DEPARTMENT OF HEALTH & HUMAN SERVICES
Centers for Medicare & Medicaid Services
7500 Security Boulevard, Mail Stop S2-26-12
Baltimore, Maryland 21244-1850

**Center for Medicaid and State Operations**

AUG 15 2007

Kathy Hudson, Ph.D.
Director
Genetics and Public Policy Center
1717 Massachusetts Ave., NW, Suite 530
Washington, DC 20036

Dear Dr. Hudson:

Thank you for your letter petitioning the Centers for Medicare & Medicaid Services (CMS) to create a "genetic testing specialty" under the Clinical Laboratory Improvement Amendments of 1988 (CLIA). You also suggested the adoption of standards for proficiency testing (PT) for genetic tests.

The CMS and the Genetics and Public Policy Center (the Center) share a common interest in ensuring that laboratories perform accurate and reliable laboratory testing. We appreciate your consistent advocacy for the proper oversight of the field of genetics.

We have carefully considered your petition. We have concluded that the arguments and supportive evidence do not justify rulemaking to establish a new genetics specialty under CLIA at this time. We will continue to vigorously apply existing quality control and other CLIA requirements to genetic testing and monitor further developments in the field of genetics. We hope to continue working with you and others to identify the most appropriate methods of responding to emerging issues in this dynamic field.

In conducting rulemaking, agencies are required to conduct a number of analyses under various statutes and Executive Orders (EOs). For example, EO 12866 limits agency rulemaking to instances in which regulations "are required by law, are necessary to interpret the law, or are made necessary by compelling public need."[1] Furthermore, in deciding "whether and how to regulate," EO 12866 requires agencies to assess all "costs and benefits of available regulatory alternatives, including the alternative of not regulating."[2] Agencies are obligated to select from available alternatives "those approaches that maximize net benefits."[3] In the end, each agency must "adopt a regulation only upon a reasoned determination that the benefits of the intended regulation justify its costs,"[4] and then "tailor its regulations to impose the least burden on society...consistent with obtaining the regulatory objectives... ."[5]

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[1] Exec. Order No. 12866, § 1(a), 58 Fed. Reg. 51,735 (Sept. 30, 1993).
[2] *Id.*
[3] *Id.*
[4] Exec. Order 12866, § 1(b)(6)
[5] Exec. Order 12866, § 1(b)(11)

Upon careful review of the petition's facts and reasoning, we find that it does not establish an adequate basis to support the agency conducting rulemaking to create a new genetics specialty. At this time, the agency finds that a cost benefit analysis of additional rulemaking compared to the continued application of current regulations, including current regulations for quality control which apply to moderate and highly complex testing that characterizes almost all genetic tests, favors continued application of the current regulations.

**CLIA Specialties and the Key Issues in Genetic Testing**

First, the petition does not establish that creation of a genetic testing specialty would significantly advance resolution of the key issues in genetic testing. For example, the petition identifies proficiency testing as a key element in determining a laboratory's competence,[6] but fails to establish that the absence of a genetics specialty is a principal or even central reason that few proficiency tests in genetics currently exist. Today only about 16 proficiency tests are available for well over 1,000 different genetic tests. The petition's assertions and supporting arguments fail to counter our conclusion that the primary barriers to the availability of such proficiency tests are related to technological and financial issues, as well as the fast pace of innovation and the high degree of specialization involved in the various genetic tests. The petition fails to provide persuasive evidence that would support a conclusion that the creation of a genetic testing specialty, or the specification of standards that such proficiency tests must meet, would substantially contribute to many more proficiency tests being created.

The petition asserts that the private sector might be more likely to invest in and create new proficiency tests and test programs if there were a prospect that all laboratories might quickly be required to utilize the proficiency test under the aegis of proficiency testing requirements under a genetic testing specialty. However, this rationale is not supported by evidence in the petition and is contravened by the industry's recent experience in cytogynecological proficiency testing, which is discussed below.

Further, to be persuasive, the petition would need to support the contention that the creation of a genetics specialty would spur the development of genetic proficiency tests, and that such tests would be available in sufficient quantity, and for a sufficiently broad range of genetic tests, so as to allow for the establishment of nationwide genetics proficiency testing programs. Such supporting evidence would be necessary to conclude that the proposed genetic testing specialty might stimulate test development in such a manner as to create reasonable assurance of widespread availability throughout the great diversity of genetic testing.

