.e., virtual medical genetic testing). These clinical protocols take place under the oversight of the medical director, including clear guidelines for genetic counselors and standard procedures used from the informed consent process to test facilitation and interpretation. Ms. Phelan explained that DNA Direct works closely with health care providers as an extension of physician services. She said genetic testing ranged from standard prenatal testing, to carrier testing, to drug response testing. DNA Direct works with various CLIA-certified laboratories, depending on the type of test being ordered.

DNA Direct's process begins with assessing test appropriateness by determining whether there is an action the consumer could take based on the results. Ms. Phelan explained that consumers are provided with pre-test information to help them understand the pros and cons of testing. Information from DNA Direct questionnaires help determine whether testing is appropriate and personal or family medical history is used to build a personalized Web-enabled report that is provided along with the test results. A

medical geneticist reviews all customers' medical charts, questionnaires, and test results before releasing results to consumers.

Ms. Phelan said all patient samples are sent to CLIA-certified laboratories using unique identifiers to protect anonymity. All tests are provided with transparency regarding pricing, and DNA Direct does not mark up laboratory fees. Laboratory costs are passed on directly to the customer, and the company charges only for interpretation and consulting services. There is a network of more than 60 genetic counselors affiliated with DNA Direct so that the consumer can choose whether to have a phone consult or in-person consult. All reports include a physician letter with specific information about the significance of the test result and appropriate clinical guidelines. Data are secured by keeping shipping, billing, and personally unique identifiers separate from genotype and phenotype correlations.

Ms. Phelan said consumers use their services for several reasons. The company provides access for those who live in regions where testing is not available or when the consumer's doctor does not want to conduct testing. Some consumers seek the anonymity provided by DNA Direct. Ms. Phelan stated that 46 percent of their customers have a family history for the tested condition; 18 percent have a personal diagnosis for the condition; and. 21 percent have a known family mutation. A combined 53 percent have both a family and a personal history. She noted that 34 percent of customers test positive for a mutation compared to 5 percent to 10 percent in a traditional genetics clinic. This finding indicates that DNA Direct is testing its customers appropriately, with clinically valid tests.

Ms. Phelan noted that different genetic tests require different support services. Diagnostic testing for serious disorders such as Huntington disease is best facilitated in a bricks-and-mortar setting with in-person evaluation by genetic experts and clear physician oversight. Predictive testing for serious health concerns such as breast cancer can be conducted with a genetic consultation by phone and physician oversight. Academic health centers acknowledge that phone consults can work well, and Web-enabled education is growing in use. Ms. Phelan said that genetic screening for carrier testing, risk assessment, and drug response probably does not need to be conducted in a physician's office and could be facilitated through the Web or by phone. She asked whether there should be different guidelines for genome-wide SNP analysis or full sequencing than traditional clinical genetic testing.

Ms. Phelan said many countries are considering what kinds of additional regulation are needed for DTC companies. She stated that that the industry in the United States was working on a code of best practice to move the field ahead in a responsible manner.

Ms. Au asked all panel members to come to the front of the room for the roundtable discussion**.**

Roundtable Discussion with Personal Genome Service Providers

Dr. FitzGerald asked the panel members if they would sacrifice the fiscal bottom line of their companies to achieve the goal of improved health care, particularly in the area of access to their services. Ms. Phelan replied that from an investor's perspective DNA Direct had always sacrificed the bottom line, because it was constantly thinking about how to provide a quality service in a responsible manner. Ms. Avey stated that 23andMe did not take typical venture capital investments and was lucky to have supporters such as Google and Genentech, whose short-term objectives were not financial reward. Dr. Gulcher said that deCODEme was involved in a publicly funded cardiovascular project to conduct genotyping at cost with a 1 million chip array for several hundred individuals. The results would be provided back to participants. Dr. Stephan said he had been working in the academic, nonprofit world for 15 years, doing research to identify the genetic drivers of disease; however, implementing genotyping as a service did not fit within

the academic, nonprofit model. He asked what proportion of the service-based medical infrastructure was not-for-profit, pointing out that physicians and diagnostic companies operate on for-profit models. He did not consider a for-profit model a negative.

