DEPARTMENT OF HEALTH AND HUMAN SERVICES

Twenty-Second Meeting of the
SECRETARY'S ADVISORY COMMITTEE ON
GENETICS, HEALTH, AND SOCIETY
June 15-16, 2010

Meeting Summary

Washington Plaza Hotel
10 Thomas Circle NW
Washington, DC 20005

Prepared by the Office of Biotechnology Activities
National Institutes of Health

Participants

June 15, 2010

Committee Member Present

Steven Teutsch, M.D., M.P.H., Chair
Mara Aspinall, M.B.A.
Janice V. Bach, M.S., CGC
Paul Billings, M.D., Ph.D., FACP, FACMG
David C. Dale, M.D. (by telephone)
Gwen Darien
Rochelle Dreyfuss, M.S., J.D.
Charis Eng, M.D., Ph.D.
James P. Evans, M.D., Ph.D.
Andrea Ferreira-Gonzalez, Ph.D.
Barbara Burns McGrath, RN, Ph.D.
Samuel Nussbaum, M.D.
Charmaine Royal, Ph.D.
Sheila Walcoff, J.D.
Marc S. Williams, M.D., FAAP, FACMG
Paul Wise, M.D., M.P.H.

Ex Officio Members/Alternates Present

Michael A. Carome, M.D. (Office for Human Research Protection)
Denise Geolot, Ph.D., R.N. (Health Resources and Services Administration)
Eric Green, M.D., Ph.D (National Institute of Health)
Adam B. Kanis, M.D., Ph.D. (Department of Defense)
Muin Khoury, M.D., Ph.D. (Centers for Disease Control and Prevention)
Elizabeth Mansfield, Ph.D. for Alberto Gutierrez, Ph.D. (Food and Drug Administration)
Douglas Olsen, Ph.D., RN for Ellen Fox, M.D. (Department of Veterans Affairs)
Jennifer Weisman, Ph.D. for Robinsue Frohboese, J.D., Ph.D. (Office for Civil Rights)

SACGHS Staff

Sarah Carr, Executive Secretary
Kathryn Camp, M.S., RD
Symma Finn, Ph.D.
Cathy Fomous, Ph.D.
Darren Greninger, J.D.
Allison Lea, M.A.
Kimberly Taylor, Committee Management Staff

Speakers

Bin Chen, Ph.D. (Centers for Disease Control and Prevention)
Emily Edelman, M.S., CGC (National Coalition for Health Professional Education in Genetics)
William G. Feero, M.D., Ph.D. (Maine-Dartmouth Family Medicine Residency Program)

Kathy Hudson, Ph.D. (National Institute of Health)
David Hunt, M.D. (Office of the National Coordinator for Health Information Technology)
Martin Reese, Ph.D. (Omicia)
Clifford Reid, M.B.A., Ph.D. (Complete Genomics)
Richard Sharp, Ph.D. (Cleveland Clinic)
Dietrich Stephan, Ph.D. (Ignite Institute for Individualized Medicine)
Steven Teutsch, M.D., Ph.D. (SACGHS Chair)

Public Commenters

Martin Naley (Life Technologies Corporation)
Mark Sobel, M.D., Ph.D. (Association of Molecular Pathology)

June 16, 2010

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Paul Wise, M.D., M.P.H.

Ex Officio Members/Alternates Present

Sarah Botha, J.D. (Federal Trade Commission)
Michael A. Carome, M.D. (Office for Human Research Protection)
Phyllis Frosst, Ph.D. for Eric Green, M.D., Ph.D. (National Institute of Health)
Denise Geolot, Ph.D., RN (Health Resources and Services Administration)
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Elizabeth Mansfield, Ph.D. for Alberto Gutierrez, Ph.D. (Food and Drug Administration)
Douglas Olsen, RN, Ph.D. (Department of Veterans Affairs)
Iliana Peters, Ph.D. for Robinsue Frohboese, J.D., Ph.D. (Office for Civil Rights)
Jeffrey Roche, M.D. (HHS/Centers for Medicare and Medicaid Services)
Jennifer Weisman, Ph.D. for Robinsue Frohboese, J.D., Ph.D. (HHS/Office for Civil Rights)

