Subcommittee Meeting on Genetics

September 10, 1997

Summary

Table of Contents

Record of Attendance

Committee Members

Dr. Patricia Charache
Dr. Jaime Frias
Dr. Susanne Gollin
Dr. Paul Ing
Dr. Kenneth Pass
Dr. Morton Schwartz
Dr. Lawrence Silverman
Ms. Stephanie Smith

Ex Officio Members

Dr. Carlyn Collins, CDC
Dr. Joseph Hackett, FDA
Ms. Judith Yost, HCFA

Executive Secretary

Dr. Edward Baker

Centers for Disease Control and Prevention

Dr. Rex Astles
Ms. Carol Bigelow
Dr. Joe Boone
Ms. Gail Bosley
Ms. Diane Bosse
Ms. Cheryl Coble
Ms. Deborah Coker
Ms. MariBeth Gagnon
Ms. Sharon Granade
Dr. Thomas Hearn
Dr. Ed Holmes
Ms. Stacy Howard
Dr. Richard Keenlyside
Dr. John Krolak
Dr. Harvey Lipman
Mr. Kevin Malone
Dr. Adam Manasterski
Dr. Toby Merlin
Ms. Anne O'Connor
Ms. Doris Pattillo
Dr. John Ridderhof
Mr. Darshan Singh
Ms. Elva Smith
Mr. Gregory Smothers
Dr. Roger Taylor
Ms. Glennis Westbrook
Ms. Rhonda Whalen
Ms. Laurina Williams

Welcome and Introductory Information

The meeting was called to order by Genetics Subcommittee Chairman Dr. Wendell O'Neal. Mr. Kevin Malone, CDC's Office of the General Counsel, explained that the Genetics Subcommittee will provide technical advice to the Clinical Laboratory Improvement Advisory Committee (CLIAC), which will then advise the CDC. In addition, Mr. Malone discussed conflicts of interest as related to an individual's participation in the Genetics Subcommittee (See Addendum C-1). Members then made self-introductions and disclosure statements as they relate to the topics to be discussed during the Genetics Subcommittee meeting.

Genetics and Public Health

Dr. Richard J. Jackson, Director of the National Center for Environmental Health, CDC, presented the following concerns in the area of genetic testing:

(1) Science may outstrip public health policy in this arena and policy decisions made as a "knee jerk" reaction may impede access to medical care;
(2) Policy decisions may be made by individuals with narrow fiscal interests; a participatory process with input from all interested parties results in better policy decisions;
(3) Actions by certain groups may exceed reasonable interventions and cause emotional reactions in the scientific and public policy communities; and
(4) Patients and practitioners will be faced with information overload in this area.

Dr. Jackson noted that embedded in the concerns are opportunities for disease prevention, professional development in genetic testing, and forging new partnerships in the public health and laboratory communities.

Subcommittee Discussion:

Subcommittee members raised concerns about the definition of genetic testing, the need for training in genetic testing, public health involvement in policy making, and the proprietary nature of knowledge gained from genetic testing, i.e. patenting of genes.

Charge to the Subcommittee:

Dr. Edward L. Baker, Director of the Public Health Practice Program Office at CDC, explained that CDC had selected Subcommittee members with technical and policy expertise who could advise CLIAC on the challenging issues related to genetic testing. The Subcommittee would

receive feedback on how advice from the Subcommittee is used. Dr. Baker then presented the following charge to the Genetics Subcommittee:

(1) Provide recommendations to the full CLIAC on genetic testing;
(2) Provide technical advice to the full CLIAC on the minimum standards for quality of genetic testing;
(3) Define genetic testing; and
(4) Determine the scope of CLIA with respect to genetic testing (it was noted that CDC will work with the Healthcare Financing Administration [HCFA] to define CLIA applicability and coverage of genetic testing).

Subcommittee Discussion:

One Subcommittee member asked if genetic screening tests are covered under CLIA. Dr. Baker responded that screening tests used in a medical/health context fall under CLIA.

Overview of CLIA: How Should Genetic Testing Be Handled Under CLIA?