Dr. Licinio asked if these services were really ready for consumer-based health care, and whether the public could understand the difference between the provision of information and what is important for their medical care. Dr. Gulcher stated that most companies offered tests that had been widely replicated in multiple independent populations, which was the new standard for publication in some journals. He said the companies offer genetic counseling and emphasize that consumers should talk to their physicians about the information they receive. He noted that consumers need to be aware that results provide risk information and are not determinative, which is clearly stated in the companies' disclaimers. Dr. Lucinio said he found it confusing that the deCODEme website states that the company provides anonymous information service not a medical service, and it is not designed for medical decision-making. Therefore, it is not covered by health insurance companies. Dr. Gulcher replied that the service is not a substitute for a physician or genetic counselor and is not reimbursed. It is important to inform consumers that the testing does not provide a diagnosis.

Dr. Khoury stated that the information provided by the companies was not "ready for prime time." He said it was important to determine what this information meant in terms of clinical validity and utility and how it would improve health outcomes without causing harms. He stated that more clinical trials were needed to see if the tests do more good than harm on a population level. Ms. Avey said the DTC companies needed a centralized way to collect information so they could standardize it across many people and across many diverse groups. She stated that the Web 2.0 environment would be a powerful tool in this regard and that all the organizations needed to work together on this goal.

Ms. Dreyfuss asked Dr. Church if his work was affected by patents. For example, whole genome sequencing includes the BRCA gene. How much did the cost of licensing add to the total cost of testing? Dr. Church replied that he did not see patents as a huge barrier as companies can work with Myriad to perform BRCA testing. He said that patents could become a problem, but they are not right now.

Dr. Williams noted that nontraditional research funding mechanisms were needed and said it was important to acknowledge that some of that funding was now coming directly from the consumer. He added that the companies were talking in their presentations about clinical plausibility, not clinical validity or utility. He asked Dr. Gulcher if his primary care physician knew how to interpret the results that indicated he was at risk for prostate cancer. Dr. Gulcher said he provided his doctor with descriptions of the company's report contents, which emphasize that the tests address risk factors, not determinative genetic factors.

Ms. Aspinall asked the panel members how they would reconcile the inconsistent results that Mr. Duncan received when his DNA was tested by multiple companies. Dr. Gulcher explained that there was no discrepancy in the raw genetic data, but there are different ways to converting odds ratios to relative risk, which can lead to different results. The companies represented here are working with the Personalized Medicine Coalition to agree on standards for annotation and determining relative risk. Ms. Aspinall also asked whether the companies' systems were ready to integrate electronic medical records (EMRs). Ms. Avey said they were looking to companies such as Google and Microsoft, which are partnering with retail pharmacies and health entities such as the Cleveland Clinic and Kaiser to create personalized health records (PHRs) and EMRs that include prescription information. She envisioned two-way communication that would allow genetic information to be transferred from the PHR to the EMR or in the other direction.

Dr. Miller noted the research enterprise aspect of 23andMe and asked Ms. Avey if the company's research studies were subject to Federal human subjects' regulations, including oversight by Institutional Review Boards (IRBs) and requirements for informed consent. Ms. Avey said their scientists must go through Office of Human Research Protections (OHRP) training, and all customers sign an informed consent. 23andMe is also talking to a commercial IRB, but its research protocol is not well defined so discussions are ongoing. Dr. Church also worked with an IRB, which he said took 1 year to involve initially and 3.5 years to achieve the scaled-up version.

Dr. Collins was concerned that health care providers might take unnecessary actions because they do not fully understand how to interpret test results. They might worry about litigation if they do not order every possible test. He asked the panel how this might play out as either a benefit or risk to the public. Dr. Gulcher said they emphasize that the results indicate clinical risk factors, similar to family history or environmental factors, and all the factors must be combined to determine whether further action is necessary.

Dr. Teutsch thanked the panel and the Committee for engaging in a lively and open discussion and ended the roundtable.

Ms. Au introduced Dr. Kathy Hudson, who spoke on public policy considerations for the emerging field of DTC personal genome services.

Public Policy Issues Surrounding Personalized Genome Services
Kathy Hudson, Ph.D.
Director, Genetics and Public Policy Center

Dr. Hudson stated that the companies the Committee heard from represented a subset of the companies offering health-related testing services. She said there was a tension between the new paradigm in genetics and personalized genomics and the old precepts of genetic medicine. She explained that the old precepts required pre- and post-test genetic counseling and health care provider involvement. Genetic tests for highly penetrant mutations for conditions with no available intervention were considered the highest risk, and genetic information was special.

