

Clinical Laboratory Improvement Advisory Committee

Genetic Testing Subcommittee

Summary Report
July 30-31, 1998



U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service



Genetic Testing Subcommittee

July 30 - 31, 1998

Summary

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Record of Attendance

Workgroup Members

Dr. Regina Benjamin
Dr. Patricia Charache
Dr. Susanne Gollin
Dr. Kathy Klinger
Dr. Toby Merlin
Dr. Wendell O'Neal
Dr. Kenneth Pass
Ms. Sharon Radford
Mr. Mark Rothstein
Dr. Morton Schwartz
Dr. Lawrence Silverman
Ms. Stephanie Smith

Ex Officio Members

Dr. Carlyn Collins, CDC
Ms. Cecelia Hinkel, HCFA (representing Ms. Judy Yost)

Executive Secretary

Dr. Edward Baker

Centers for Disease Control and Prevention

Ms. Nancy Anderson
Dr. Rex Astles
Ms. Carol Bigelow
Dr. Joe Boone
Ms. Gail Bosley
Ms. Genoria Bridgeman
Ms. Cheryl Coble
Ms. Carol Cook
Ms. Sharon Granade
Dr. Tom Hearn
Dr. Ed Holmes
Dr. Dick Keenlyside
Dr. John Krolak
Dr. John Ridderhof
Ms. Renee Ross
Mr. Darshan Singh
Mr. Gregory Smothers
Ms. Glennis Westbrook
Ms. Rhonda Whalen
Dr. Laurina Williams

Welcome and Introductory Information

The meeting was called to order by Genetic Testing Workgroup Chair Dr. Wendell O'Neal. The Workgroup members made self introductions, and Dr. O'Neal briefly reviewed the agenda and described the process for the meeting.

Overview of Progress to Date

Dr. Carlyn Collins, Director, Division of Laboratory Systems, Public Health Practice Program Office, presented an overview of the progress made by the Genetic Testing Workgroup and the Clinical Laboratory Improvement Advisory Committee (CLIAC) on issues pertaining to clinical laboratory standards for genetic testing. She explained that at the meeting on May 27 - 28, 1998, individual workgroups for the pre-analytic, analytic and post-analytic phases of genetic testing addressed issues for their respective phases. The full Workgroup then considered a number of the issues, but did not have sufficient time to complete discussion on all of the relevant topics. Dr. O'Neal presented a report to the CLIAC for consideration on May 28, that included those issues which the full Workgroup had addressed, and identified the areas which the Workgroup needed more time to discuss.

Dr. Collins noted that in considering the Workgroup report, the CLIAC made recommendations on all of the issues addressed by the full Workgroup. In addition, the CLIAC provided input on some topics which the Workgroup had not yet fully discussed. 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".

Genetic Test Definition

The Workgroup reviewed the two working definitions for genetic testing proposed by the CLIAC. Several members stressed the importance of developing definitions that are concise and specific, yet flexible enough to accommodate the future. After a brief discussion of whether it is necessary to identify that "individuals, families or populations" are the subject of genetic tests in both definitions, the Workgroup decided that it is not needed. Other minor revisions were proposed, and the working definitions that resulted from the Workgroup discussion are as follows:

Molecular genetic and cytogenetic tests - The analysis of human DNA, RNA, and chromosomes, in order to detect heritable or acquired disease-related genotypes, mutations, phenotypes, or karyotypes for clinical purposes. Such purposes include predicting risk of disease, identifying carriers, and establishing prenatal or clinical diagnoses or prognoses.

Biochemical genetic test - The analysis of materials derived from the human body, including human proteins, and certain metabolites predominantly used to detect inborn errors of metabolism, heritable genotypes, or mutations for clinical purposes. Such purposes include predicting risk of disease, identifying carriers, and establishing prenatal or clinical diagnoses or prognoses. [Tests that are used primarily for other purposes, but may contribute to diagnosing a

- S The laboratory shall assist its clients in ordering tests to meet clinical expectations including suggesting follow-up tests when appropriate.
- S Non-written requests for new tests must follow confidentiality and informed consent requirements as defined elsewhere in these regulations.
- **Ownership of specimen** - It was previously suggested that specimen ownership is not under the purview of CLIA, but that it is addressed through the agreements and policies of individual institutions and review boards. Points raised during this Workgroup discussion pertained to informed consent for retaining and/or re-using specimens (with or without patient identifiers), and valid reasons for a laboratory to retain, and possibly re-use specimens. A sample may be kept in case tests improve in the future, to confirm an original result or diagnosis, or for use in quality control or new test development.

Analytic phase

- **Specific quality control** - The Workgroup reviewed the CLIAC discussion on quality control. One member recommended, and the Workgroup agreed, that the phrase “but not processed” be deleted from the suggested requirement “A specimen should be stabilized but not processed until the clinical information for accurate testing is available”. The Workgroup discussed the listed items required to perform a test, and noted that a number of these are currently included in the CLIA requirements for a test requisition. The Workgroup proposed that any items not currently in the CLIA regulations be added to the regulations, instead of the Surveyor Guidelines. After a brief discussion on the CLIAC proposal regarding quality control checks to monitor contamination, the Workgroup had no suggestions for revisions.
- **Specimen integrity** - As with the list of items required for the previous topic, the Workgroup discussed the elements that CLIAC suggested as necessary to ensure specimen integrity and identification, and noted that these items should be in the CLIA regulations, if they are not currently included. Several Workgroup members proposed that “where necessary, include” be part of the introduction to this list, as all items may not be required for every test. A member also suggested general language to cover the requirements for specimen integrity (see Addendum).
- **Proficiency testing and alternatives** - Several questions were raised by the Workgroup in considering proficiency testing (PT) for genetic testing, including the definition of an analyte (e.g. DNA, RNA, point mutation, disease diagnosis). The Workgroup agreed that PT should be required for genetic testing if available, at the same frequency as required under CLIA for other analytes. Dr. Collins asked the Workgroup what is appropriate for PT of genetic tests, and whether surrogate or generic PT could be developed. A few members stated that the CLIA PT requirements for genetic testing should be very general,

and asked that the Centers for Disease Control and Prevention (CDC) consider what is appropriate, especially for tests where PT does not currently exist.