Since public funding does not directly pay for the costs of proficiency testing, the expense of developing and administering a proficiency test must be recouped by charges levied upon laboratories that undergo the testing. The fact that there are so many different genetic tests covering a great diversity of techniques and skill sets (ranging from molecular genetic tests to biochemical tests to cytogenetic tests) means that there is a limited number of laboratories that would be in the market for any one particular proficiency test. Given the high costs of proficiency testing development and the limited market for most types of genetic tests, it would

[6] Petition for Rulemaking, Genetics and Public Policy Center, September 26, 2006, p. 4

likely be difficult for testing entities to recoup those costs. This limitation on volume serves as a significant financial barrier to development of more proficiency tests. In addition, technological barriers create their own inherent limitations as prospective testing sponsors struggle to devise, field test, validate, and market new proficiency tests for diverse and complicated genetic tests.

As the development of new proficiency tests tends to be slow and painstaking, while the rate at which genetic tests are developed continues to expand, there will continue to be a very significant disparity between the availability of proficiency tests and the number of genetic tests being used. Therefore, other means of ensuring quality will, in all probability, continue to govern the preponderance of genetic testing. We therefore anticipate that we will continue to rely upon quality requirements that are already in the current regulations, as discussed later in this letter.

The above observations are based not on conjecture, but on our experience with proficiency testing, particularly recent experience in proficiency testing for cytogynecological examinations. As the petition points out, laboratory errors in Pap smear examinations was one of the principal imperatives behind passage of CLIA. Proficiency testing for such examinations was specified in the original CLIA legislation in 1988, and a cytology specialty has long existed in regulations. That specialty designation obliged laboratories to undertake proficiency testing when available. However, for five years after passage of the law, CMS could not mandate this proficiency testing due to the lack of a program with sufficient materials to provide widespread test availability. In 1994, sufficient materials were available in the State of Maryland when a State law and statewide program took effect. Despite strenuous efforts by CMS and the Centers for Disease Control and Prevention (CDC), no nationwide cytogynecological proficiency testing became available until 2005, almost 17 years after passage of CLIA. Only then was CMS in a position to require that all applicable laboratories undergo the proficiency testing. In short, the fact that there had long been a cytology specialty, and a mandate to undergo proficiency testing when available, did not make proficiency testing a reality. For many years, the prospect that proficiency testing would eventually be mandatory was not sufficient to stimulate development of a nationwide proficiency testing program. And this was just for one type of testing, not 1,000+ different tests.

Instead of focusing on a new regulation and the prospect of proficiency tests that are generally unavailable at this time, we believe a more cost-effective and efficient approach is to foster partnerships among the professional and public organizations that can advance the overall goal of quality control, as well as collaborate on development of new proficiency tests. To this end, CMS has been actively working with the Clinical Laboratory Standards Institute (CLSI) and others on a variety of projects designed to increase quality in laboratories subject to CLIA. These professional, consensus standards could be incorporated, where appropriate, into CMS' Surveyor Interpretive Guidelines as examples of how laboratories might facilitate effective quality practices.

Development of genetic test proficiency testing can also be facilitated through the collaboration of the three Federal agencies responsible for CLIA, i.e., the FDA, CDC, and CMS, as well as partnerships with professional associations. This collaboration is an element of our Action Plan (enclosed with this letter), and we invite your suggestions as to the manner in which we may facilitate advancements in the field.

