THE SECRETARY OF HEALTH AND HUMAN SERVICES
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Edward R. B. McCabe, M.D., Ph.D., Chair
Secretary's Advisory Committee on Genetic Testing
6705 Rockledge Drive, Suite 750
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Dear Dr. McCabe:

I thank you and other members of the Secretary's Advisory Committee on Genetic Testing (SACGT) for the valuable and thoughtful report, *Enhancing the Oversight of Genetic Tests.* The SACGT is to be commended for not only the quality of the final product but also the thorough and comprehensive process – including public consultations – it undertook to prepare the report. The report provides a solid basis for federal oversight of genetic testing. As the SACGT well recognizes, enhancing such federal oversight will require a coordinated effort across HHS agencies as several agencies share responsibilities for different aspects of genetic testing.

As you know, the Assistant Secretary for Health and Surgeon General, Dr. David Satcher, charged a small working group consisting of representatives from the Food and Drug Administration (FDA), the Centers for Disease Control and Prevention (CDC) and the Health Care Financing Administration (HCFA) to review the SACGT report and develop a proposed response, in consultation with staff from the Office of Public Science and Health (OPHS) and the Office of the Assistant Secretary for Planning and Evaluation (OASPE). In December 2000 a draft response was presented to the HHS Interagency Working Group on Genetic Testing, which is composed of representatives from OPHS, OASPE, FDA, CDC, HCFA, and the National Institutes of Health (NIH), the Health Resources and Services Administration (HRSA), the Agency for Healthcare Research and Quality (AHRQ), the Office for Human Research Protections (OHRP), and the Office of General Counsel (OGC). The Interagency Working Group endorsed the proposed approach for enhanced oversight of genetic testing, plans to refine it further prior to implementation, and will keep the SACGT apprised as the work progresses.

However, in the interim, I am providing you with an overview of what the Department is prepared to undertake to enhance oversight of genetic tests and genetic testing. The HHS oversight plan capitalizes on the authorities provided by existing statutes and regulations and, where needed, the promulgation of new rules. Under the authorities of the Clinical Laboratory Improvement Amendments (CLIA) of 1988 to the Public Health Service Act and the Medical Devices Amendments of 1976 to the Food, Drug and Cosmetic Act, the Department intends to integrate HCFA's certification of clinical laboratories with FDA's oversight of medical devices, and CDC's Genetic Testing Assessment Program to develop a program that we believe will be responsive to a broad range of SACGT's recommendations, with particular emphasis on the following:

- IRB review should be conducted of all research protocols for genetic tests in which individually identifiable human subjects or samples are used, regardless of the funding source. Informed consent must be obtained from all subjects participating in such research.

- The CLIA regulations should be augmented to provide more specific provisions for ensuring the quality of laboratories conducting genetic tests.

- FDA should be the federal agency responsible for the review, approval, and labeling of all new genetic tests that have moved beyond the basic research phase.

- Development of data formats for post-market information gathering to update the utility of genetic tests should be the responsibility of CDC in collaboration with FDA, other federal agencies, and private sector organizations as appropriate. Post market collection, aggregation, and analysis of data should be performed under the auspices of the CDC, and may be required of the test developer, as well as other payers for the approved tests. The focus of this effort is to attain a full understanding of the clinical utility of the test.

In developing its regulatory approach, the Department is stipulating three general principles. One, HHS would apply, to the extent feasible, the SACGT's proposed methodology for classification of genetic tests and its templates for collection of data on the analytical validity, clinical validity and clinical utility of genetic tests.

Two, informed consent, the principal foundation for ensuring the protection of human subjects, will be required for research protocols in which individually identifiable human subjects or samples are used. In the near future, OHRP will be revising and updating its Institutional Review Board Guidebook, including the section on Human Genetic Research. Furthermore, the National Human Research Protections Advisory Committee will also be addressing this issue. OHRP, working closely with the relevant HHS agencies, will coordinate development of appropriate Department-wide policies and/or guidance on this matter.

Three, oversight of genetic tests will cover clinical genetic testing services (so called "home brews") as well as genetic test kits.

