Clinical

Laboratory

Improvement

Advisory

Committee

Summary Report

January 29-30, 1998

U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Clinical Laboratory Improvement Advisory Committee

January 29-30, 1998

Summary

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Record of Attendance

Committee Members
Dr. Regina Benjamin
Dr. Lemuel Bowie
Dr. Mary Burritt
Dr. Ronald Cada
Dr. Patricia Charache
Dr. Susanne Gollin
Dr. Verlin Janzen
Dr. Bereneice Madison
Ms. Diana Mass
Ms. Deborah McHugh
Dr. Toby Merlin
Dr. Glenda Price
Ms. Sharon Radford
Dr. Patricia Saigo
Mr. Elliott Segal

Ex Officio Members
Dr. Carlyn Collins, CDC
Dr. Steve Gutman, FDA
Ms. Judith Yost, HCFA - represented by Ms. Joan Simmons (HCFA) on 1/30

Liaison Representatives
Dr. Fred Lasky (HIMA)

Executive Secretary
Dr. Edward Baker

Centers for Disease Control and Prevention
Ms. Nancy Anderson
Ms. Annette Baird
Ms. Rosemary Bakes-Martin
Ms. Carol Bigelow
Dr. Joe Boone
Ms. Gail Bosley
Ms. Diane Bosse
Ms. Cheryl Coble
Ms. Carol Cook
Ms. MariBeth Gagnon
Ms. Sharon Granade
Dr. Thomas Hearn
Dr. Ed Holmes
Dr. John Krolak
Dr. Harvey Lipman
Mr. Kevin Malone
Dr. Adam Manasterski
Dr. John Ridderhof
Ms. Renee Ross
Dr. Shahram Shahangian
Ms. Marianne Simon
Mr. Darshan Singh
Ms. Elva Smith
Mr. Gregory Smothers
Dr. Steven Steindel
Dr. Roger Taylor
Ms. Julie Wasil
Ms. Glennis Westbrook
Ms. Rhonda Whalen
Ms. Laurina Williams

Clinical Laboratory Improvement Advisory Committee

The Secretary of Health and Human Services is authorized under Section 353 of the Public Health Service Act, as amended, to establish standards to assure consistent, accurate, and reliable test results by all clinical laboratories in the United States. The Secretary is authorized under Section 222 to establish advisory committees.

The Clinical Laboratory Improvement Advisory Committee (CLIAC) was chartered in February 1992 to provide scientific and technical advice and guidance to the Secretary and the Assistant Secretary for Health regarding the need for, and the nature of, revisions to the standards under which clinical laboratories are regulated; the impact on medical and laboratory practice of proposed revisions to the standards; and the modification of the standards to accommodate technological advances.

The Committee consists of 20 members, including the Chair. Members are selected by the Secretary from authorities knowledgeable in the fields of microbiology, immunology, chemistry, hematology, pathology, and representatives of medical technology, public health, clinical practice, and consumers. In addition, CLIAC includes three ex officio members, or designees: the Director, Centers for Disease Control and Prevention; the Commissioner, Food and Drug Administration; the Administrator, Health Care Financing Administration; and such additional officers of the U.S. Government that the Secretary deems are necessary for the Committee to effectively carry out its functions. CLIAC will also include a non-voting liaison representative who is a member of the Health Industry Manufacturers Association and such other non-voting liaison representatives that the Secretary deems are necessary for the Committee to effectively carry out its functions.

Due to the diversity of its membership, CLIAC is at times divided in the guidance and advice it offers to the Secretary. Even when all CLIAC members agree on a specific recommendation, the Secretary may not follow their advice due to other overriding concerns. Thus, while some of the actions recommended by CLIAC may eventually result in changes to the law, the reader should not infer that all of the advisory committee's recommendations will be automatically accepted and acted upon by the Secretary.

Welcome and Introductory Information

The meeting was called to order by CLIAC Chairman Dr. Morton Schwartz. The committee members made self-introductions and disclosure statements of their relevant financial interests as they relate to the topics to be discussed during the CLIAC meeting. Dr. Edward L. Baker, Director of the Public Health Practice Program Office (PHPPO) at the Centers for Disease Control and Prevention, thanked the Genetic Testing Subcommittee, that met on January 27 - 28.

