Highlights of the Thirteenth Meeting of the
Secretary's Advisory Committee on Genetic Testing
May 14-15, 2002
Baltimore, Maryland

The thirteenth meeting of the Secretary's Advisory Committee on Genetic Testing (SACGT) was held in public session May 14-15, 2002, in Baltimore, Maryland. The meeting included an update on the status of the Department's implementation of SACGT's oversight recommendations; a report on the outcomes of the genetics education conference; presentations of draft reports and preliminary white papers from the Informed Consent/IRB Work Group, and draft reports from the Access Work Group and Rare Diseases Work Group; and an overview and analysis of the public comments received on the draft information brochure on genetic testing.

DAY ONE

After opening remarks from SACGT Chair, Dr. Edward McCabe, the morning session began with a briefing from Dr. Sherri Hans, senior advisor to Dr. Eve Slater, Assistant Secretary for Health (ASH). Dr. Hans updated the Committee on the efforts of the ASH regarding the implementation of SACGT's recommendations on the oversight of genetic testing. At present, the office is collecting information and perspectives from various offices and agencies that have the responsibility of moving the recommendations forward. The Food and Drug Administration (FDA) is currently reviewing its statutory authority to regulate home-brew genetic tests, the completion of which is expected prior to the August 15-16 SACGT meeting. In the coming weeks, representatives of these offices and agencies will meet to discuss the status of efforts in implementing the recommendations, identify where additional work may be warranted, and prepare for a briefing of the Secretary on the activities of the Department and Committee.

Next, Dr. Joann Boughman, chair of the Education Work Group, presented the outcomes of the conference, *Genetic Testing and Public Policy: Preparing Health Professionals*, convened by SACGT on May 13, 2002. The meeting was the culmination of more than a year of information gathering, analysis, and consultation with experts in the field. Dr. Boughman first reviewed the goals and format of the conference. The major goal of the conference was to define the challenges and barriers to integrating genetics into curricula and practice of health professionals and to propose recommendations to address these barriers. The morning session of the conference consisted of a plenary session of three speakers and panel session discussing the roles of various health professionals in the provision of genetics services and their differing levels of genetics education and training. In the afternoon, four concurrent focus groups addressed genetics content and curriculum; genetics in training, examinations, and accreditation criteria; genetics tools and resources; and implementations of new developments in genetics.

Dr. Boughman organized the outcomes of the meeting according to five main action themes: integrate, institutionalize, implement, investigate, and identify needs. While genetics issues are under discussion in many forums, the conference revealed a lack of consistency and constancy in the integration of genetics concepts in teaching, training, or practice, making the institutionalization of genetics necessary. Implementation of new genetic testing and

technologies was recognized in all four focus groups as the biggest challenge to the full integration of genetics through all phases of healthcare education and practice. Time was seen as the greatest barrier to the incorporation of genetics material into curricula, clinical training and active practice. To establish new standards of practice, it is imperative that evidence-based medicine be pursued to demonstrate the efficacy of new developments and their implementations. Also, more research is needed to facilitate the translation of new genetic knowledge into practice. In addition, data must be gathered and carefully analyzed to fully assess competing models of practice. Among the needs identified were funding for investigation, teaching and faculty development programs, and training of geneticists utilizing a collaborative team approach.

Although a number of specific recommendations emerged from the focus groups, members recognized that some of the recommendations were beyond the jurisdiction of the Department of Health and Human Services (DHHS) and would need to be addressed by private organizations. However, the Committee agreed that it would be important to recognize the need for action by private groups and acknowledge organizations that may be best suited to address these needs. Other issues that were discussed were access to genetic services and rural health, the roles of allied health professionals in the provision of genetic services, barriers to reimbursement, and public education. The Education Work Group will work over the summer to synthesize the conference proceedings and develop recommendations to present to SACGT in August.

One public commenter noted that several health professions education and training programs were in need of reauthorization this year and suggested that SACGT may wish to consider making a recommendation to the Secretary about the importance of the programs and the value of incorporating provisions for genetics education and training into the authorization. Following some discussion of the merits of the programs, the Committee agreed to draft a letter to the Secretary that would affirm the importance and urge reauthorization of Title VII (Health Professions Education Act) and Title VIII (Nurse Education and Training Act) of the Public Health Service Act and that would recommend the addition of provisions to those statutes authorizing support for programs to train genetic specialists and to enhance general genetics education and training for all health professionals. Subsequent to the meeting, the Committee learned that the programs' authority does not expire until 2003 and that given this timetable they decided to include recommendations about the programs in the Education Work Group's report.