- **Personnel qualifications** - Several Workgroup members indicated that for genetic testing, the title for Technical Supervisor be changed to Technical Director, to better reflect the qualifications and level of responsibility of this position. Other members stated that this term is used only under CLIA, and that the title of an individual in an organization or laboratory is not required to be the same as stated in the CLIA regulations. In fact, in some institutions, the same person may fulfill the qualification requirements for several of the CLIA personnel categories and serve multiple roles.

General Supervisor - The proposed General Supervisor qualifications for genetic testing differ from the current CLIA standards for this position in the experience that would be required in high complexity genetic testing in the relevant subspecialty. Rather than one year of experience as is currently required for General Supervisor, under the Workgroup proposal, individuals with an M.D., D.O., Ph.D. or Master's degree would need two years of appropriate experience, and individuals with a baccalaureate degree would need three years of appropriate experience.

Clinical Consultant - The major issues considered by the Workgroup relative to the qualifications for Clinical Consultant for genetic testing were whether or not Board certification should be required for a Ph.D. or a Master's degree (in genetic counseling) individual, and whether or not a "grandfather" clause should be included to ensure that no one would be disenfranchised. The Workgroup stressed that for the future, Board certification is an important requirement, but a "grandfather" provision is needed to allow currently employed individuals to continue performing counseling. They also asked that the CDC provide current information on the numbers of genetic counselors who have graduated from accredited programs, but who are not Board certified.

Testing Personnel - The Workgroup reviewed the current CLIA requirements for Testing Personnel and suggested that they are adequate for genetic testing, except to add the word "relevant" to the experience requirement.

- **Personnel responsibilities** - No changes for genetic testing were proposed to the current personnel responsibilities for Laboratory Director, General Supervisor, or Testing Personnel. In addition to the current responsibilities, the Workgroup proposed that the Technical Supervisor must ensure that reports include pertinent information required for specific patient interpretation, and suggested that the Clinical Consultant responsibilities be revised to require that they "assist clients in ordering appropriate tests to meet clinical needs".
- **Validation of tests** - The Workgroup suggested that several items be added to the requirements for validation of new test procedures, including the significance of clinical parameters in validating a test in a specific population. One Workgroup member stated that some of the concerns regarding test validation are adequately addressed in

professional standards.

Post-analytic phase

- **Special reporting requirements** - The Workgroup discussed the CLIAC proposals for issues pertaining to results reporting, with some suggestions for minor revisions. To clarify one point, it was suggested that the reports should be “meaningful to” a non-geneticist healthcare provider, rather than “understandable by”. Several members expressed concern about providing information regarding the implications of test results for other family members.
- **Consultation to non-geneticist caregivers, use of test data** - These were addressed as part of the discussion of topics applicable to all phases of testing.
- **Record/specimen retention** - Although this work topic had not been previously considered, the Workgroup proposed that it be included for the post-analytic phase of genetic testing. Ms. Rhonda Whalen reviewed the current CLIA requirements for retention of records and specimens, and the Workgroup discussed aspects of genetic testing that may need to be specifically addressed in the regulations. They suggested that patient reports should be retrievable for a minimum of ten years, and that electronic records are acceptable. They raised issues pertaining to the storage and maintenance of patient specimens, and the need to balance practicality with patient needs. Several members stressed that significant space and resources are required to maintain specimens in a usable state after testing has been completed. The Workgroup proposed that the laboratory be required to have a policy defining specimen retention practices, but did not specify what that policy should be.

Topics applicable to all phases of testing

- **Informed consent** - The Workgroup reported that informed consent is appropriate for some genetic tests, and may be needed for re-use of patient specimens. However, one member suggested that it may be hard to define “tests of a sensitive nature” and gave alternative language that could be incorporated in the CLIA regulations (see Addendum). The Workgroup endorsed the proposal, noting that the laboratory can ensure that appropriate informed consent forms and processes are developed, but can not ensure that test results, limitations, and consequences are always adequately discussed with patients.
- **Re-use of previously tested specimens** - The Workgroup agreed that the laboratory must always have informed consent when patient identifiers are not removed, if excess material from patient specimens is to be used for any purpose. Several members suggested that it is appropriate for a laboratory to have a mechanism to notify all patients that their specimens may be re-used and to give patients the option to request that their specimens not be re-used. However, the Workgroup expressed concern that it may be difficult to implement policies and procedures for this in all institutions. In discussing the re-use of specimens for research or development of new genetic markers, and the use of patient

specimens for profit, the Workgroup noted that these issues are not under the purview of the CLIA regulations, and did not address them any further.

- **Genetic counseling (role of the laboratory)** - The Workgroup stated that this topic was addressed as part of the discussion on personnel qualifications and responsibilities.
- **Confidentiality** - Due to the many complex issues related to confidentiality and privacy, the Workgroup deferred discussion on this subject.

Concluding Remarks

Dr. O'Neal noted that the Workgroup report will be presented to the CLIAC at their meeting on September 16 - 17, 1998, and adjourned the Workgroup meeting.

I certify that this summary report of the July 30 - 31, 1998, meeting of the Genetic Testing Workgroup is an accurate and correct representation of the meeting.

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