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Janice Bach, M.S., CGC (SACGHS Committee Member)
Adam Berger, Ph.D. (Institute of Medicine)
Sarah Copeland, M.D. (Health Resources and Services Administration)
R. Rodney Howell, M.D. (Secretary's Advisory Committee on Heritable Diseases in Newborns and Children)
Elizabeth Mansfield, Ph.D. (SACGHS *Ex Officio*, Food and Drug Administration)
Charmaine Royal, Ph.D. (SACGHS Committee Member)
Marc Williams, M.D., FAAP, FACMG (SACGHS Committee Member)

Tuesday, June 15, 2010

Opening Remarks

Dr. Steven Teutsch, Chair of the Secretary's Advisory Committee on Genetics, Health and Society (SACGHS) welcomed everyone to the 22nd SACGHS meeting and described the agenda for the next two days. He then made note of several updates, including:

- SACGHS finalized its report on *Gene Patents and Licensing Practices* and *Patient Access to Genetic Tests and Direct-to-Consumer Genetic Testing*, both of which were transmitted to the Secretary in spring 2010.
- The Committee's draft report on genetics education and training was released for public comment on May 24, 2010; the comment period will close June 30, 2010.
- At the February 2010 SACGHS meeting, the Committee approved a commentary for submission to a medical journal. It was submitted to *The New England Journal of Medicine* in May.
- In March 2010, Committee members Jim Evans and Rochelle Dreyfuss briefed the NIH Director Francis Collins on the patents report findings, conclusions, and recommendations.

Dr. Teutsch also thanked departing SACGHS *ex officios* Barry Straube, Centers for Medicare & Medicaid Services (CMS) and Robinsue Frohboese, Office of Civil Rights (OCR) and welcomed Jeffery Roche and Jim Rollins as the new CMS *ex officios* and Jacqueline Berrien as the new *ex officio* from the Equal Employment Opportunity Commission.

SACGHS Executive Secretary, Sarah Carr, concluded the opening remarks by reminding the Committee of the standards of ethical conduct for employees of the executive branch.

Selected Federal Updates

Overview of the Genetic Testing Registry and a New Partnership with FDA on Translational Research

Kathy Hudson, Ph.D., Chief of Staff at the National Institute of Health (NIH) briefed the Committee on the recently developed Genetic Testing Registry (GTR) and issues affecting personalized medicine. She reported on the recent formation of the NIH-Food and Drug Administration (FDA) Joint Leadership Council, which is co-chaired by Dr. Collins and FDA Commissioner Dr. Margaret Hamburg. The objectives of the Joint Leadership Council include improving translational science, making science "regulatory review ready," and speeding the development of new medical products. She discussed the impact of health care reform legislation on NIH, particularly the Cures Acceleration Network (CAN). The goal of CAN is to advance development of new treatments and cures for debilitating and life-threatening diseases by reducing barriers between laboratory discoveries and clinical trials and to promote innovation in technologies supporting the research, development, and production of high-need cures. The definition of a high-need cure encompasses drugs, biologics and devices (e.g. development of a new diagnostic test).

With regard to the development of the GTR, Dr. Hudson discussed GTR goals, which were inspired by the SACGHS oversight report to improve research and public health by enhancing the transparency of genetic testing, increasing access to information on genetic tests, and increasing marketplace competition. To gather broad public input, a Request for Information was published in the *Federal Register* on June 11, 2010.

Discussion. The Committee posed questions to Dr. Hudson about the accuracy of information in the GTR,

the unintended consequences of including information such as clinical utility, the possible expansion of the GTR to include all clinical tests, and the importance of involving clinicians in it's development. Dr Hudson noted that all of these points are important and would be explored and discussed with the further development of the GTR.

Update on Comparative Effectiveness Research

Dr. Marc Williams, SACGHS Committee member, reviewed the May 2010 *Report on Obligations, Expenditures, and Unobligated Balances for Comparative Effectiveness Research* from the Agency for Healthcare Research and Quality (AHRQ) and NIH. AHRQ's funding for comparative effectiveness research (CER) activities involves identification of new and emerging comparative effectiveness issues, evidence gap identification, evidence synthesis, evidence generation, dissemination and translation, and research training and career development. Dr. Williams noted that virtually all of AHRQ's $300 million for CER is in the process of being obligated, and all of its funding announcements are closed. As of March 2010, NIH had committed $342 million of its $400 million for CER and is in the final stages of making awards for the remaining $58 million. An example of genomic-specific CER is funding for a Center for Comparative Effectiveness Research in Cancer Genomics (CancerGen).