For example, CDC has been conducting activities to promote the quality and appropriate use of genetic testing in clinical and public health practice, including improving the availability of reference materials that may be used for quality control, proficiency testing, and method validation for genetic testing. In 2000-2002, CDC competitively funded two projects to develop positive samples needed by both testing laboratories and proficiency testing or external quality assessment programs for quality assurance and performance evaluation activities. In 2003-2004, CDC organized three working meetings to develop recommendations for establishing a sustainable process to make quality control/proficiency testing materials available to the genetic testing community. Based on the recommendations, CDC, in partnership with the genetics community, established the Genetic Testing Quality Control Materials (GTQC) Program, which has recently been renamed the Genetic Testing Reference Materials (GeT-RM) Program. The GeT-RM Program coordinates a self-sustaining community process to improve the availability of appropriate materials with confirmed mutations for purposes such as quality control, proficiency testing, test development, method validation, and research. Since 2005, this program has coordinated community efforts to enrich public availability of reference materials for genetic testing of a number of conditions, including Fragile X syndrome, cystic fibrosis, the Ashkenazi Jewish disease panel, Huntington disease, and other disorders. The program also facilitates and coordinates information exchange between users and providers of quality control/proficiency testing materials for genetic testing, and coordinates efforts for material contribution, development, verification, and distribution. Further information on this program and its ongoing activities is available at http://www.phppo.cdc.gov/dls/genetics/qcmaterials/default.aspx.

Additional CDC efforts to improve the performance and application of genetic tests include:

- The CDC Newborn Screening Quality Assurance Program, which provides comprehensive quality assurance and proficiency testing challenges for laboratories performing newborn screening testing. Currently, participants include 73 domestic laboratories and one or more laboratories in 53 other nations (http://www.cdc.gov/nceh/dls/newborn_screening.htm).

- Assuring appropriate understanding and use of genetic test results in clinical and public health practice. CDC has facilitated partnerships of professional organizations, government agencies, clinical and public health care providers, laboratory professionals, payers, information specialists, educators, and policy makers, to develop a standard framework for reporting genetic test results to achieve clinical and public health benefits (http://www.phppo.cdc.gov/dls/genetics/comm052003.aspx).

- A collaborative effort of federal agencies, professional societies, advocacy organizations, academic institutes, industry, and other stakeholders, to improve the availability, accessibility, and quality of genetic testing for rare diseases (http://www.phppo.cdc.gov/dls/genetics/RareDiseaseConf.aspx). This effort led to, and has been providing input to, the Collaboration, Education and Test Translation (CETT) Program, which is funded by the Office of Rare Diseases of the National Institutes of Health to promote the translation of rare disease genetic tests from research phase to patient care (http://www.cettprogram.org).

- The Evaluation of Genomic Applications in Practice and Preventions (EGAPP) model project, which was established in 2004 to develop and evaluate a coordinated, systematic process for assessing genomic applications in transition from research to clinical and public health practice. Currently, this project is conducting evidence reviews under collaboration or contract for the following genetic tests: hereditary nonpolyposis colorectal cancer screening, genomics tests for ovarian cancer detection and management, testing of cytochrome p450 polymorphisms in adults with depression, and UGT1A1 testing in colorectal cancer patients treated with irinotecan (http://www.cdc.gov/genomics/gTesting.htm).

- Recently CDC initiated the process and acquired approval to publish an issue of their prestigious Morbidity and Mortality Weekly Report that will contain educational information for genetic testing laboratories to facilitate quality testing.

**Specialties are not required in CLIA**

The CLIA statute requires the promulgation of standards "to assure the consistent performance by laboratories issued a certificate under this section of valid and reliable laboratory examinations and other laboratory procedures." (42 U.S.C. 263a(f)(1)). In developing these standards the Secretary is required to take into account:

- The examination and procedures and the methods employed,
- The degree of independent judgment involved,
- The amount of interpretation involved, the difficulty of calculations involved, the calibration and quality control requirements of the instruments used, the type of training required to operate the instruments used in the methodology, and
- Such other factors as the Secretary considers relevant.

In taking the considerations of 42 U.S.C. 2361(f)(2) into account, the Secretary established a regulatory scheme based on three categories of tests: waived or "simple" tests, moderate complexity tests, and high complexity tests.

Under the CMS-promulgated regulations, some moderate and high complexity tests are subject to additional "specialty" quality and PT requirements. However, neither the statute nor the CLIA regulations affirmatively require that all moderate and high complexity tests fall within a specialty area. The petition fails to establish that all genetic tests must belong in such a genetic specialty area. If the CLIA statute did require these specialties, the CLIA provision providing for laboratories performing non-specialty area tests having to "establish and maintain the accuracy of [their] testing procedures" and to "verify the accuracy of [their] test results at least twice a year" would be superfluous. (See 42 CFR 493.801 (a)(2)(ii)). A basic cannon of statutory and regulatory construction is that one should not read the text in a manner that renders portions of it superfluous. This leads to the discussion of current requirements, explained below.