In the afternoon, Dr. Judith Lewis, Chair of the Access Work Group, presented the Work Group's draft report, *Billing and Reimbursement for Genetic Education and Counseling Services*. The report focused on specific problems in current billing and reimbursement for genetic education and counseling services and their impact on access to such services. Six gaps were identified that were seen to impede billing and reimbursement for genetic education and counseling provided by a range of qualified healthcare professionals: 1) existing Current Procedural Terminology® (CPT) codes do not adequately reflect the preparation and follow-up time and extended duration of patient sessions that may be needed for genetic education and counseling; 2) the Health Care Professionals Advisory Committee of the American Medical Association (AMA) does not currently include certified genetic counselor representation (this is currently under AMA review); 3) because certified genetic counselors are not listed in Medicare statute for direct or "incident to" billing purposes, they are limited in how they may bill

Medicare; 4) certified genetic counselors are not eligible for provider identifier numbers; 5) licensing and credentialing standards for clinicians providing genetic education and counseling are lacking; and 6) data on the value of genetic testing are greatly lacking. Dr. Lewis also presented results from a small survey conducted by the Access Work Group, as well as a similar survey conducted by the California Department of Health, that qualitatively demonstrated the potential for the current reimbursement rates to limit access to and availability of these services. Twelve recommendations were proposed to address these identified gaps and survey findings.

SACGT voted to draft a letter to the Secretary expressing an urgent need for data on the health and economic value of genetic services, including genetic testing and genetic education and counseling, and requesting an assessment of existing data and delineation of additional data needs and research strategies, methodologies and priorities be conducted. They further agreed public comments could be solicited on the remaining proposed recommendations.

Drs. Victor Penchaszadeh and Benjamin Wilfond, co-chairs of the Informed Consent/IRB Work Group, presented the group's revised recommendations in the group's draft report, *Improving Decision Making and Informed Consent for the Use of Genetic Tests in Clinical and Public Health Practice.* At February's SACGT meeting, Drs. Barbara Koenig (past co-chair) and Wilfond presented an overview of the issues considered by the work group in the development of the report, including the reasons why a focus on informed consent in genetic testing was important. The Committee generally concurred with the conceptual framework of the report -- that certain test characteristics were key to considering the nature of the consent process -- as well as the report's explanation of those factors and the way they can affect consent. However, some concerns were expressed about how the level of informed consent would be determined and implemented. In addition, many members expressed concerns about the proposal that FDA be involved in the determination of the level of consent. The Committee reasoned that the involvement of FDA in this role could interfere with the patient/provider relationship and might undermine the primacy that the needs of individual patients should have in determining the nature of the consent process.

The revised recommendations presented at this meeting attempted to address the concerns of the Committee by limiting FDA's role in assuring informed consent to those tests that cross the threshold of complexity and warrant an extensive consent process. The revised recommendations focused on the development of professional guidance; DHHS support of social science research to improve consent and the private sector efforts to develop guidance for specific genetic tests; dissemination of test information to help facilitate and enhance consent; FDA involvement in identifying highest complexity tests requiring extensive informed consent; and the role of the laboratory in verifying consent for highest complexity tests.

While the Committee expressed appreciation for the Work Group's effort to refine the recommendations and reiterated their support for the conceptual framework, members remained concerned that a governmental role in this area might infringe on the practice of medicine and that an educational rather than a regulatory approach was needed. While rejecting the recommendations about FDA in assuring consent, the Committee did support the recommendations related to the convening of a national conference on informed consent; the

development and dissemination of information about genetic tests; the development of guidelines on informed consent developed by professional societies in collaboration with patients, public, and informed consent and legal scholars; Federal funding of guideline development efforts and social science research on informed consent; and reimbursement for the time and effort involved in the provision of informed consent. The Committee requested that the Work Group further refine the recommendations taking account of the Committee's views and present a revised set for the Committee's consideration in August.

Dr. Michele Puryear presented an initiative from the Health Resources and Services Administration (HRSA) regarding the recommendation calling for national discussion on informed consent for genetic tests used in clinical and public health practice. Dr. Puryear reported that HRSA would be sponsoring a national conference on informed consent with the University of California, Los Angeles, on November 21-22, 2002. The conference will be held in association with SACGT and cosponsored by the National Institutes of Health (NIH) and the Centers for Disease Control and Prevention (CDC). HRSA has offered to provide an opportunity for SACGT to present the informed consent report and recommendations and gather broader perspectives on the ideas developed in the report.

