Highlights of the Seventh Meeting of the Secretary's Advisory Committee on Genetic Testing November 2-3, 2000 Bethesda, MD

The seventh meeting of the Secretary's Advisory Committee on Genetic Testing (SACGT) was held in public session on November 2-3, 2000, in Bethesda, Maryland. The Committee was updated on the progress of the SACGT working groups, which were formed in August 2000 and are composed of SACGT members and ad hocs, and heard presentations in three broad areas: the advertising, labeling, and promotion of medical devices; reimbursement issues in genetic testing services; and informed consent issues in clinical and research settings. The Committee was also briefed on data collection and oversight activities of CDC, FDA, and CLIAC.

At its August 4 meeting, SACGT established work groups to explore five broad high-priority areas: informed consent and IRBs; data elements/data collection; rare disease testing; access to genetic tests and services; and genetics education of health professionals and the public. Short-term and long-term tasks were identified for each group. Since the August 4 meeting, each group convened at least one teleconference to review the scope of issues that were initially identified and to begin work on the tasks. Work group chairs presented progress reports to the full Committee throughout the two-day November meeting followed by discussion by SACGT and the public.

The Committee also reviewed and revised the classification methodology developed by the Classification working group and endorsed by the full Committee in August. SACGT decided to reconsider the methodology in response to a number of issues raised by professional groups regarding the feasibility of the methodology in its present form. The methodology is intended to be a tool for classifying tests according to the level of review warranted.

DAY ONE

On November 2, four of the five chairs reported to the full Committee on their group's progress. Dr. Wylie Burke, chair of the Data Team, was first to present her group's efforts. The group's primary short-term task was to develop a pre- and post-test information template that displays the basic elements of a test for health professionals. The goals of the template were to identify what health professionals should know about a genetic test; and what represents complete information about a test. The workgroup identified seven key data elements, developed 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 test, a test's analytical validity, clinical validity, and clinical utility, and the cost of a test. The team is currently soliciting input from a range of individuals and organizations on the data template. SACGT endorsed the group's efforts and requested a report on its progress at the next SACGT meeting.

Ms. Mary Davidson, chair of the Rare Disease Testing Team, reported on her group's progress. The major short-term task of the team was to define test volume as proposed in the test classification methodology. The group's efforts since the August meeting included gathering information from laboratory experts and the rare disease testing community on their experiences with well-established rare disease genetic tests and exploring criteria for what determines when a Level I test should move to Level II. Ms. Davidson presented background information on the reasons for selection of test volume as the first criterion in the test classification schema and highlighted concerns that have been raised regarding that criterion. The use of FDA's Humanitarian Device Exemption for certain low volume genetic tests was also discussed. The team will continue to gather data from laboratorians and the rare disease community regarding their experiences with rare disease testing and the impact of FDA review on rare disease testing, and develop a set of criteria that would raise the level of review for particular rare disease tests. As recommended by SACGT in the oversight report, the team, in collaboration with HCFA, CDC, and relevant private sector organizations, will also begin developing technical assistance models to help small private or academic laboratories meet CLIA regulations.

Dr. Judy Lewis, chair of the Access Working Group, discussed the group's efforts to solicit comments on the five areas being explored by the work groups, briefly reviewed an analysis provided by NHGRI of ELSI's research grant portfolio on intellectual property, and presented a draft version of a letter to the Secretary on gene patenting and licensing for the Committee's consideration. The letter discussed concerns heard by SACGT at its June 2000 meeting regarding the impact of gene patenting and licensing on access to and cost and quality of genetic tests and recommends that the Secretary consider whether further study of the issues is warranted. Members discussed the letter's focus and balance, suggested changes, and agreed to review the letter again the next day. Dr. Lewis also described presentations organized by the group on reimbursement of genetic testing services for the next morning. A range of experts representing the public and private sector, including Medicaid and Medicare, indemnity insurance, and managed care was invited to educate the Committee on their policies and practices for reimbursement of genetic testing services. The Access Working Group will continue to study issues related to reimbursement of genetic testing services and focus on health care disparity issues related to genetic testing.