Further, in 2003 CMS promulgated final regulatory amendments that reduced the number of specialties under CLIA in order to reduce complexity, standardize the requirements and reflect current technologies that may overlap specialties. Through the same regulatory amendments,

CMS *increased the quality control requirements* that would apply to all laboratories conducting moderate or high complexity testing, so that the existence of a specialty area would be less of a factor.

**Current Requirements and Alternatives to Creation of a Genetic Testing Specialty**

Laboratories that conduct genetic tests of moderate or high complexity are already subject to CLIA requirements to the extent that they test human specimens for health care purposes. This includes quality control, personnel qualifications and responsibilities, recordkeeping, quality assurance, and PT requirements. The 1992 regulations already covered genetic tests, were further enhanced in 2003 for all laboratories, and include quality control requirements.

The petition does not establish that the creation of a genetic testing specialty through new regulation would be superior to effective application of existing regulations.

Under existing regulations, all laboratories performing genetic testing of moderate or high complexity must maintain the accuracy of their testing procedures, and at least twice annually must verify the accuracy of any genetic test or procedure they perform. (*See* 42 CFR § 493.801(a) (2) (ii) and 42 CFR 493.1236 (c)(1)). CLIA does not prescribe the approaches laboratories must use to evaluate the performance of their genetic tests; however laboratories performing genetic testing must have in place and must follow performance evaluation procedures that are adequate to meet §493.1236(c) and other applicable requirements. Current approaches used by laboratories include:

- Analyzing split patient or control samples with another laboratory instrument or method.
- Incorporating known value samples as unknowns in the test procedures.
- Participating in available proficiency testing or equivalent quality assurance programs. where available. Data from the College of American Pathologists (CAP) genetic survey programs, state programs, and published studies (McGovern et al, 1999, McGovern et al, 2003, Dequeker et al, 2003) indicate that many laboratories performing genetic testing have been participating in available proficiency testing or equivalent quality assurance programs, as a means to meet the CLIA performance evaluation requirement or laboratory accreditation requirements.
- Reciprocal testing; and
- Developing alternative approaches in adherence to professional practice guidelines and good laboratory practices, especially in circumstances when formal proficiency testing or equivalent quality assurance programs are not available.

The CMS intends to continue to ensure that laboratories fulfill their regulatory obligations to meet the requirements of §493.1236(c).

Each laboratory that performs nonwaived testing must also meet the applicable requirements under subpart J-Facility Administration, 42 CFR §§ 493.1101 through 493.1105. Those sections of the regulation address facility design, requirements for transfusion services, equipment, record preservation and retention requirements, and adherence to State and local laws. In particular, § 493.1101(a) (3) requires the laboratory to be constructed, arranged, and maintained to ensure that molecular amplification procedures that are not contained in closed systems have a

unidirectional workflow. Note that these were several of the recommendations made by advisory committees that were either of general applicability (enhanced confidentiality) or that addressed identified problems (e.g., use of a uni-directional workflow to eliminate contaminated specimens) that were incorporated into the 2003 regulations.

CLIA also imposes requirements for personnel qualifications and quality testing responsibility for certain required positions in laboratories performing moderate complexity testing (42 CFR §§ 493.1403 through 493.1425) and for laboratories performing high complexity testing (42 CFR §§ 493.1441 through 493.1495) with the laboratory director having the overall responsibility for ensuring test accuracy and reliability. The vast majority of genetic tests are categorized as high complexity at this time, including all genetic tests that are laboratory-developed. The testing personnel that perform such tests must meet the more stringent, high complexity CLIA personnel requirements and laboratories must retain the additional required position of a general supervisor, who is responsible for day-to-day operations. These requirements apply regardless of whether the personnel conducting the testing are in a specialty area or not.