The final presentation of the day was by Ms. Sarah Carr, Executive Secretary of SACGT. Ms. Carr presented an overview and analysis of the public comments submitted in response to a request for public comments on the informational brochure *Some Basic Questions and Answers about Genetic Testing*. At the last SACGT meeting, the Informed Consent/IRB Work Group presented the draft informational brochure and SACGT recommended that they solicit public comments on the brochure. The 30-day public comment period was held from March 19 to April 20. In order to gather public comments from a wide range of individuals and groups, SACGT solicited comments via the *Federal Register*, the SACGT web-site, and a target mailing to 2800 individuals and organizations.

Two hundred eighty-seven comments were submitted to SACGT. The majority of comments were generally favorable, and most thought the brochure would be useful in informing patients, health professionals and members of the general public about genetic testing. Many commenters had specific suggestions about the content of the brochure and a number submitted specific editorial changes. A number of commenters expressed concerns about the document's reading level for general audiences and its appropriateness for diverse communities. After discussing the comments, SACGT decided that the brochure should be revised based on public comments and tested in focus groups composed of diverse representatives of the general public and patients/consumers before it is finalized. The Committee also decided that a report to the Secretary should be developed to highlight the importance of public understanding of genetic testing; call for the development and dissemination of information about genetic tests to the general public and to patients/consumers considering genetic testing; call attention to the need for informational materials tailored to particular communities, including groups linked by ethnicity, culture, or language; and transmit the final brochure as an example of the type of information needed to enhance public understanding and as a model, along with other such brochures, for the preparation of additional brochures on specific tests and categories of tests. Regarding the dissemination of the brochure, SACGT recommended that the final brochure be made available on the SACGT website (as well as to any others that wish to post it) in a

downloadable format and that it be reviewed periodically to ensure continuing currency and accuracy.

DAY TWO

SACGT has had extensive discussions in previous meetings about the critical importance of supporting ongoing data collection and analysis of genetic tests in both the pre-market and post-market phases. Its July 2000 oversight report included recommendations about the need for coordinated efforts in data collection. Since issuing that report, SACGT, largely through the efforts of the Data Work Group and its chair, Dr. Wylie Burke, has sought to understand in more specific detail the challenges involved in achieving this goal. At its August 2001 meeting, SACGT decided that more specific information was needed about the efforts of relevant DHHS agencies to support the advancement of knowledge of the clinical validity and utility of genetic tests. In the fall of 2001, SACGT sent letters to the heads of Agency for Healthcare Research and Quality, CDC, Centers for Medicare & Medicaid Services (CMS), FDA, HRSA, NIH, and the Office of Human Research Protections (OHRP) requesting information on their activities regarding the support of efforts to advance knowledge of clinical validity and clinical utility of genetic tests.

At its February meeting, SACGT heard presentations from the agencies on their activities and an overarching analysis of the totality of effort underway across the HHS in these areas. The extent and scope of the activities were impressive to the Committee, but questions were raised about DHHS's vision for genetics and genetic testing, including whether genetics is considered a targeted programmatic area or an integral part of health and medicine generally, and the need for more systematic planning and coordination efforts. Before coming to final conclusions and recommendations about the adequacy of efforts to advance knowledge of clinical validity and clinical utility, and the Department's role in advancing those efforts, the Committee decided that a phase II study was needed to gather data in several specific areas using a case study approach. The second phase would help elucidate the different steps in the translation process, including the role of the private sector, and highlight successful approaches to coordination and collaboration among the agencies. Three case studies were presented: population-based testing for hemochromatosis, susceptibility testing for breast cancer, and newborn screening for sickle cell disease and other hemoglobinopathies.

Dr. Muin Khoury presented the first case study on hereditary hemochromatosis (HHC). Dr. Khoury opened his presentation with an overview of the multi-step process from gene discovery to diagnosis, treatment, and prevention of disease. HHC is an autosomal recessive disease characterized by iron overload leading to organ damage. The hemochromatosis gene was discovered in 1996 and two main variants were identified: C282Y and H63D. Population screening for HHC was considered because of the high prevalence of the mutation, lack of early-onset clinical manifestation, lack of specificity of clinical findings, low cost of diagnosis and efficacious treatment (phlebotomy), and the high cost and low success rate of late diagnosis and treatment. Shortly following the gene discovery, federal research and public health agencies, as well as academia, consumer advocacy groups and the private sector, came together to address questions of screening, testing, and treatment. In 1997, CDC and the National Human Genome Research Institute convened a conference to determine if public screening was warranted for HHC. The attendees favored a movement toward routine adult screening but recognized that

much more needs to be learned about the prevalence and penetrance of the mutations. Between 1997 and 2002, NIH funded 45 projects on HHC. At present, the existing gaps in knowledge about HHC include its natural history including penetrance and the role of other genetic and non-genetic factors, the public health impact, screening and genetic testing, and efficacy of early treatment.