The Office of the Secretary has $400 million for CER, and as of March 2010, it had an unobligated balance of $388.3 million. About $246 million of this unobligated balance have been put into funding opportunity announcements that are now closed, about $53 million are in funding announcements that are still open, and approximately $85 million are uncommitted. Dr Williams suggested that SACGHS could make a recommendation to the Office of the Secretary about how some of those remaining funds could be allocated to research in genomics and personalized medicine. He proposed some ideas based on prior SACGHS reports and priorities, which included methodological issues, such as evidentiary standards, and the ability to capture genomic information in electronic health records (EHRs) to enable CER.

Discussion. Dr. Teutsch noted that all the CER funding from the American Recovery and Reinvestment Acts (ARRA) must be expended by September 30, 2010, so there is a very narrow window for advising the Secretary. Given the impending deadline, Dr. Williams volunteered to draft a letter to the Secretary for discussion the following day. The letter—suggesting priority areas for CER funding—will be based on the Committee's prior reports and correspondence.

Updates and Developments from the Office of the National Coordinator for Health Information Technology

David Hunt, M.D., Chief Medical Officer of the Office of Health Information Technology Adoption, Office of the National Coordinator for Health Information Technology (ONC), began with a recap of his February 2010 presentation to the Committee on the Health Information Technology for Economic and Clinical Health (HITECH) Act. ONC's priorities for implementing HITECH are to define meaningful use of EHRs and support the medical community in meeting that definition, establish public trust, and foster health information technology (IT) innovation. The final goals are to improve individual and population health outcomes, increase transparency and efficiency, and advance the ability to study and improve health care delivery.

Dr. Hunt described the Strategic Health IT Advanced Research Projects (SHARP), a $60 million program that supports research in the following areas: security of health IT, cognitive support (leveraging IT to assist care delivery), network platform architecture, and the secondary use of EHR data. He reported that the final rule implementing provisions in ARRA that provide incentive payments to eligible professionals

and hospitals participating in Medicare and Medicaid programs and demonstrating meaningful use of certified EHR technology will be issued soon. The final rule focuses on expectations of meaningful use of EHRs for the 2011 period and may include some of the expectations for the second and third periods of meaningful (in 2013 and 2015). Also expected soon is the final rule for standards, implementation specifications, and certification criteria for EHRs.

Dr. Hunt noted the creation of 15 Beacon Communities that encompass the continuum of care (i.e., including long-term care facilities, skilled nursing homes). These Communities will focus on specific and measurable improvement goals in health systems improvement, to demonstrate the ability of health IT to transform local health care systems. He reported that two additional Beacon Communities will be funded and that the Department of Defense and Department of Veterans Affairs are working together in a somewhat parallel program. In addition, the Regional Extension Center Program has established 60 centers nationwide that will provide technical assistance to providers and practices—particularly small practices and those in rural locations—to achieve meaningful use of EHRs.

Discussion. In response to a question about de-identification and privacy, Dr. Hunt reported that Joy Pritts, J.D., has been appointed as the ONC Chief Privacy Officer to help inform ONC's policymaking with regard to security and privacy, particularly the de-identification of information and its secondary use. He also noted the work of the National Health Information Network (NHIN), which has released a set of standards and protocols called NHIN Direct that provide fundamental requirements for encrypting, anonymizing, and sharing data. Dr. Jennifer Weisman, SACGHS *ex officio* from the HHS Office for Civil Rights (OCR), added that OCR held a two-day workshop in March 2010 on the topic of the de-identification standard and the HIPPA Privacy Rule. A link to the webcast and presentation materials is available on the OCR website (http://www.hhs.gov/ocr/privacy/hipaa/understanding/coveredentities/De-identification/deidentificationworkshop2010.html).