Dr. Hudson explained that all these precepts could now be challenged. Concerning pre- and post-test genetic counseling, she said there are too many genes and not enough genetic counselors, and it is too expensive. In addition, the old model of genetic counseling was built on reproductive genetic testing and highly penetrant disorders such as Huntington's disease. She said the precept of no testing without a health care provider as an intermediary was no longer viable, as there are many genetic tests and not all require physician involvement. They pose different risks for interpretation and intervention. Concerning actionable or non-actionable information, Dr. Hudson said studies indicated that the public can handle genetic information, even when there is nothing they can do about it. She suggested that we should focus our attention on the validity of tests that are actionable. If consumers are going to take a drug or not take a drug, have surgery or not have surgery based on the test results, then the validity of those tests is of utmost importance. Lastly, Dr. Hudson said there is reason to believe that the public no longer considers genetic information special compared with other medical information.

Dr. Hudson stated that there used to be a systematic way of translating genomics or biomedical research into health impacts. The current path skips over some of those steps, which made many people uncomfortable. She asked what the response to concerns about DTC genomic testing should be and

suggested support for needed policy changes. These concerns include consumers not being able to understand results, getting tested without thinking about their family members, and forgoing standard treatments or getting unnecessary treatments. Instead of speculating about these concerns we should be support studies to obtain information about them.

On the policy side of the equation, Dr. Hudson said there were concerns about the adequacy of privacy protections, the validity of tests, the competency of laboratories, the evidence to support the claims being made, protections for research participants, and surreptitious testing of individuals without their permission. She noted the enormous gaps in the oversight of the quality of genetic tests and praised the recommendations the Committee sent to the Secretary in this area. She pointed out that there was no HHS authority over false claims made by companies, although there had recently been some Federal Trade Commission (FTC) investigations. There is also a lack of clarity in terms of who is authorized or should be authorized to order and interpret tests, limited applicability of the Health Insurance Portability and Accountability Act (HIPAA), and limited applicability of the Common Rule for protection of research subjects. She said it was important to note that the Common Rule does not necessarily extend to all research, including some that is conducted by DTC companies.

Dr. Hudson said there was an opportunity for professional groups and industry to develop voluntary guidelines and said a number of statements from professional groups had been issued. The American Society of Human Genetics (ASHG) said some tests were appropriate for DTC marketing, but they must be accurate and reliable. The American College of Medical Geneticists (ACMG) took a different position and recommended that health care providers be involved in ordering and interpreting all genetic tests. The American Medical Association (AMA) recommended that States restrict the performance of clinical and laboratory genetic testing to individuals under the personal supervision of a health care professional. She added that the States have always had a role in laboratory testing, as they administer CLIA and can impose higher standards than CLIA requires (e.g., New York). The States also determine who is an authorized person to order and receive laboratory tests.

Dr. Hudson discussed several policy options moving forward. They included a "buyer beware" stance, a demand for transparency, third-party review of accuracy and safety, taking action against false claims, creating a category of laboratory developed tests (LDTs) that would be the moral equivalent of over-the-counter drugs, expanding HIPAA to include DTC companies as covered entities, and/or expanding the Common Rule.

Dr. Teutsch thanked Dr. Hudson and opened the public comment period.

Public Comments

Michele Schoonmaker, Ph.D.
Association for Molecular Pathology

Dr. Michele Schoonmaker represented the Association for Molecular Pathology (AMP). AMP is an international medical professional association representing approximately 1,500 physicians, doctoral scientists, and medical technologists who perform laboratory testing based on the knowledge derived from molecular biology, genetics, and genomics. Dr. Schoonmaker said AMP recommended several topics for consideration by the Committee. First, they encouraged the Committee to investigate the current mechanisms for funding outcomes research for clinical diagnostic tests. Specific areas included implementation and performance of tests in clinical practice settings, the impact of the physician ordering practices and patient decisionmaking on test utilization, and the impact of test interpretation on patient

management and family decisionmaking. Second, Dr. Schoonmaker said coverage and reimbursement decisions were increasingly being made based on the comparative effectiveness of various treatments. She said genomic information might identify population subgroups that contradicted aggregate population study findings and challenge population-based treatment decisions. She asked that the Committee explore the role genomics will play in this emerging trend in health policy research. Third, AMP recommended that the Committee survey the clinical decision support tools currently under development and explore future needs for the integration of genomic information into clinical decision support tools, including the development of standards and specific clinical services. Fourth, AMP requested that the Committee continue to examine the structure and consequences of non-traditional genetic testing and how these test results will be interfaced with traditional genetic medical practice. Finally, they requested that the Committee continue monitoring oversight efforts concerning reimbursement and coverage for genetic tests.