Dr. Michele Puryear next presented the case study on newborn screening for sickle cell disease (SCD) and other hemoglobinopathies. Dr. Puryear began with a general overview of sickle cell disease and the milestones in the development of newborn screening. Currently, 44 states, the District of Columbia, Puerto Rico, the Virgin Islands, Guam, and Saipan provide universal newborn screening for SCD; the remaining six states provide newborn screening for SCD upon request. In 1972 and 1978, the Sickle Cell Disease Act and the National Genetic Disease Act were enacted, respectively. Under these authorities, NIH transferred funds to the Maternal and Child Health program to develop community-based sickle cell education, screening, and counseling services. Between 1972 and 1992, more than 50 million dollars were devoted toward funding sickle cell clinics, couples counseling, psychosocial support for patients and families, newborn screening, and programs for young adults with SCD. In 1986, NIH-funded clinical trials indicated that children with SCD have an increased susceptibility to bacterial infections and should receive oral penicillin prophylaxis. In 1987, a NIH-HRSA consensus conference recommended universal newborn screening for SCD. However, national newborn screening still has not been achieved and there is a lack of consistent adherence to national guidelines for follow-up and treatment. In addition, there is a need for improved education for both the general public and health professionals regarding SCD and the establishment of a hemoglobinopathy reference laboratory for accurate identification of abnormal hemoglobins detected by newborn screening.

Dr. Burke presented the third case study on BRCA1/2 susceptibility testing for breast cancer. In 1994 and 1995, the breast cancer susceptibility genes, BRCA1 and BRCA2, were identified, respectively. Shortly thereafter, in 1996, commercial testing was introduced (Myriad Genetics owns the exclusive licensing rights for the BRCA1 and BRCA2 genes). Several organizations have developed clinical guidelines and position statements regarding the use of and criteria for susceptibility testing for breast cancer. Since the identification of BRCA1 and BRCA2, a number of papers have been published on the risks of cancer in BRCA1/2 carriers, the prevalence and penetrance of BRCA1/2 mutations, the identification and prevalence of mutations in the Ashkenazi Jewish population, and the psychosocial, educational/counseling and informed consent issues associated with BRCA1/2 susceptibility testing. More recently, studies have focused on the clinical correlations of BRCA1/2 carriers and outcomes of preventive surgery and screening. Several federal initiatives have supported translational research efforts related to BRCA1/2. These include Requests for Applications to stimulate research in particular areas (notably the Cancer Genetic Studies Consortium and Department of Defense breast cancer initiatives); the development of research infrastructures (notably the Cancer Family Registries and the Cancer Genetics Network); and federal support of educational and information resources, including research projects addressing educational needs of patients as well as the National Cancer Institute's CancerNet/PDQ system and the GeneTests-GeneClinics web-site. Some of the remaining issues regarding research on BRCA1/2 testing include the role of the test offerer in on-going research, a re-evaluation of current research structures and the potential need for new

collaborations or databases, and a need for ongoing secondary analyses and long-term studies on the ethical, legal, and social implications of breast cancer susceptibility testing.

Dr. Burke led the discussion following the case studies. A number of topics were discussed including the importance and continued need for public-private collaborations, the role of the commercial sector, and need for follow-up studies and new research strategies to enhance knowledge of clinical validity and clinical utility. The Committee decided that the Data Work Group should take the lead in assessing the case studies and developing draft recommendations to propose to SACGT in August about steps DHHS could take to enhance research, development, and translation of genetic tests.

Ms. Kate Gottfried, Executive Director of NHRPAC, updated SACGT on the activities of NHRPAC and its newly reconstituted Genetics Working Group. Following up on a presentation the NHRPAC chair, Dr. Mary Faith Marshall, made to SACGT in February, Ms. Gottfried reported that the Committee had revised its recommendation regarding informed consent of third parties and forwarded its revised statement to the Assistant Secretary of Health in April. The Genetics Work Group expects to address issues of community consultation, stored tissue research, blanket consent for use of samples in research, and disclosure of research results. Partly in response to a recommendation of SACGT, the Work Group is currently updating a genetics research chapter in OHRP's 1993 guidebook for institutional review boards.