Other Committee discussion focused on interoperability, the integration of genomics and personalized medicine within the Beacon Communities, and plans to expand these Communities into more populated areas.

CLIAC Recommendations for Good Laboratory Practices for Biochemical Genetic Testing and Newborn Screening

Bin Chen, Ph.D., from the Division of Laboratory Systems at the Centers for Disease Control and Prevention (CDC) reviewed the recommendations of the Clinical Laboratory Improvement Advisory Committee (CLIAC) that address good laboratory practices for biochemical genetic testing and newborn screening for inherited metabolic disorders. Good laboratory practices are intended to improve the quality of laboratory genetic services, enhance the oversight of genetic testing under the current regulatory framework, and improve health care outcomes from genetic testing. The CLIAC recommendations encompass the pre-analytic, analytic, and post-analytic phases of biochemical genetic testing and newborn screening. Good laboratory practices in the pre-analytic phase address information provided to users of laboratory services (e.g., health care providers, patients, payers) such as indications for testing, test methodology, and cost information when possible and practical; necessary information to make an informed decision about testing, specimen submission and handling requirements, and pre-analytic system assessment. Recommendations for the analytic phase include performance characteristics and verification, control procedures, and proficiency testing or alternative performance assessment. Recommended practices for the post-analytic phase address the laboratory's report of test results and any information necessary to understand the results, retention of the laboratory report and tested specimens, and post-analytic systems assessment.

Discussion. During the discussion, Committee members asked for clarification about the meaning of electronically compatible laboratory reports, recommended that the good laboratory practices address reimbursement for genetic counseling and recognize that certified professionals with Ph.D.s meet CLIA requirements for high-complexity testing, and suggested dissemination and discussion of good laboratory practices at workshops for laboratory professionals.

Public Comments

Martin Naley, Chief of Staff, Life Technologies, made comments related to the upcoming session on implications of affordable whole-genome sequencing (WGS). His suggestions to the Committee included establishing rapid biomarker review mechanisms to ensure responsiveness in incorporating biomarker knowledge into treatment decision rules, consideration of evaluation criteria for genomic technologies used in medicine, continued facilitation of the development of information exchange networks incorporating genomic patient data, and investing in continuing education and training for health professionals. He also explained two measures of accuracy in WGS. One is the accuracy of raw sequence data, and the other is the accuracy of the data after analysis, which can be considered processed data accuracy. He noted that that raw accuracy is the ultimate driver of quality and cost for genetic information. Mr. Naley remarked that whole-genome sequencing is compatible with the other cost-saving programs in the Health Care Reform Act as it will lead to specific treatment decisions for patients and better health outcomes.

Mark Sobel, M.D., Ph.D., Executive Officer, Association of Molecular Pathology (AMP), commended SACGHS for choosing to focus on WGS and the challenges related to policy and private practice issues. He then discussed AMP's concern with clinical applications of WGS such as issues related to ethical practice (e.g., the appropriateness of masking data irrelevant to the test prescriber's indication), limitations on interpreting WGS data and reporting results due to DNA patents on specific sequences, reimbursement policies, clinical utility, liability, accurate diagnostic analysis, communication gaps, data storage and handling, and access to WGS data. Dr. Sobel noted that AMP had formed a working group on whole-genome analysis.

Implications of Affordable Whole-Genome Sequencing

Committee members Dr. Paul Billings and Dr. Charis Eng led the session on affordable WGS, which included a series of presentations from a panel of experts.

Overview of WGS

Dietrich Stephan, Ph.D., President and Chief Executive Officer (CEO) of Ignite Institute for Individualized Medicine provided an introductory overview of the current state of WGS. He discussed the value of WGS in both clinical and research settings, key definitions and performance metrics associated with WGS, the evolution of first-, second-, third-, and fourth-generation technologies, and analysis and interpretation on the genome.

Quality and Management of WGS Data

Cliff Reid, M.B.A., Ph.D., President and CEO of Complete Genomics, discussed the accuracy of WGS, the magnitude of data generated through WGS, and how the data are best managed. He explained that genomic sequencing utilizes information theory, and accuracy is improved by using redundancy to correct errors and gaps in the information. The most accurate published human genome (published in *Science* in early 2010) had an error rate of 1 in 100,000 bases, which means 30,000 errors in a 3 billion base genome.