Dr. Carlyn Collins briefly reviewed the history of CLIA (See Addendum C-2), noting that CLIAC was chartered in 1992 and that Drs. Wendell O'Neal and Morton Schwartz were members of the original Committee. She discussed the purpose of CLIAC, the responsibilities of the federal agencies (HCFA, CDC, and the Food and Drug Administration) involved in CLIA, the key features of the CLIA law, and the guiding principles of CLIA. She emphasized that under CLIA, laboratory standards are based on the complexity of testing. Dr. Collins noted that categorization of tests as moderate complexity (65% of all tests) or high complexity (33% of all tests) and approval of waived tests (2% of all tests) are performed by CDC. About 20,000 test systems have been categorized as moderate or high complexity and 475 test systems (16 analytes) have been approved as waived tests.

Laboratories performing moderate complexity testing must meet certain requirements, while laboratories performing high complexity testing must meet more stringent requirements, especially in the area of personnel. Dr. Collins explained that laboratories which perform waived tests are exempt from CLIA, except they must pay a fee and register with HCFA, follow manufacturers' instructions for waived test performance, and waived laboratories are subject to random or complaint inspections. She noted that the CLIA requirements are minimal standards to ensure quality testing.

Dr. Collins explained that all genetic tests performed for diagnostic or health assessment purposes are subject to CLIA. Most genetic tests would be categorized as high complexity and CLIA certification is required for laboratories performing genetic tests. Uncategorized genetic tests are high complexity. Dr. Collins commented that the CLIA regulations contain general requirements applicable to genetic testing and specific requirements for cytogenetic testing.

Subcommittee Discussion:

There were many questions about the applicability of CLIA to genetic screening tests, other genetic tests, and testing performed in research laboratories. Dr. Collins explained that laboratories performing research procedures which are not linked to a specific individual are exempt from CLIA. When a laboratory reports a test result with a patient identifier to a healthcare provider, the test becomes subject to CLIA regulations. She said that this would include screening tests performed for health assessment.

One Subcommittee member commented that laboratories performing genetic testing subject to CLIA could be identified through billing procedures. According to another member, some patients pay cash for tests to ensure confidentiality. It was noted that some research laboratories don't bill for tests and may be unaware that their testing is subject to CLIA regulation. Dr. Collins emphasized that the issue is whether a laboratory is providing a service, i.e. reporting a test result for patient care to a healthcare provider, not whether the laboratory is billing for a test.

In response to concerns that laboratories performing genetic testing may not know that the testing is subject to CLIA, Dr. Baker suggested that the Genetics Subcommittee might want to consider a mechanism for providing information to the community on genetic testing. Noting that some small laboratories may not be registered under CLIA because of concerns about cost and perceived difficulty in meeting the CLIA requirements, Dr. Collins felt that if these laboratories had more information, CLIA might not seem so burdensome.

One Subcommittee member commented that certain laboratories are exempt from CLIA, and Dr. Collins confirmed that laboratories performing pure research or forensic testing and the Veteran's Administration (VA) laboratories are exempt from CLIA. She noted that VA laboratories must meet VA standards for laboratory practice. Department of Defense laboratories are not subject to CLIA but have separate laboratory standards equivalent to CLIA.

American College of Medical Genetics

Dr. Stephen I. Goodman, representing the American College of Medical Genetics, reviewed the recommendations on genetic testing made by the Task Force on Genetic Testing created by the National Institutes of Health-Department of Energy Working Group on Ethical, Legal, and Social Implications of Human Genome Research. He then presented the Task Force's definition of genetic testing and reasons why genetic testing is different from other laboratory testing (See Addendum C-3). He stressed that genetic expertise is essential in determining which tests should be done (pre-analytic phase) and interpreting the results (post-analytic phase), but said that the testing procedures (analytical phase) can be performed by most physicians/scientists trained in laboratory medicine.

Subcommittee Discussion:

Subcommittee members emphasized the importance of training medical geneticists (neurologists and pediatricians may be good candidates) and the lack of funds for training. One Subcommittee member presented definitions of three types of genetic testing: molecular genetics, molecular diagnostics, and molecular pathology (See Addendum C-4). He then asked whether the Subcommittee is to consider only molecular genetics testing (genetic disease testing) or molecular diagnostics in total. Dr. O'Neal indicated that this topic would be included in later discussions.