Amy Miller, Ph.D.
Public Policy Director, Personalized Medicine Coalition

Dr. Amy Miller stated that the Personalized Medicine Coalition (PMC) represents all stakeholders in personalized medicine, including academic researchers, medical institutions, diagnostic companies, pharmaceutical companies, insurance companies, and *ex officio* Government officials. Dr. Miller said PMC had met with leading companies to discuss the possibility of working together toward standards of operation and basic guidelines in consumer genomics. PMC was also looking at the role it could play in fostering such conversations and reaching consensus around this issue.

Ann Willey, Ph.D., J.D.
Director of the Office of Laboratory Policy and Planning, Wadsworth Center
New York State Department of Health

Dr. Ann Willey addressed the role of the New York State regulatory program in DTC marketing. She stated that the New York State Clinical Laboratory Reference System had been responsible for the oversight of clinical laboratories performing analytical testing on specimens collected in New York since 1964. The categories of testing covered are specified in the enabling statute and its implementing regulations. The clinical laboratory permit requirements include personnel standards, credentialing of the laboratory director, physical facility inspection, proficiency testing, test authorization requirements and result reporting standards, and business practice requirements, among others. Category-specific standards are stated in the regulations and/or in the interpretive standards, which are issued by the program. Standards for genetic testing related to cytogenetics were added in 1972 for genetic testing, with biochemical genetics and molecular or DNA-based genetic testing added in 1990. Other genomic types of testing, which might include nuclear DNA, RNA, or gene expression profiles, are covered in other categories, such as molecular oncology. Key elements of the oversight of genetic testing laboratories include the training and experience of the responsible laboratory director in the relevant areas of genetics and the performance of tests that are generally accepted in laboratory medicine or approved by the FDA as cleared or approved in vitro diagnostic devices. Since 1990, the Department has reviewed all laboratory developed genetic tests as to their analytical validity and clinical validity prior to their approval for addition to the test menu of any permitted laboratory. Genetic testing based on a single genome sequence or gene product detection or multiplexed assays detecting multiple targets concurrently, including those used in the various genome profiles, are all subject to similar review standards.

Dr. Willey stated that the recent explosion of Internet marketing of various genetic profiling assays for individualized genome information systems raised new paradigms for patient or consumer access to such

laboratory analysis. The Department routinely monitors the Internet for entities purporting to offer laboratory services of any kind. Laboratory services in its system are defined as the performance of an analytical analysis on specimens derived from the human body and the reporting of individualized results for almost any purpose. All entities identified on the Internet are routinely notified that in order to offer their services in New York, the testing entity must seek and obtain a clinical laboratory permit from the Department and meet all relevant requirements and standards. These requirements apply regardless of the physical location of the entity. In the previous year, they sent notices to 31 entities that they must seek permits to offer genetic testing services. The letters indicated that in the absence of a permit, the service could not be offered in New York.

Dr. Willey said increasing numbers of entities were purporting to offer genomic profiling. She stated that although more than 150 laboratories held New York State permits for various genetic testing menus, none of the major entities marketing consumer access to genetic profiling or their contract laboratories held New York State permits for that purpose. The Department was in discussions with several entities concerning the requirement for submission by the testing laboratory of the necessary assay descriptions, analytical validation data, and documentation of the clinical validity for the use of genetic markers in advising the client about health issues. They also needed to resolve the business relationship between the marketing entity, the data management and interpretation process provider, and the testing laboratory. Within the constraints of New York law, there can be no inducement, no payment, and no contractual arrangement between the individual requesting the test and the laboratory. The third matter under discussion was the physician-patient relationship between the person authorized to order the test and the person tested, and the relationship of that provider with the marketing entity, the data management and interpretation entity, and the laboratory. Laboratories under New York State permit are prohibited from performing testing on New York residents, except as requested by a person authorized by law to use those test results. The authorized person is generally a health care provider with an established provider-patient relationship with the tested individual. The New York program views these genome profiling scenarios as no different than any other clinical laboratory genetic testing menu and expects providers to comply with all applicable permit and business model requirements.