About 300 of these errors would occur in the regions of the genome that code for proteins, or about 1 percent of genes will have an error, which is unacceptable for clinical use. Dr. Reid estimated that an error rate of 1 in 10 billion bases (about 3 errors in the protein-coding regions) would approach the necessary accuracy for clinical testing and would take 6 to 10 years to achieve.

In discussing the magnitude of WGS data, Dr. Reid explained that one complete human genome generates 3 terabytes of data. Currently, it costs about $5,000 per year to store this amount of data, so storing a genome for a few years costs more than sequencing. Because it would be prohibitive to store raw data, they are converted to sequence reads, which are 10 times smaller and 10 times cheaper to store. Dr. Reid noted that with the decreasing sequencing costs, it will soon become more cost effective to resequence the genome than to store the data. He also touched on issues related to the validation and quality control of WGS data, interpretation of sequence variants, and formatting the data in a standardized way for EHRs.

Preparing and Managing WGS Data for the Clinical Setting

Martin Reese, Ph.D., CEO and Co-Founder of Omicia, discussed how to translate WGS data into a usable resource for clinical application. The overall workflow of the data included sequencing, traditional bioinformatics, gene annotation, clinical integration, reporting and technical interpretation, and finally clinical interpretation. Dr. Reese reviewed examples of the emerging clinical use of WGS data to inform disease predisposition (e.g., cardiovascular disease, cancer, diabetes) and drug response (e.g., warfarin) and to identify mutations for rare genetic diseases. He addressed quality assessment and control, integrated systems for technical interpretation, and clinical assessment. He noted that quality assessment and control should include identity testing to confirm that the specimen matches the donor, verification experiments (e.g., orthogonal technology validation), and data security measures. Integrated systems for technical interpretations involve variant ranking by quality and phenotype severity; rule-based decision support systems are needed, and their development should be transparent. Clinical interpretation should consider family history and environmental background as well as integration into the electronic health record.

Approaches to Using WGS Data and Clinical Utility

W. Gregory Feero, M.D., Ph.D., Research Director from the Maine-Dartmouth Family Medicine Residency Program, spoke of the concerns related to primary care application of WGS. Referencing the 1997 report from NIH-Department of Energy Task Force on Genetic Testing, Dr. Feero explained that clinical utility is the balance of benefits to risks that accrue from both positive and negative tests. He noted that some in the primary care community, especially those who practice outside of academic centers, question the value of genetic testing due to the lack of evident utility. In considering clinical utility, he cautioned that the rank and file health care provider who is facing an ever-mounting number of patients and ever lowering reimbursement may view utility differently than specialists who routinely order genetic tests. Dr. Feero remarked that evidence-based medicine often takes a rigorous approach to examining the evidentiary base that supports the use of a proposed new technology. For genetic testing, there are extremely limited data that would meet the high bar of evidence of reducing morbidity and morality. He emphasized that additional studies in the later stages of translational research are needed to demonstrate that genetic testing will improve patient outcomes. Dr. Feero concluded with a discussion of related to data storage, sequencing accuracy, accounting for behavioral and environmental factors in disease, and developing phenotype definitions and readying EHRs for genomic medicine.

Impact of WGS on the Practice of Health Care

Emily Edelman, M.S., CGC, Project Director, National Coalition for Health Professional Education in Genetics, spoke about the future of WGS in health care, how it will be applied to clinical practice, and how will it change the practice of medicine. She presented a mock scenario between a patient and doctor to demonstrate how WGS could be applied in a typical health care setting and discussed the steps that need to be taken to realize this type of scenarios. These steps include establishing clinical validity and utility data for specific gene-disease or variant-disease associations; developing data management and decision-support systems; attaining payer recognition; encouraging professional societies to develop recommendations and guidelines; and expanding education for clinicians, patients, and consumers. In concluding, Ms. Edelman remarked that affordable WGS will occur before the clinical importance of all the data is understood, and it will be extremely challenging to educate clinicians and consumers during this phase of rapidly changing information. She noted that risk communication principles for WGS data are similar to those for traditional genetic medicine, but they will be applied in a different context.

