Highlights of the Eighth Meeting of the
Secretary's Advisory Committee on Genetic Testing
February 15-16, 2001
Bethesda, MD

The eighth meeting of the Secretary's Advisory Committee on Genetic Testing (SACGT) was held in public session on February 15-16, 2001, in Bethesda, Maryland. The Committee was briefed on DHHS's response to SACGT's oversight recommendations and steps that are being taken to implement the recommendations. The Committee was also briefed on FDA's Genetics Action Plan. After reviewing public comments, SACGT engaged in further deliberation about the proposed test classification methodology for review purposes and the format for test summaries for health professionals.

SACGT also heard progress reports from four of the five work groups formed to explore several high-priority areas: genetics education of health professionals and the public, informed consent and IRBs; access to genetic tests and services; and rare disease testing. Four Working Groups met during the two-day meeting.

DAY ONE

In January 2001, the Committee received a letter from then Secretary of Health and Human Services, Donna E. Shalala, outlining the Department's response to SACGT's report on *Enhancing the Oversight of Genetic Tests: Recommendations from the SACGT*. Dr. William Raub, Acting Assistant Secretary for Planning and Evaluation and Science Advisor, briefed the Committee on the Department's response to SACGT's recommendations for oversight of genetic tests and the steps that are being taken to implement the recommendations. Dr. Raub indicated that HHS agreed that enhanced oversight should involve both home brews and genetic test kits and that informed consent should be required for all genetic testing research studies in which individually identifiable human subjects or samples are used. He then outlined actions to be taken by the Health Care Financing Administration (HCFA), the Food and Drug Administration (FDA), and the Centers for Disease Control and Prevention (CDC) in response to the oversight recommendations.

Dr. David Feigal, Director of FDA's Center for Devices and Radiological Health (CDRH), amplified on Dr. Raub's presentation by providing a report on FDA's Genetic Action Plan for implementing oversight of genetic tests, including tests provided as a laboratory service (known as in-house or "home brew" tests). Dr. Feigal presented a phased-in program for regulation of all genetic tests, which involves registration and listing, test classification, development of review templates and standards, phased-in review of all tests, and implementation of premarket review. The FDA plan will be voluntary until a rule to require premarket submission of applications is promulgated. FDA is in the process of developing an application form specific to genetic tests that is intended to expedite the review process. Dr. Steven Gutman, director of the Division of Clinical Laboratory Devices at CDRH, presented the draft review template with an example of a genetic test. The template would require data on analytical validity, clinical validity, quality control and quality assurance, and clinical interpretation among other areas.

The remainder of the first day was focused on review of public comments and discussion of SACGT's proposed test classification methodology which has been under development since August 2000. The proposal set forth two levels of review and three criteria for determining into which category a test would fall: analytical validity, population screening, and rare or common disease or condition. Public comment was solicited through a *Federal Register* notice, a mailing to all those who commented on the oversight report, and a posting on SACGT's web-site. The Committee received 34 comments from individuals and organizations, including patient advocacy groups, academic organizations, professional societies, and industry. The comments raised a number of concerns regarding the feasibility of the classification methodology and the extent to which the proposed criteria would succeed in addressing the aspects of genetic testing that raise the greatest concern. For example, the absence of a criterion for the purpose of the test, i.e., diagnostic or predictive, was of concern to a number of commenters.

After careful consideration of public comments and further discussion, the Committee concluded that accurately categorizing tests based on a few elements in a simple, linear fashion was not the preferred methodology and therefore, should not be used by FDA as an a priori way of determining review level. Instead, SACGT tentatively endorsed the use of the review template presented by FDA to incorporate into the review process the critical elements identified in the classification methodology. SACGT has requested that FDA continue to evaluate how the template approach would be effective in identifying tests that warrant a more in-depth review without causing delays in the review process. The Committee also asked the agency to provide additional examples for different types of genetic tests.

Dr. Pat Charache, liaison to the CLIAC, updated the Committee on the recent CLIAC meeting and decisions regarding CDC's Notice of Intent to strengthen CLIA regulations for genetic testing.