Dr. Teutsch thanked those who provided comments and turned the floor over to Dr. Burns McGrath for an update on the work of the Education and Training Task Force.

Presentation of Proposed Action Plan of SACGHS Task Force on Education and Training
Barbara Burns McGrath, R.N., Ph.D.

Dr. Burns McGrath said that during the discussion of priority issues the previous day, several topics that were ranked slightly lower than the top 20 could be incorporated into the work of the Education and Training Task Force. These included consumer access to genomic information, electronic health records, public health applications of genomics, coverage and reimbursement, and health disparities. She stated that the goal for the session was to reach consensus on the Task Force Charge and the draft Action Plan. She noted that at the February SACGHS meeting the Committee suggested narrowing the scope of stakeholders. The initial list was quite broad and included professionals outside of point-of-care health delivery, such as hospital administrators, policy makers, and members of health professional governing bodies (e.g., National Board of Medical Examiners). Dr. Burns McGrath read the revised draft charge developed by the Task Force for the Committee's consideration:

"Advances in genetics and genomics are leading to a better understanding of disease processes and improved application of genetic testing to guide health decisions. With increased integration of genetics into other medical disciplines, however, health professionals with or without training or expertise in

genetics are challenged to keep pace with this dynamic and rapidly evolving field. Education will have to address the growing importance of genetics in common diseases, which likely will require more knowledge and understanding about risk assessment and communication. In addition, the accelerated growth of direct-to-consumer genetic services highlights the need for informed decisionmaking. To realize the benefits of genetic technologies and protect against potential harms, the education of health care professionals, the public health work force, and the general public is critical. For these reasons, the Secretary's Advisory Committee on Genetics, Health, and Society has formed a Task Force to build on the findings of the Committee's 2004 resolution on genetic education and training of health professionals.

The Task Force is charged with developing a plan to identify the education and training needs of health professionals, the public health work force, and the general public in order to optimize the benefits of genetic and genomic services for all Americans. This plan will also outline the steps required to meet these needs and evaluate the efficacy of educational and training efforts. This plan includes but is not limited to the following activities:

- Assembling evidence to determine which recommendations from the 2004 SACGHS education resolution were implemented and which ones require additional efforts;
- Identifying the education and training needs specific to genetics and genomics for health care professionals;
- Identifying the education and training needs of the public health work force;
- Identifying the education needs of patients and consumers to assist them in informed decisionmaking about the use of genetic services and enhance their understanding and utilization of results and how these results impact decisions about prevention or treatment;
- Identifying effective educational tools that can be incorporated into electronic health records, personal health records, and clinical decision support systems that would enhance the appropriate integration of genetic and genomic technologies throughout the health care system without adversely impacting privacy, access, and work flow. In addition, identify gaps where such tools do not currently exist and develop recommendations on how to address these gaps;
- Assessing the use of evaluative research methods to determine the efficacy of genetics and genomic education and training."

Dr. Burns McGrath described the activities of the Task Force members since the previous SACGHS meeting. They held a conference call in March 2008 and broke into three workgroups to focus on health professionals, public health providers, and consumers and patients. Each workgroup held conference calls to address their area of focus. On June 3, Dr. McGrath met with the workgroup chairs by teleconference to discuss integrating the activities of the three workgroups and developing an action plan. The primary goal of the action plan was to produce a report by 2010 that would identify gaps and make recommendations. The draft action plan proposed a clinical case model with specific cases to highlight the needs of various groups. The framework of the model was designed to address the needs of various audiences for different types of testing at different stages of testing and in different settings. It would also address how education or training could best be provided and evaluated.