In the afternoon, the Committee was briefed on CDC activities by Drs. Muin Khoury and Joe Boone, on CLIAC by Dr. Pat Charache, and on FDA by Dr. Steve Gutman. Dr. Khoury reviewed a system for collecting and evaluating data on genetic tests, including an assessment of the availability, quality, usefulness, and dissemination of data. Dr. Boone updated the Committee on the recent Genetics Laboratory Forum meeting and summarized the group's concerns regarding SACGT's classification methodology. Dr. Charache updated the Committee on the recent CLIAC meeting and decisions regarding CDC's Notice of Intent to strengthen CLIA regulations for genetic testing. Dr. Gutman briefed the Committee on FDA's professional in vitro diagnostics (IVD) roundtable meeting on October 24, held to brainstorm on how the enhanced oversight of genetic testing might be implemented.

SACGT next heard presentations from Mr. Matthew Daynard of the Federal Trade Commission and Mr. Byron Tart of FDA on their agency regulations governing the labeling, promotion, and advertising of medical devices. FTC and FDA have an interagency liaison agreement defining each agency's jurisdictional boundaries. FTC has primary jurisdiction for the advertising of foods (including supplements), over-the-counter drugs, devices, and cosmetics. FDA has primary jurisdiction for the labeling of these products and for both advertising and labeling of prescription drugs. Mr. Daynard reviewed FTC's advertising principles and emphasized that true and substantiated health claims are an important part of FTC's mission. Mr. Tart discussed FDA's regulations governing device labeling, promotion, and advertising, how they might apply to genetic testing, and how they address off-label use. Mr. Tart stated that FDA does not distinguish between professional and direct-to-consumer marketing. Both agencies require substantiation of claims and review the evidence supporting a claim. The two speakers joined Committee members in a roundtable discussion and reviewed hypothetical advertisements for genetic tests.

The final presentation of the day was by Dr. Joann Boughman, chair of the Genetics Education work group. Dr. Boughman presented the work group's guiding principle of promoting a partnership between health care professionals and the public so that genetic testing can be used effectively even while knowledge is continuously expanding and evolving. Dr. Boughman described the group's efforts to gather information on current genetic educational efforts in the public and private sectors. SACGT recommended that a white paper be drafted to summarize current efforts in genetic education, identify where gaps or needs in genetics education exist, and make recommendations to the Secretary about how they might be addressed. The group will report back to the full Committee in February with a draft document for review and consideration.

DAY TWO

On November 3, Dr. McCabe announced that the SACGT oversight report, *Enhancing the Oversight of Genetic Tests*, had been received by Secretary Shalala and that the report was now publicly available. Copies were distributed to meeting attendees and the report will be posted on SACGT's web-site (http://www4.od.nih.gov/oba/sacgt.htm).

The morning was devoted to a session on *Reimbursement Practices for Genetic Testing Services*. The goal of the session was to provide background information on the current practices and policies for reimbursement of genetic test services by various types of public and private payors. The panel was composed of five representatives from the public and private sectors: Ms. Jackie Sheridan of the Health Care Financing Administration (Medicare and Medicaid), Dr. David Witt of Kaiser Permanente of Northern California (not-for-profit managed care), Dr. Allan Bombard of Aetna US Healthcare (for-profit managed care, PPO, POS, and indemnity), Dr. Victor Villagra of CIGNA Healthcare (for-profit managed care), and Mr. Cecil Bykerk of Mutual of Omaha (for-profit indemnity). The presenters discussed how their respective organizations determine coverage policies, what genetic tests are currently covered, and the impact that

FDA review of genetic tests would have on coverage decisions. A roundtable discussion was held with presenters from the panel and Committee members.