DAY TWO

The morning was devoted to a review of public comments and discussion on the proposed format for genetic testing summaries for health professionals. At the November meeting, the Data Team, chaired by Dr. Wylie Burke, presented an information template for health professionals that displays the basic elements of a genetic test. The proposed template contains seven key data elements, definitions for each element, and specified sources for each data element. The seven elements relate to the purpose of the test, clinical condition for which the test is performed, definition of the test, analytical validity, clinical validity, and clinical utility, and the cost of a test. Public comment was solicited through a *Federal Register* notice, a mailing to 87 health professional organizations, and a posting on SACGT's web-site. The Committee received 16 comments from individuals and organizations, including patient advocacy groups, academic organizations, and professional societies. Overall, the comments were supportive of the goal of educating health professionals on genetic tests and their appropriate uses and agreed that the seven data elements outlined in the template were key information items that health professionals should have knowledge of when ordering a genetic test. Some commenters raised concerns regarding the burden on laboratories as the source of information for the majority of data

elements. The Committee will continue discussions on the provider test summaries at the May meeting.

In the afternoon, the chairs of the working groups reported to the full Committee on their group's progress. Dr. Joann Boughman, Chair of the Genetics Education Work Group, reported on the efforts to address issues regarding the genetics education of health professionals. Dr. Boughman described the development of a background report on current efforts to enhance genetic education of health professionals in the public and private sectors. If the Group finds gaps in the efforts to enhance the education of health professionals, it will present them to SACGT for discussion of whether to recommend approaches to the Secretary on how any gaps might be addressed. The Group will also specifically address the role of informatics and its impact in provision of knowledge to health care providers and patients/consumers. The Group will carry out analyses of educational (basic, advanced, and continuing) and training programs, workforce needs, and desired behaviors and outcomes of enhanced genetics education. Dr. Boughman concluded that the Group would endeavor to complete its work in time for presentation to the full Committee at the May meeting.

Dr. Barbara Koenig, Chair of the Informed Consent/IRB Working Group, reported on several tasks the group is currently undertaking. The Group is in the process of developing an informational brochure, *What Every Patient and Consumer Should Know About Genetic Tests and Informed Consent.* The brochure will describe general concepts about genetic tests and informed consent issues in a format appropriate for patients and consumers.

SACGT previously charged the Informed Consent/IRB Work Group with developing principles for informed consent in the clinical setting with specific attention to criteria for determining the level of consent that should be required for different kinds of genetic tests. Dr. Koenig reported that the Group discussed a conceptual framework for guiding the development of recommendations. The Group's task is to define criteria for which tests warrant documented consent. Dr. Koenig reported that the Work Group's goal is to develop by fall 2001 overarching principles of informed consent for genetic testing in clinical practice, including criteria identifying what types of tests warrant documentation of informed consent process and what levels of and approaches to consent should be required for different types of tests; and recommend sources of information to ensure an informed decision.

Future projects for the Informed Consent/IRB Work Group might include the development of additional guidance for investigators about when experimental genetic test results may appropriately be returned to research participants (taking account of the need for basic oversight elements such as laboratory quality assurance provisions and current regulations such as CLIA). The Group is considering commissioning a white paper on how consent issues evolve as tests move through a development continuum from early research to clinical and public health practice to direct-to-consumer access to tests. The paper will include special consent issues raised by multiplex testing. The Group will also follow developments with regard to promulgation of the HHS privacy rule and, depending on its final outcome, consider whether specific guidance regarding privacy and confidentiality of investigational genetic test results may be needed for investigators and IRBs.

Dr. Judith Lewis, Chair of the Access Work Group, discussed the Group's efforts to address reimbursement and health care disparities issues as they relate to genetic testing. The Group is in the process of developing a framework of genetic services benefits to serve as a model for insurers, employers, and providers. The development process will include a request for public comment in the *Federal Register*. The Group will be exploring current limitations in coverage of genetic tests and genetic counseling services. Dr. Lewis also reported on a presentation by Irene Stith-Coleman, Ph.D., Senior Public Health Advisor to the Assistant Secretary of Health, about DHHS initiatives addressing health care disparities. In the future, the Work Group will be briefed by Department agencies on their specific efforts to address health disparities. The Group will explore the availability of culturally appropriate genetic services, the inclusion of broad populations in the test development process, and scientific developments in understanding the relevance and significance of human genetic variation and SNPs to health status, health promotion and disease management.

Ms. Mary Davidson, Chair of the Rare Disease Testing Work Group, updated the Committee on the Group's efforts. In collaboration with HCFA, CDC, and relevant private sector organizations, the Group is beginning to develop technical assistance models to help small private or academic laboratories meet CLIA regulations. The Group also will monitor the impact of CLIA certification and the continued availability of genetic tests for rare disorders. In addition, the team will work towards the development of a consensus definition of rare diseases to harmonize current multiple definitions.

At the next meeting in May, FDA will report on the further development of the review templates and SACGT will continue discussions on review process. The Committee will hear progress reports from the work groups and review any work products ready for full Committee consideration.