The historical overview provided in Attachment I contains recommendations from several Secretarial advisory committees to "augment CLIA with a genetic specialty". However, after thorough review and evaluation, we find that the documents and reports lack sufficient evidence to support the advancement of newly detailed, prescriptive regulations for genetic tests or to establish the superiority of a new regulation over the existing regulation. That is, there is no data or other information to indicate that a new regulation creating a genetic testing specialty would be of greater benefit than relying on current regulations. Instead, CMS will provide technical training and ongoing communication to its State surveyors to promote testing accuracy, collaborate with its sister federal agencies and professional organizations to educate laboratories, and expand its Website to provide laboratory quality information. See Attachment II for CMS' Action Plan.

**Costs versus Benefits**

The petition fails to adequately consider the costs of promulgating a new regulation creating a genetic testing specialty, and fails to weigh these costs against the benefits, or to compare those costs and benefits to reliance on the existing regulations.

A generally accepted definition of a genetic test has not been established. This limitation confounds the development of specific requirements for "genetic tests", and increases the chance of unintended consequences and unforeseen costs. In fact, the Secretary's Advisory Committee on Genetic Testing (SACGT) admitted in a 2001 report[7] that categorizing genetic tests was "exceedingly complex" and provided no obvious basis upon which to build a regulatory infrastructure.

[7] Secretary's Advisory Committee on Genetic Testing, September 2001 report, Development of a Classification Methodology for Genetic Tests: "Conclusions and Recommendations of the Secretary's Advisory Committee on Genetic Testing." "After consideration of the public comments and additional discussion, the Committee concluded that fundamental, irresolvable questions had been raised about the feasibility of categorizing tests for oversight purpose based on limited set of elements in a simple, linear fashion. Thus, the Committee decided that further efforts to develop a classification methodology for genetic tests should be curtailed for the present."

Various tests that we would all regard as "genetic tests" are in actuality dispersed throughout different operational sections of the laboratory and many are found in different existing CLIA specialties. Creation of a new genetic testing specialty would require not only greater precision in the current definitions, but would also require a teasing out of certain tests from some existing specialties, and cause some disruption to existing regulatory and payment structures.

The fact that over 1,000 genetic tests have been developed in a relatively short period of time suggests that the current CLIA regulatory structure is not an impediment to progress in this very dynamic field. We are concerned that regulatory creation of a genetic testing specialty (with detailed genetic testing controls) would become quickly outdated during the multi-year promulgation process under the Federal Administrative Procedures Act. Outdated regulations would then hinder laboratories' abilities to be creative and take advantage of new technologies.

Finally, there are opportunity costs involved in promulgating a new regulation. The promulgation process invariably takes time, resources, and attention away from effective enforcement of current regulations. We have witnessed some laboratories that have sought to escape detection and avoid CLIA quality controls, and have redoubled reconnaissance in collaboration with the FDA and CDC to ensure that such laboratories are identified and monitored. We have also ensured that enforcement action is taken when we find that a laboratory is improperly contending that CLIA regulations do not apply. We have implemented an Action Plan (see Attachment II) to strengthen application of current regulations. These efforts would inevitably be circumscribed by promulgation of a new regulation that offers uncertain benefits and contains other disadvantages.

Opportunity costs also apply to other parties that would be involved in the promulgation of a new regulation, redirecting resources from key issues, such as the dangers of direct marketing to consumers, the veracity of advertising, privacy protections for individuals (for whom genetics testing is performed), or the utility of genetics tests themselves, which all merit attention. Most of these tests are not currently approved or cleared by the FDA and therefore, not necessarily reviewed for clinical validity, making them more vulnerable to inaccuracies in laboratories that do not incorporate appropriate quality control procedures to ensure the accuracy and reliability of their testing.

**Conclusion**

At this time, we do not intend to advance a genetic testing regulation because it has not been established that creation of a genetic testing specialty or specific proficiency testing standards for genetic tests under CLIA would address the key issues in genetic testing, nor would it address the ethical, legal, and social issues that are not soluble through the authority of CLIA. In addition, the petition does not establish an adequate basis to support creation of a new genetics specialty compared to continued application of current regulations.