The core elements of the HHS approach are as follows:

CLIA Oversight of Genetic Testing

HCFA will immediately begin to identify and register all clinical laboratories that are providing genetic test results to patients or their care providers but are not already CLIA certified. For such certification, HCFA will develop new surveyor guidelines that will include an emphasis on methods for validating the various genetic tests that are performed by the laboratories, appropriate training for surveyors who have not yet been required to review genetic tests per se,

and a broader educational effort involving CDC, FDA, accrediting organizations and professional societies. The clinical laboratories themselves will also have to be educated with respect to CLIA requirements and HCFA's expectations.

In addition to the above, HCFA, working with CDC, will develop new CLIA regulations for expanded oversight of genetic testing laboratories. A *Notice of Intent* to add a genetic specialty under CLIA has been published and HCFA and CDC are currently reviewing the public comments that have been submitted. The Notice also predicates the addition of specific requirements for informed consent, confidentiality, quality assurance, genetic counseling, laboratory personnel, and record keeping.

Introduction of FDA Regulatory Controls

A critical step in providing oversight of genetic tests is to ensure that the proposed test is properly labeled and that information is collected on clinical validity to ensure its availability to health providers for pre and post-test counseling. FDA proposes to:

- Require establishments engaged in the manufacture of genetic tests to register their establishment with the FDA and to list their tests in accordance with section 501 of the Federal Food, Drug, and Cosmetic Act. The FDA registration process calls for general information on the name, ownership, and location of establishments; the listing process calls for general information on the name and classification of the devices produced. In implementing such a requirement, FDA will make every effort to minimize the administrative burden on affected laboratories.

- Work with professional organizations, CDC, HCFA, and others to develop appropriate templates and standards for premarket data collection.

- Investigate the feasibility of using the methodology proposed by SACGT to categorize genetic tests into medical device classes established under the Food, Drug and Cosmetic Act. To this end, FDA will develop lists of devices and convene its relevant advisory committees to refine classification criteria and to assign devices to appropriate classes. FDA will attempt to use the SACGT methodology to classify genetic tests based on risk and knowledge about these devices, with each class subject to a different set of regulatory controls.

- Explore mechanisms for providing premarket review of these tests, once classified, and ensuring their accurate labeling. As recommended by SACGT, such review, to be phased in over time, would "delineate review processes for premarket evaluation of genetic tests, using criteria informed by standards already in place in professional organizations and based on and integrated with existing regulations such as the Clinical Laboratory Improvement Amendment (CLIA)."

CDC-Coordinated Information System on Genetic Tests

CDC will develop a voluntary, integrated system for collection and dissemination of information on genetic tests. This will involve interagency coordination and collaboration in the development of standard templates for collection of data from the research phase through the premarket phase and into the postmarket phase. Using the templates proposed by SACGT as a point of departure, CDC, in conjunction with other agencies, will refine these templates to capture data on analytical validity, clinical validity and clinical utility. CDC's efforts would result in development of model data templates, the creation of a pilot database(s) to store the information for subsequent analysis, and dissemination and the establishment of an information system that would be publicly accessible.

Concurrent with efforts to refine the data templates, CDC, working through public-private partnerships and interagency work groups, will develop procedures for collecting, analyzing, and disseminating information on the analytical and clinical validity as well as the clinical utility of a broad range of genetic tests. In addition, as various genetic testing programs and initiatives are implemented by either government agencies or private organizations, CDC would develop methods to monitor the status, quality and impact of such genetic testing efforts and, where possible, capture relevant data that could be added to the database. This activity is already underway as a CDC pilot program, the Genetic Assessment Program (GAP). CDC would expand GAP's data gathering activities, coordinate development of integrated data systems with other agencies, and provide data analysis and dissemination of information on genetic tests.

Collectively, the activities described above will provide a regulatory framework that will go measurably further to enhance the oversight of genetic tests and genetic testing in the United States. Given the breadth and complexity of these activities, HCFA, FDA and CDC will be implementing them on an incremental basis, moving steadily forward as resources will allow. In the interest of reaching their respective goals in an efficient manner, all three agencies intend to implement their activities concurrently so that maximum progress can be achieved in approximately the same timeframe.

SACGT has offered a number of other recommendations that are not addressed here. The Department will communicate its response to SACGT at a later date.

In keeping with its mission to improve public health, HHS remains committed to safeguard the public from flawed or inappropriately applied genetic tests while encouraging continued development of genetic tests and their assimilation into health care practice.

Sincerely,

Donna E. Shalala