Ethical Implications of WGS

Richard Sharp, Ph.D., Director of Bioethics Research at the Cleveland Clinic discussed physicians' genomic competencies and noted that Cleveland Clinic survey data indicate that nearly all physicians lack proper genetic and genomic education and training, and they are ill equipped to answer their patient's questions. He suggested that not only are physicians limited in their current knowledge of genetics but more basically, are not well-prepared to respond to a foundational paradigm shift—from reactive to proactive medicine—that is signaled by the appeal of WGS data.

Dr. Sharp described a study that aims to describe patients' and genetic professionals' attitudes and beliefs about the (1) types of diagnostic possibilities that should be discussed prior to large-scale clinical mutation testing and (2) types of diagnostic results that should be returned after testing. The goal of the study is to develop practice guidelines on the return of diagnostic results from genomic tests. Preliminary findings from extended meetings with small groups of genetic professionals in six regional sites include:

- Genetic professionals do not believe that highly multiplexed genetic tests are ready for routine clinical use
- Many geneticists feel that there is insufficient data to support the clinical utility of multiplexed genetic testing
- Widespread use of multiplexed genetic tests may result in unnecessary medical follow up of false test results or findings that are not immediately relevant to the patient's clinical presentation
- Genetic professionals struggled to identify which kinds of test results should be high priority to review with patients
- Many clinical geneticists favored a more targeted approach to disease diagnosis in which a clinician orders only those tests that are suggested by a patient's presentation or history
- Since WGS will reveal many types of genetic information that are not immediately relevant to patient care, geneticists saw WGS as raising multiple problems of information management

Dr. Sharp's primary concerns were patients believing genetic information is more predictive than it is and the lack of outcomes data related to the impact of genetic risk information on behavior.

Economic Value of Whole Genome Sequencing

Dr. Teutsch, in his professional capacity as Chief Scientific Officer of the Los Angeles County Health Department presented on a method for economic evaluation and presented a formula to measure cost over quality-adjusted life year (QALY), noting that cost effectiveness does not always imply cost savings.

He focused on six scenarios of a screening model for WGS—testing an asymptomatic patient—and discussed the possible outcomes of this model. Five of the six scenarios generated increased health care costs due to false positives that lead to unnecessary follow-up tests or false negatives that give a false sense of reassurance and may cause harm if appropriate follow up does not occur. One of the scenarios indicated cost savings and benefit to the patient. Dr. Teutsch suggested a list of steps necessary to preserve the value of WGS, while preventing the overuse of screening. These steps include delivering services that demonstrate health benefits and provide good value, developing financing to cover costs and reimbursement, and developing a system to assure the appropriate use of WGS.

Discussion. The Committee asked about the timeline for affordability and implementation of WGS into clinical practice. The speaker panel suggested that the cost of WGS could level at $1,000 - $2000 over the next few years and noted that its highest utility and value lies in cancer sequencing. In response to a question about research priorities, Dr. Teutsch suggested the following areas of study: clinical validity of whole-genome sequencing (i.e., identifying variants associated with disease risk or a particular phenotype), appropriate outcome measures to evaluate WGS technologies, risk communication and education, and using WGS to understand disease pathways. Other areas of discussion included evidentiary standards for assessing the clinical utility of WGS, clinical standards for using WGS testing, and the training and resources that will be necessary for clinicians to use sequencing technologies optimally.

In light of the many questions related to WGS, the Committee decided to form a task force to stay abreast of emerging issues. The task force will be co-chaired by Dr. Billings and Dr. Eng and include Janice Bach, Jim Evans, Andrea Ferreira-Gonzalez, Charmaine Royal, Gwen Darien, and Muin Khoury.

Wednesday, June 16, 2010

Opening Remarks

Dr. Teutsch opened the second day of the meeting by thanking Dr. Eng, Dr. Billings and SACGHS Staff member Cathy Fomous for their work on the WGS session. He then gave an overview of the day's session topics and introduced the first speaker.