New York State Department of Health (NYSDOH)

Dr. Ann Willey presented an overview of the New York Clinical Laboratory Evaluation Program, which was instituted in 1964 (See Addendum C-5). She noted that New York regulates all laboratories with the exception of physician office laboratories (POLs) in the state, including those non-POLs performing forensic, insurance, and employment testing. Laboratories outside the state that perform tests on New York State (NYS) residents are also required to hold a NYS permit. NYS has been licensing cytogenetic laboratories since 1972; since 1990, permits have been issued for biochemical genetic testing and DNA-based genetic testing (germline testing). Unique features of the NYS program include:

(1) Cytogenetic laboratories are required to obtain the outcomes of all prenatal monitoring;
(2) Reports must be interpretive and written in a narrative form comprehendible to non-geneticist physicians;
(3) For oncofetal antigen, the laboratory must obtain (a) the signature of the requesting physician and the informed consent of the patient being tested, and (b) the designation of a provider to provide follow-up if the test result is abnormal;
(4) Permits are assay-specific; and
(5) Fees are based on the revenue generated by the laboratory.

Subcommittee Discussion:

One Subcommittee member thought that the NYS program should be a model for consideration by the Subcommittee. Dr. O'Neal said that the Subcommittee might or might not choose to use all or part of the NYS program as a model. He noted that some NYS requirements exceed what is usually considered to be the laboratory's responsibility.

The Subcommittee discussed the requirement for laboratories to obtain statements of informed consent for oncofetal antigen testing.

Why is Genetic Testing Different?

Dr. Pat Murphy, who has directed a genetic laboratory, presented her reasons why genetic testing is different from other laboratory testing (See Addendum C-6). She felt strongly that the Genetics

Subcommittee should not use the New York State program as a model. Emphasizing that the content of her presentation represented her personal opinions, she suggested that the BIO Group (a biotech/pharmaceutical lobbying group representing about 10 laboratories) might present a more balanced industry viewpoint.

College of American Pathologists (CAP)

Dr. Henry Travers, representing the CAP, presented pathology community concerns that federal efforts to specifically address genetic testing could be problematic and the CAP position that genetic testing should be treated no differently than any diagnostic test performed in the clinical laboratory (See Addendum C-7). CAP does not see a need for additional CLIA regulations to address genetic testing, although minor changes in the existing regulations may be necessary. CAP feels that ensuring the quality of genetic testing would best be accomplished through existing accreditation programs such as CAP's Laboratory Accreditation Program. CAP and the American College of Medical Genetics are actively working to develop a comprehensive accreditation program addressing all aspects of quality assurance in genetic testing.

Subcommittee Discussion:

Several Subcommittee members presented reasons they consider genetic testing to be different from other laboratory testing, while others said genetic testing should be treated the same as any other laboratory test. Two Subcommittee members felt that accreditation would be preferable to expanded regulations. One member emphasized, however, that the role of the laboratory in genetic testing should go beyond the analytic phase of testing. Dr. Travers agreed that the pathologist laboratory director should be part of a clinical team in genetic testing. In general, the CLIAC members agreed that the individual who interprets the results of genetic testing should be trained specifically in medical genetics.

Summary of Genetic Testing Issues

Subcommittee Discussion:

After discussion, the members determined that the following issues should be presented to CLIAC as possible topics for discussion at future Subcommittee meetings.

1. Define genetic testing.
    a. **Appropriateness**, what tests are appropriate and under what circumstances.
    b. **Interpretation**, the extent to which regulations should address pre- and post-analytical considerations.

2. Screening vs. diagnostic vs. prognostic may need to be considered in defining genetic testing.

3. Scope of the regulations needs to be defined, with consideration given to whether specific requirements for requisitions and collection of information should be included.

4. Regulatory structure needs to accommodate new technologies; more important for genetic testing than other types of testing.

5. Review the current CLIA general requirements for application to genetic testing. Determine whether the existing requirements are adequate for genetic testing, revisions are needed, or a genetic specialty should be created. Specifically consider:
   a. Approaches to proficiency testing
   b. Possible changes in patient test management
   c. Appropriate quality control requirements
   d. Determine personnel qualifications
   e. Review quality assurance as it applies to genetics

6. Difficulty in assuring registration of laboratories performing genetic testing. Finding, registering, and educating genetic testing laboratories that have not previously been regulated under CLIA may be challenging.

7. Whether a different registration process is needed for very small laboratories/research laboratories. The transition of testing procedures from the developmental phase to the production phase should not be inhibited.

I certify that this summary report of the September 10, 1997, meeting of the Genetics Subcommittee of the Clinical Laboratory Improvement Advisory Committee is an accurate and correct representation of the meeting.

/S/ Wendell R. O'Neal, Ph.D.
Chairman