Ms. Judy Yost, Director of the Division of Laboratories and Acute Care, which administers the CLIA program, at CMS, briefed the Committee on efforts to develop a *Frequently Asked Questions* document on CLIA certification. Ms. Yost reviewed the major provisions of CLIA, highlighting those that are considered high priority in ensuring quality assurance, and the flexible approach CMS surveyors take in compliance review. Ms. Yost noted that the quality assurances of genetic testing research laboratories are considered to meet CLIA requirements.

Next, Ms. Mary Davidson and Dr. Michael Watson, co-chairs of the Rare Disease Work Group, updated the Committee on the progress of the group's white paper and highlighted key issues that the paper addresses in its present draft. Ms. Davidson reviewed the work of the group and summarized the session on rare diseases held at last November's SACGT meeting. Ms. Davidson described the core challenge facing genetic testing for rare diseases as the balance between assuring the quality of rare disease testing and continued access to such tests. The goals of the white paper are to define rare diseases, describe the steps in the research, development, and translation of tests for rare diseases, review current oversight, describe resources for rare diseases and pending legislation, and propose recommendations to enhance the development, translation, oversight, availability and accessibility of genetic tests for rare diseases. Ms. Davidson also reviewed the past recommendations relating to rare disease testing put forth by a 1994 Institute of Medicine report and the 1997 report by the NIH-DOE Task Force on Genetic Testing.

Dr. Watson then described the special considerations for rare diseases including genetic heterogeneity, differences between the incidence and prevalence of disease, particularly across populations, and the associated test volume. A rare disease can have a rare diagnostic test but a common screen or carrier test, which raises a different set of issues. Some of the barriers to

translating rare disease tests into clinical practice include the lack of research funding for data collection to validate tests, the lack of institutional support to provide the test as a clinical service, and the lack of interest from the commercial sector to provide rare disease testing due to the low profitability of such tests.

The current oversight applicable to rare disease testing is the Orphan Drug Act and Humanitarian Device Exemption (HDE) administered by FDA, and CLIA. The definitions of rare/orphan diseases differ in the Orphan Drug Act and Humanitarian Device Exemption (less than 200,000 persons in the U.S and fewer than 4,000 individuals per year, respectively). Although FDA has encouraged the submission of HDE applications for any qualifying medical disease or condition, many genetic tests for rare diseases may not qualify for the program because they could not meet the definition of HDE (fewer that 4,000 tests per year). With regard to CLIA oversight, a survey conducted by the American College of Medical Genetics and the American Society of Human Genetics confirmed that some rare disease testing laboratories are unfamiliar with the CLIA regulations. To assist these laboratories to meet CLIA regulations, respondents identified a need for different types of assistance such as protocol books and workshops on CLIA regulations.

During the Committee's discussion, a number of issues were identified for the Work Group to consider including the need for increased funding for translational research for rare diseases, establishment of a database of patients with rare diseases for research and follow-up studies, assessing how FDA's HDE mechanism can be improved for rare disease genetic testing, and assessing why past recommendations regarding rare disease testing have not been implemented. The Work Group expects to present a first draft of recommendations at SACGT's next meeting in August.

Dr. Lewis next presented the second of the Access Work Group's reports addressing issues on more global coverage and reimbursement of genetic testing services. The purpose of the report is to provide a broad look at coverage and reimbursement for genetic services, identify challenges in obtaining and providing reimbursement for these services, and develop recommendations for addressing these challenges. To help identify challenges and develop recommendations, Dr. Lewis proposed a roundtable be convened with individuals who have a role in or are affected by coverage and reimbursement decisions for genetic services. The Committee concurred that a roundtable would be a valuable next step.

Before adjourning, Dr. McCabe reviewed the preliminary agenda for the August 15-16 meeting to be held in Bethesda, Maryland. Dr. McCabe proposed that the Committee set aside time to evaluate the Committee's role, effectiveness, impact, and accomplishments since SACGT's inception as well as future goals. In this regard, the Committee was reminded that they should remain mindful of the criteria articulated by Dr. Francis Collins in August 2000 in deciding which issues and projects SACGT commits itself to, such as whether the issue falls under the Committee's charter and whether the Committee's contribution will have an important impact. The Committee concurred that it would be appropriate to reflect on its impact and accomplishments at the next meeting. Other expected topics for the August meeting include a briefing on FDA's oversight authority, follow-up on work group projects, and discussion of a draft report on HHS programmatic efforts in the research, development, and translation of genetic tests into the clinical and public health setting.