In view of our obligation to maximize net benefits to the public, and to weigh all alternatives, we conclude that we can more effectively oversee genetic testing under existing regulations and infrastructure. We believe that our Action Plan for enhancing the oversight of genetic testing will yield equivalent or superior benefits than rulemaking to create a genetic testing specialty, and will do so faster and without disruption to the existing CLIA specialties and infrastructure.

We look forward to continuing to work with you and the many other professionals and citizens who are working hard to advance accurate, reliable, and useful genetic testing. I will also provide this response to each of the petitioners.

Sincerely,

Dennis G. Smith
Director

Enclosures

**The Centers for Medicare & Medicaid Services' Historic Timeline for Oversight of Genetic Testing**

- **October 1988,** Section 353 of the Public Health Service Act (42 U.S.C. 263a) was amended by Congress with enactment of the Clinical Laboratory Improvement Amendments of 1988 (CLIA) on October 31, 1988. The Act established minimum quality standards for all laboratory testing to ensure the accuracy, reliability, and timeliness of patient test results regardless of where the test was performed.

- **February 1992**, CMS (then the Health Care Financing Administration (HCFA)) published final CLIA regulations.

- **September 1997**, The National Institutes of Health (NIH)/Department of Energy (DOE) Task Force report recommended that CLIA regulations be augmented to strengthen clinical laboratory practices for genetic tests by requiring specific provisions for quality control, personnel qualifications and responsibilities.

- **September 1997,** The Clinical Laboratory Improvement Advisory Committee (CLIAC) convened to determine the adequacy of existing CLIA requirements and the need of a genetic testing specialty. The CLIAC also recommended that the Centers for Disease Control and Prevention (CDC) and CMS (then HCFA) collaborate to define CLIA applicability and coverage of genetic testing. The CLIAC presented the following issues as possible topics for discussion at future CLIAC Subcommittee meetings:

  - Approaches to proficiency testing
  - Possible changes in patient test management
  - Appropriate quality control requirements
  - Determination of personnel qualifications
  - Quality assurance as applied to genetics
  - Finding, registering, and educating genetic testing laboratories that had not previously been regulated under CLIA.

- **January 1998,** The CLIAC convened a Genetic Testing Workgroup. After first developing a working definition for genetic testing, the workgroup went on to develop recommendations that encompassed both general issues such as informed consent, confidentiality, and personnel requirements, as well as specific technical issues for each phase of laboratory testing.

- **May 1998,** The Genetic Testing Workgroup convened to discuss whether the CLIA regulations were appropriate for preanalytic, analytic, and postanalytic phases of genetic testing, or if revisions to the requirements were needed to address genetic testing.

- **June 1998**, The Secretary of Health and Human Services (**HHS**), Donna Shalala, chartered the Secretary's Advisory Committee on Genetic Testing (SACGT) in response to recommendations of two working groups commissioned jointly by the NIH and the DOE for the Human Genome Project. These groups identified the need for broad-based public policy development to help the Nation address the benefits and challenges of genetic knowledge and genetic testing.

**The CMS' Historic Timeline for Oversight of Genetic Testing**

- **September 1998,** The CLIAC made recommendations on all of the issues addressed by the full Workgroup for each phase of genetic testing. The CLIAC also reviewed the working definition of a genetic test, and proposed that it be separated into "molecular genetic and cytogenetic tests" and "biochemical genetic tests." The CLIAC recommendations can be found on the CDC website at http://www.phppo.cdc.gov/dls/cliac/default.asp.

- **June 1999,** Dr. David Satcher, Assistant Secretary for Health and Surgeon General, asked SACGT to assess, in consultation with the public, the adequacy of oversight of genetic tests and, if warranted based on a consideration of the public comments and an analysis of the issues, to recommend options for additional oversight and to ensure public access to quality genetic tests. Subsequently, SACGT drafted a document, *A Public Consultation on Oversight of Genetic Tests*, and solicited public comments. **October 1999,** The SACGT convened to discuss oversight issues and finalize plans for consulting with the public on oversight issues. The SACGT identified several options for oversight of analytical validity and clinical validity application of genetic tests. These included strengthening CLIA regulations.

- **January 2000,** The SACGT held a public meeting to gather perspectives on issues related to the adequacy of oversight of genetic testing.