In the afternoon, the Committee heard a presentation from Dr. Nancy Press, an Associate Professor in the Department of Public Health and Preventive Medicine at the Oregon Health Sciences University, on informed consent issues in the clinical and research setting. Following Dr. Press's presentation, Dr. Barbara Koenig, chair of SACGT's informed consent/IRB work group, presented the group's progress report. Dr. Koenig reviewed the goals of the group, including to develop an informed consent checklist, determine how informed consent should be implemented and documented for different tests, and coordinate the work group's activities with other ongoing oversight activities. Among the group's short-term tasks was to develop a letter to the Secretary recommending the advisory committee to the Office of Human Research Protections (OHRP) clarify the regulations regarding secondary research subjects and OHRP prioritize updating its Human Genetic Research chapter of the IRB guidebook. Long-term tasks of the group included assisting OHRP in updating the genetic research chapter, reviewing NBAC's recommendations on human biological materials and building upon the genetic test-related recommendations, and considering issues related to disclosure of research results. The Committee recommended that the group develop a genetic test checklist for research participants, patients, and consumers outlining basic questions that should be asked about a genetic test before deciding whether to be tested; explore the utility of a central IRB for genetic testing studies; develop recommendations for consideration by the full Committee regarding informed consent challenges in direct-to-consumer marketing; and continue to build on the work of other groups.

SACGT returned to a discussion of the test classification methodology for determining the level of review for genetic tests. The Committee focused primarily on the criteria of test volume and the intended use of a test, as either diagnostic or predictive. The Committee's initial reasons for selecting test volume as the first criterion included reducing the number of tests requiring a Level II review, a more time-consuming and detailed data analysis. In addition, SACGT wished to reduce the cost and burden of review to laboratories providing a small number of tests per year, particularly those in the academic setting. For the criterion of test volume, concerns were raised about the ability to accurately estimate the projected use of a new test or to gauge how quickly the use of a test might expand. Also, initial attempts to define the threshold number for test volume proved difficult.

For the intended use criterion, concerns were raised that a Level II review could slow the introduction of a diagnostic test to the market. Since many genetic tests can potentially be used for multiple purposes, a large number of tests may fall into Level II review since they can be used for predictive purposes as well as diagnostic. Of even greater concern was the potential for off-label use. For example, a test approved for the claim of diagnosis of a disease (Level I review) could be used for the unapproved claim of prediction of disease (Level II review).

To address the concerns raised with these two criteria, Drs. Wylie Burke and Muin Khoury led a discussion that resulted in a revised classification schema. The revised classification methodology reprioritizes and redefines the Committee's goals for determining an appropriate level of review for a test. The revised classification schema maintains the two levels of review originally identified, Levels I and II, but determination of review level would be based on three criteria instead of four. As shown in Figure 1, the revised classification schema would begin with a determination of whether a test is analytically valid. The addition of analytical validity to the classification schema makes explicit the Committee's view that if a test is not analytically valid, it should not be commercially available and, therefore, be automatically rejected.

If a test is shown to be analytically valid, it moves on to a second criterion that defines whether the test is intended for use on a population (the same criterion as in the original classification schema). If a test is intended for population screening, the test would receive a Level II review.

If a test is not intended for population screening, the next determination is whether a test is to be used to detect a common or rare disease. The Committee proposed using rare disease as a criterion instead of test volume since it can be more accurately determined based on prevalence or incidence. SACGT proposed defining the term *rare* as having a prevalence of one in 2,000 or an incidence of one in 10,000. If a test is for a rare disease, it would receive a Level I review. If a test is for a common disease, it would receive a Level II review. In dividing genetic tests into categories of rare (Level I review) and common (Level II review) as the final determinant of review level, the Committee eliminated the intended use of a test (diagnostic or predictive) as a criterion. All tests, regardless of purpose, for the detection of disease with a prevalence greater than one in 2,000 or prevalence of one in 10,000, would receive a Level II review.

Other criteria that were eliminated from the original classification schema included the questions about whether a proven intervention was available and whether there is potential for significant medical or social risks. Rather than being criteria for classifying genetic tests, SACGT would expect to see these factors considered during the review process. SACGT agreed to solicit public comment on the revised classification schema before finalizing it.

At the next meeting in February, SACGT will hear progress reports from the five work groups and review finalized and draft documents from the groups. SACGT will also discuss a sixth area of interest -- the influence of genetic test information on concepts, definitions, and perceptions of ancestry, ethnicity, and identity.

Figure 1. Revised Draft Test Classification Scheme Formulated by SACGT on November 3, 2000