Updates from the Food and Drug Administration (FDA)

SACGHS *ex officio*, Dr. Elizabeth Mansfield, FDA, reported on direct-to-consumer (DTC) genetic testing and noted the calls from many quarters—including SACGHS—for increased oversight of these tests. She explained that FDA became quite concerned when Pathway Genomics announced a plan to sell DTC tests, including pharmacogenomic test, through Walgreens. FDA sent an "It has come to our attention letter" to Pathway Genomics, and the marketing plan with Walgreens was abandoned. On June 10, 2010, FDA sent letters to five companies—23andMe, Navigenics, Illumina, deCODE, and Knome—requesting them to work with FDA to determine which claims require oversight and how to manage the submission process. Dr. Mansfield also noted the Congressional interest in DTC companies and the letters the Energy and Commerce Committee sent to these companies requesting information about their tests. She mentioned the possibility of a Congressional hearing in the next few months.

Dr. Mansfield continued with the announcements of two upcoming FDA public meetings. On June 30, 2010, FDA will host a meeting to discuss array-based copy number testing. The intent of the meeting is to gather information on regulatory approaches for nontargeted testing (e.g., arrays, WGS), which will likely be different than for single-analyte targeted testing. On July 19-20, 2010, FDA will hold a meeting about FDA's intent to implement risk-based oversight of laboratory-developed tests (LDTs). General

expectations are that FDA will initially require registration and listing and then phase in a risk-based oversight system, with precautions to avoid disruption to access to tests. Dr. Mansfield also mentioned that FDA is working on draft guidance for companion diagnostics (i.e., diagnostics required for safe and effective administration of a drug) and an informational document on the co-development of a treatment and a diagnostic that addresses regulatory strategies and reviews issues that differ from normal drug and diagnostic development.

Based on a public comment at a previous SACGHS meeting, Dr. Mansfield reported that FDA had developed of a new product code for LDTs that enables anyone to report an adverse event and make a medical device report (MDR) for LDTs. FDA had already received several reports. She also remarked that FDA had received several complaints about its 510(k) process. As a result, FDA is conducting an internal review of the process and the Institute of Medicine (IOM) is conducting an independent review. Recommendations are expected later this year.

Discussion. Areas of discussion included concerns about overlap of required registration and listing of LDTs with the Genetic Testing Registry, differences in the regulation of traditional cytogenetics (e.g., karyotyping, fluorescence in situ hybridization) vs. array technologies, and the interplay between FDA regulations for LDTs and the oversight of laboratories via the Clinical Laboratory Improvement Amendments (CLIA).

Genomic Data Sharing

Dr. Charmaine Royal, SACGHS member, presented an update and overview of the Committee's work on genomic data sharing (GDS), which included the formation of a steering group in 2009 and a session at the February 2010 SACGHS meeting that explored a number of GDS models. She then discussed the steering group's fact-finding efforts, which included a literature review and consultations with two genomic data program directors, three secondary data users, and one bioethics researcher. The central GDS issues that emerged from the literature review were the blurred line between research and clinical practice, potential for group harms, and privacy concerns of current and future information technology capabilities. The consultations revealed the following concerns: patients' perception of data breeches, limited data on environmental exposures in genomic datasets, the ability to link genomic data to EHRs is not fully developed, lack of clear guidance on who should communicate incidental findings, lack of standards for characterizing phenotypic data, limited incentives to make data available for secondary use, inadequate informed consent processes. Based on these findings, Dr. Royal asked whether the Committee should continue to examine the GDS topic, and if so, what the specific focus should be.

Discussion. The Committee had concerns related to topic overlap with other groups and committees and about whether these issues were too broad to tackle. After much discussion, the Committee decided to pursue this topic by forming a WGS task force, with the goal of creating a narrower charge centered on group-related issues. The task force will be chaired by Charmaine Royal and include Gwen Darien, Rochelle Dreyfuss, Barbara McGrath, Sheila Walcoff, David Dale, Mike Carome, Mike Amos, Michele Lloyd-Puryear, Laura Lyman Rodriguez, and Doug Olsen and *ad hoc* members Sylvia Au, Julio Licianio, and Kevin FitzGerald.