- **February 2000,** The SACGT met to review the public input received and to develop conclusions and recommendations on the adequacy of oversight of genetic testing. The meeting identified key recommendations and recommended that CLIA be augmented to provide more specific provisions for ensuring the quality of laboratories conducting genetic testing.

- **May 2000,** CDC published a Notice of Intent (NOI), *Genetic Testing Under the Clinical Laboratory Improvement Amendments*, as a recommendation of the CLIAC with the support of the SACGT. The NOI advised the public that HHS would be preparing a proposed rule to establish a genetic testing specialty in CLIA and solicited public comments. The NOI also informed the public of specific requirements for informed consent, confidentiality, quality assurance, genetic counseling, laboratory personnel, and record keeping.

- **June 2000,** The SACGT met to review public comments and finalize conclusions and recommendations on oversight of genetic tests.

- **July 2000,** The SACGT issued a report, *Enhancing the Oversight of Genetic Tests, Recommendations of the SACGT* (available at: http://www4.od.nih.gov/oba/sacgt.htm). The report stated that:

    - Criteria were needed to assess the benefits and risks of genetic tests.
    - Benefit/risk criteria should be used to categorize tests.
    - A mechanism was needed to assign genetic tests to categories.
    - Processes were needed to collect, evaluate and disseminate data on tests and groups of tests in each category.
    - Options were needed for the oversight of genetic tests, and
    - Appropriate levels of oversight were needed for each category of genetic test.

## CMS' Historic Timeline for Oversight of Genetic Testing

- **August 2000,** The SACGT convened to discuss the report, *Enhancing the Oversight of Genetic Tests*, review a test classification methodology developed by SACGT working group, plan a course of action for future projects, and establish workgroups to explore five broad high-priority areas: informed consent and Institutional Review Board (IRB); data elements and data collections; rare disease testing; access to genetic tests and services; and genetics education of health professionals and the public.

- **September 2000,** The CDC compiled the NOI comments and provided a summary report at the CLIAC meeting on September 28, 2000. After considering the analysis of the public comments, the CLIAC felt that additional consultation was needed and formed a second Genetics Workgroup to evaluate the NOI comments and provide input to assist the Committee in making further recommendations on genetic testing.

- **November 2000,** The SACGT convened and identified seven key data elements for genetic testing. The seven elements relate to the purpose of the test, clinical condition for which the test is performed, definition of a test, a test's analytical validity, clinical validity, and clinical utility, and the cost of the test.

- **December 2000,** The Genetics Workgroup met to analyze the NOI comments and suggested modifications to the initial CLIAC recommendations to address establishing a genetic testing specialty under CLIA.

- **January 2001,** Based on the conclusions from the July 2000 SACGT report, *Enhancing the Oversight of Genetic Tests*, HHS Secretary Donna Shalala recommended that the CLIA regulations be augmented to provide more specific provisions for ensuring the quality of laboratories conducting genetic tests.

- **February 2001,** A report of the recommendations by the second Genetics Workgroup was presented to the full CLIAC. The CLIAC reviewed each recommendation of the Workgroup and supported the additional modifications. The SACGHT recommended that HHS proceed with development of a proposed rule including the revised CLIAC recommendations for genetic testing under CLIA. The revised recommendations were for definitions and subspecialties of genetic tests, clinical validity, authorized persons to order genetic tests, confidentiality, informed consent, re-use of tested specimens, and requirements for specific testing phases.

- **September 2001,** The SACGT issued a subsequent report, *Conclusions and Recommendations of the Secretary's Advisory Committee on Genetic Testing* (available at: http://www4.od.nih.gov/oba/sacgt.htm). The SACGT acknowledged that it was exceedingly complicated to develop a meaningful classification methodology for genetic tests. It noted that there was no "simple logical breakdown" for categorizing such tests, and thus no obvious basis upon which to build a regulatory structure of appropriate requirements for the varied tests that fall under the rubric of "genetic testing."

- **May 2001 through May 2002,** The SACGT continued to meet.

**The CMS' Historic Timeline for Oversight of Genetic Testing**

- **September 2002,** The SACGT was replaced by a successor organization, the Secretary's Advisory Committee for Genetics Health and Society (SACGHS) to assist HHS in addressing complex medical, ethical, social, and legal issues associated with new technological development in human genetics.