The Task Force developed a list of seven potential case studies to highlight the educational and training needs of the three identified groups. They included: a patient diagnosis of a single gene disorder, a family history of common disease, a newborn screening situation, PGx testing, DTC testing, population research, and media reporting of research results. Each workgroup designed a plan for addressing the needs of their specific group. The Health Professionals Workgroup planned to summarize the literature and map the existing Federal ecosystem that supported education and training, including a survey of key professional

organizations. The Public Health Providers Workgroup planned to conduct an assessment of the needs of a subset of State and local health providers and review the genetic competencies of professional organizations and agencies to identify core competencies. The Consumer and Patient Workgroup planned a literature review, mapping of existing genetics education activities in public and private organizations, and consultation with experts in the field of genetics and education to better understand the needs of consumers and patients.

Dr. Burns McGrath said the next steps for the Task Force would be to execute the action plan and draft the survey findings by the spring of 2009. A draft report for public comment was planned for the summer of 2009, with a final report by early 2010. She opened the floor for discussion of the draft charge.

Discussion of the Draft Charge and Action Plan

Dr. Billings asked why the public health workgroup was separate from the health care provider workgroup. Dr. McGrath explained that for the purposes of this Task Force health care providers were considered point-of-care practitioners, and public health providers were those involved in state-level activities. Dr. Billings inquired if a person is a public health physician, would he/she be considered a health care provider? Dr. McGrath replied that there are overlaps between the two groups, but if the physician worked in a setting that would require a deep understanding of state policies (e.g., newborn screening), then he/she would be considered a public health provider. Dr. Billings said that including groups in addition to traditional providers and patients opens consideration of other stakeholders such as hospital administrators, legislators, and judges. Dr. McGrath responded that these groups were included in the initial draft charge of the Task Force, and the Committee recommended narrowing the range of stakeholders.

Dr. Michael Amos suggested that there might be a need to educate new companies on the expectations of scientific rigor that will be required for the general genetics community to accept their technologies. He asked if there had been any discussion of working with industry, as it might help the process of obtaining clinically relevant and useful diagnostic tests. Dr. McGrath said that many groups were considered for inclusion, but the Task Force agreed to include only those groups involved at the point-of-care as a way to limit the scope.

Dr. Sherrie Hans suggested that more expertise was needed for the Public Health Providers Workgroup, and said that additional members could be sought from the Centers for Disease Control and Prevention (CDC) or the American Public Health Association (APHA). Dr. McGrath said they would look into using such experts as consultants.

Dr. FitzGerald asked if the Task Force would address DTC testing. Dr. McGrath replied that this aspect of genetic testing would be included and added that it would provide a way to include industry.

Dr. Teutsch stated that with those changes, the Committee had reached consensus on the charge. He returned the group to the discussion of new priorities.

Continued Discussion of Plan for Next Steps in the Priority-Setting Process
Dr. Wise

Dr. Wise said the Committee had already achieved the goals for the session, which were to review and approve the process used to set priorities, and to achieve general consensus and suggest revisions to the categories that were worthy of further exploration. He said these categories would have issue briefs

developed so that final decisions on priorities could be made at the December meeting. Dr. Wise said it made sense to combine the discussion of priority-setting activities with the discussion of personalized medicine and DTC genetic testing issues, because the previous day's discussions clearly identified personalized medicine and DTC testing as important for the Committee to address. He stated that the Committee had agreed to act quickly on one or more issues in light of the pending transition to a new administration. He suggested discussing new priorities with an eye toward ensuring that SACGHS had a voice at the critical time of transition.

Dr. Amos commented that standards (e.g., standard reference materials, standard reference data, standard reference methods) had not been developed for most diagnostic tests. He said there are about 140 standards available internationally for different diagnostic tests, but thousands of different diagnostic tests are available. He wondered how the Committee could interject some sound science in this situation that would enable the public to make good decisions.

Dr. FitzGerald asked Dr. Wise whether decisions had been made concerning which priority topics would lead to specific products, such as large-scale reports, white papers, or letters to the Secretary. Dr. Wise said no decisions had been made on specific action steps. He suggested that the Committee provide some guidance to the Task Forces, particularly the Priority-Setting Task Force, about the most appropriate way to address specific issues. He said the focus of the Task Force's work over the next few months might be to articulate the central questions that were likely to be important to SACGHS as it moved forward.

Dr. Teutsch stated that clusters of topics had been agreed to the previous day, and he asked if any could be addressed immediately and studied in depth prior to the December meeting. He noted that some topics were moving to the Education Task Force for action.