Update on CER Funds

Dr. Williams revisited his proposal from the previous day concerning recommendations to the Secretary for spending undesignated ARRA funds. He also presented an overview of phenotyping, highlighting the deficiency of detailed phenotypic data that leads to inadequate clinical information to associate with genomic data. He then presented a draft letter to the Secretary, with suggestions on spending ARRA funds

for a research center focused on comparative effectiveness of genetic and genomic information, informatics infrastructure, and phenotypic data research.

Discussion. The Committee reviewed the recommendations and suggested revisions. Upon realizing the impending deadline to submit the letter to the Secretary, the Committee created a small working group to finalize the letter within the next week.

Carrier Screening

Sara Copeland, M.D., Deputy Director of the Genetics Services Branch, Health Resources and Services Administration and representative for SACHDNC, reviewed issues related to carrier screening such as who to screen (e.g., targeted vs. general population), how to screen (e.g., family history, genetic testing), and when to screen (e.g., newborn period, childhood, adulthood). She then explained a proposal to create a joint SACHDNC-SACGHS task force to examine these issues and develop guidelines for carrier screening.

Discussion. The Committee discussed the logistics of a joint task force and ultimately decided that SACGHS members would participate in a carrier screening work group led by SACHDNC (i.e., no joint task force). The following SACGHS Committee members and *ex officios* will participate: Janice Bach, Jim Evans, Charmaine Royal, Phyllis Frosst and Adam Kanis.

Retention and Use of Residual Dried Blood Spot Specimens after Newborn Screening

Ms. Janice Bach, M.S., CGC, SACGHS member, provided an overview and reminded the Committee of the steering group formed during the February 2010 SACGHS meeting to comment on the SACHDNC draft briefing paper on retention and use of residual dried bloodspot specimens after newborn screening (NBS).

Challenges and Opportunities in Using Newborn Screening Samples for Translational Research

Adam Berger, Ph.D., Project Director, Roundtable on Translating Genomic-Based Research for Health, IOM, gave a brief overview of newborn screening then discussed the recent IOM workshop that focused on the benefits of making NBS samples available for research, protecting the privacy and rights of individuals whose samples are used for research, and making specimens available for research without compromising the core mission of NBS programs. Meeting participants identified the following area that need to be addressed for research programs to succeed: education about the potential use of dried blood spots, funding to store specimens and support research, consent, transparency, stewardship and accountability, and policies for return of research results.

Committee Report on the Retention and Use of Residual Dried Blood Spot Specimens after Newborn Screening

R. Rodney Howell, M.D., Chair of the Secretary's Advisory Committee on Heritable Disorders in Newborns and Children (SACHDNC) reviewed previous reports and policies for the use of residual NBS dried blood spots specimens and discussed the controversy of using these specimens for research. He then discussed the SACHDNC draft report on the retention and use of residual dried blood spot specimens after NBS and reviewed the report's seven recommendations.

SACGHS Comments on the SACHDNC Draft Report

Ms. Bach provided an overview of the comments of a SACGHS steering group assigned to review the SACHDNC draft report. The steering group endorsed the draft overall but had several suggestions that included providing model legislation that could facilitate the adoption of state policies for the retention and secondary use of residual dried blood spot specimens, adding language about the provision of funding to facilitate the retention and use of these specimens, elaborating on the need for a voluntary national repository, and advising the Secretary to discourage states from making premature changes to policies that lead to shortened retention of residual NBS specimens.

Discussion. After discussion of the steering group's comments, the Committee voted unanimously to send a letter to SACHDNC formally endorsing the report with the changes suggested by the steering group.

Concluding Remarks

Dr. Teutsch thanked everyone and recapped the decisions made by the Committee. He also announced that the *New England Journal of Medicine* had accepted the commentary submitted on behalf of the Committee and that the American Medical Association House of Delegates had passed a resolution supporting legislation that would exempt those who use patented genes for medical diagnosis from claims of infringement. In closing, Dr. Teutsch noted the topics at the next Committee meeting in October 2010 would include the SACGHS draft report on genetics education and training, whole genome sequencing, comparative effectiveness research, genomic data sharing, and an update on the implementation of the Genetic Information Nondiscrimination Act (GINA).

Adjournment

The meeting was adjourned at 1:53 p.m.

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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., M.P.H.

Sarah Carr