- **January 2003,** The CMS published a final rule, *Medicare, Medicaid, and CLIA Programs; Laboratory Requirements Relating to Quality Systems and Certain Personnel Qualifications,* implementing nonwaived testing regulations that included several of the CLIAC's recommendations on genetic testing and augmented quality control requirements for all testing.

**The Centers for Medicare & Medicaid Services' Action Plan for Oversight of Genetic Testing**

The Centers for Medicare & Medicaid Services' (CMS) action plan for oversight of genetic testing under the current CLIA regulations is focused on:

- The effective, targeted application of current regulations and authority;
- Working with other federal agencies (e.g., the Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA), the National Institutes of Health (NIH)) and professional associations to promote a comprehensive approach to genetic testing that includes more availability of proficiency testing (PT); and
- Enhancing the expertise of surveyors and CMS in the area of genetic testing to better serve the community, and providing specific survey guidance to surveyors to assess compliance for these tests.

Example elements of the plan include the following:

- **Better Protections for All Testing**

  - ***2003 Regulation:*** A final rule was issued by CMS in 2003 to strengthen the quality control requirements for all laboratories performing non-waived testing. The rule included some of the genetic testing recommendations made by the Secretary's Clinical Laboratory Improvement Advisory Committee (CLIAC).

  - ***Proficiency Testing for Genetic Tests:*** CMS will work with the CDC, FDA, and the professional associations to promote the development of additional proficiency tests or alternative mechanisms for PT. Very few proficiency tests currently exist for the more than 1,000 genetic tests due to a paucity of appropriate specimens and to market concerns of PT providers.

  - ***Analytical Test Validation of Genetic Tests:*** CMS will seek assistance from CDC and the FDA for evaluation of analytical test validation of laboratory-developed tests.

- **Better Information and Knowledge**

  - ***Guidelines:*** CMS will work with professional associations, such as the Clinical Laboratory Standards Institute (CLSI), to promote the development of consensus guidelines on molecular and other genetic testing.

  - ***Coordination Among Federal Agencies:*** CMS will collaborate with CDC, FDA, the Federal Trade Commission (FTC) and NIH to ensure effective oversight of genetic tests, expansion of our coordinated efforts toward future improvements, and continuation of the regular conference calls these agencies already hold to facilitate that goal. CMS may also enlist the expertise of the CLIAC to weigh in on these issues.

**CMS' Action Plan for Oversight of Genetic Testing**

- ***Information for Surveyors:*** CMS will issue an informational alert for State Agencies (SAs) and CMS regional offices to heighten the awareness of genetic testing and clarify that genetic testing laboratories are subject to CLIA when tests are used to diagnose, prevent, assess or treat human illnesses and conditions. CMS will also seek to raise awareness in the research laboratory community of the need for laboratories to enroll in CLIA when genetic tests are used in patient care.

- ***Training for Surveyors:*** CMS will explore the development of a specific survey protocol to assess compliance in genetic laboratories where unique technologies and methodologies are utilized. We will also provide surveyors with technical training on current technologies and the quality aspects of genetic testing by subject matter experts from the field.

- ***CLIA Website Enhancement:*** CMS will coordinate with CDC to provide helpful educational genetic testing guidance and updates on its website for surveyors and laboratories.

- **Better Monitoring and Enforcement**

  - ***Application of Existing Regulations:*** CMS will seek guidance from the CMS-approved accreditation organizations (AOs) that already have specific molecular diagnostic standards. CMS will also work with SAs, AOs, and other federal partners to promote the effective application of existing regulations to ensure that genetic testing is accurate and reliable, and will explore additional mechanisms to oversee these tests. When CMS becomes aware of a non-CLIA certified laboratory that is using the Internet to market, or is performing genetic testing for use in patient care, we will take swift action to address the CLIA deficiencies.

  - ***Effective Communications:*** CMS will work with other federal agencies, SAs, and AOs to accelerate the sharing of information about new developments in genetic testing, the existence of laboratories that have failed to register for CLIA, and enforcement actions.