Ms. Aspinall suggested that the DTC/personal genomics issues be addressed immediately. She said the DTC issues should be separated from personalized medicine more broadly, and the work on personalized medicine and personal genomics should be continued. Dr. FitzGerald agreed and said many issues were embedded in DTC, which might require a large, comprehensive report. He suggested breaking out and clarifying some of the sub-issues that were highlighted concerning personalized medicine and DTC testing, such as informed consent, privacy and confidentiality, coverage and reimbursement, and clinical utility. He stated that these could be examined in a brief, focused period of time.

Dr. Randhawa suggested referring back to the list of priority topics that were agreed to the previous day before continuing the process of deciding how to address them. He stated that if the group decided to move immediately on some central issues, issue briefs might not be needed for those topics. Dr. Khoury pointed out that some priority issues fell within the scope of the Evaluation Task Force, and he asked if they would move forward before December. He said the Committee would be missing an opportunity if no work was done until the next SACGHS meeting. He suggested writing a letter to the Secretary on personal genomics. He noted that the Secretary already had a number of products from the Committee that had not been fully addressed (e.g., the oversight report, the PGx report), and SACGHS could urge the Secretary to take action on the recommendations in those reports.

Dr. Teutsch stated that to help the Committee position itself for the next administration, he had asked staff to pull together all the recommendations SACGHS had made. This information would inform a letter to officials in the new administration that would be approved by the Committee in December. In summarizing what he heard from the discussion, Dr. Teutsch noted there was a desire to move forward expeditiously on at least two issues, possibly personalized genomic services and some aspects of DTC testing. He said the Evaluation Task Force could begin work on personal genomic services. Another Task

Force could be fonned on DTC issues, if that was considered a priority to be addressed before December. Dr. Miller suggested that staff prioritize the pending recommendations and present them in the fonn of an annual report or memo from the Committee to the internal HHS transition group. Ms. Aspinall agreed, and stated that the issues within DTC testing should be prioritized based on what the Committee believed HHS should look at first. She said larger reports could be written later. Dr. FitzGerald remarked that many of the priority issues had been identified in prior reports. Excerpts from these reports could be used to put together a letter to the next Secretary. Dr. Wise said the Priority-Setting Task Force would be responsible for developing the document on the recommendations. Dr. Amos and Dr. Jim Evans noted the importance of highlighting clinical utility and evidence-based medicine. Dr. Teutsch asked Ms. Au to pull together the information the Committee heard in the past two days on personal genome services in the form of a letter to the Secretary. Dr. Williams and Dr. FitzGerald agreed to assist in that effort.

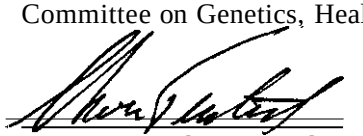
Dr. Williams suggested creating a progress report on the status of the recommendations made in various SACGHS reports. It would indicate whether the recommendations were still relevant, being continued in another Task Force, still unresolved, or moving forward. The document would be valuable both for the current Secretary and the incoming Secretary. He also said the key to the personalized medicine issue would be to use informatically-based mass customization approaches that would take advantage of robust evidence bases.

Dr. Teutsch summarized the decisions made by the Committee. Under Ms. Au's leadership, a letter would be drafted on personal genome services; under Dr. Wise's leadership, a progress report would be developed on the status of SACGHS recommendations. Ms. Aspinall said the Evaluation Task Force would develop an issue brief by the December meeting.

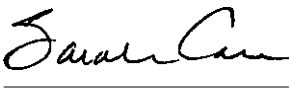
Concluding Remarks
Dr. Teutsch

Dr. Teutsch stated that the next meeting would take place on December 1 and 2, 2008. The Committee would receive an update on the activities of the Gene Patents Task Force and would review the report developed on the status of SACGHS recommendations. The priority-setting process would continue. Dr. Teutsch thanked all those who had contributed to the meeting's success and adjourned the meeting.

We certify that, to the best of our knowledge, the foregoing meeting minutes of the Secretary's Advisory Committee on Genetics, Health, and Society are accurate and correct.



Steven Teutsch, M.D., Ph.D.
SACGHS Chair



Sarah Carr
SACGHS Executive Secretary