Presentations and Committee Discussion

CLINICAL LABORATORY IMPROVEMENT AMENDMENTS OF 1988 (CLIA) UPDATE

Centers for Disease Control and Prevention (CDC) **Addendum C-1**

Dr. Carlyn Collins, Director of the Division of Laboratory Systems (DLS), PHPPO, reported that guidelines for the public health response to the regulatory closure of cervical cytology laboratories were published in the CDC Morbidity and Mortality Weekly Report on December 19, 1997. She also said that two articles on proficiency testing performance (one authored by DLS staff) would be published in the Journal of the American Medical Association on February 11, 1998. Dr. Collins announced that the CLIAC minutes from the September, 1997 meeting are posted on the Division of Laboratory Systems homepage on the Internet (http://www.cdc.gov/phppo/dls); and that since future minutes will also be posted, the CDC is considering eliminating the distribution of hardcopy minutes to the public. The CLIAC would still receive the hardcopy reports. Dr. Collins concluded by noting that the final waiver regulation is still undergoing work for final clearance, and describing recent changes in the CLIA statute to clarify that procedures cleared by the Food and Drug Administration (FDA) for home use are waived regardless of whether or not a prescription is required.

Committee Discussion:

A CLIAC member asked for clarification regarding the waiver process for tests approved by the FDA for home use. Mr. Kevin Malone stated that a request for waiver must still be submitted to the CDC for registration purposes, and Dr. Baker added that the CDC continues to have a process for requesting waiver for tests not approved by the FDA for home use. Several CLIAC members expressed concern regarding recently published FDA final rules pertaining to exemption of certain medical devices from the premarket review process, and questioned whether home use tests would fall into this category. Dr. Steve Gutman explained that the FDA is currently assembling a list of products that will not be exempt from review, and that he believes that tests for near-patient and home use will most likely be in this group of products. Dr. Schwartz asked that this issue be addressed at a future CLIAC meeting, with input from the CDC and the FDA.

Health Care Financing Administration (HCFA) **Addendum C-2**

Ms. Judy Yost, Director of Outcomes and Improvement, HCFA, presented a status report on CLIA implementation. She indicated that approximately 70% of laboratories currently hold either a certificate of waiver or provider-performed microscopy, and are not subject to routine inspections. Applications for State exemption for Florida, Georgia, and California are now under review by HCFA and CDC. Reapproval of deemed organizations is ongoing, and validation inspections of laboratories accredited by these organizations have all demonstrated that the organizations are performing satisfactorily. Ms Yost stated that HCFA is reviewing proficiency testing (PT) enrollment and performance data for 1995 - 1996 as a mechanism to evaluate CLIA implementation under the Government Performance Review Act. HCFA has noted that some laboratories fail to enroll in PT in alternate years when they are not being inspected. The CLIA fee schedule increases for certificate fees were effective as of January 1, 1998. Seventy-one comments were received in response to the Federal Register notice announcing the revised fee schedules. HCFA will monitor the fee increases and review the fees based on comments to the Federal Register notice and the impact on laboratories. Ms. Yost next noted that Medicare/Medicaid reimbursement for laboratory tests is being denied for laboratories that are not appropriately certified to perform the services. She ended her update by indicating that outcome oriented surveys have been implemented, and are being well received in the field.

Committee Discussion:

Committee members asked for clarification of several points made by Ms. Yost, including the fee increases and Medicare/Medicaid issues, and one member asked about laboratory fraud and abuse investigations. Ms. Yost explained that HCFA has pilot projects in several states to investigate billing practices. The member expressed concerns about integrating billing audits with CLIA inspections, to which Ms. Yost responded that fraud and abuse investigations are not part of the laboratory surveys to determine compliance with CLIA requirements.

GENETIC TESTING

Genetic Testing Subcommittee Report **Addendum C-3**

Dr. Wendell O'Neal summarized the activities of the January 27-28 meeting of the Genetic Testing Subcommittee. He emphasized the charge to the Subcommittee and the Subcommittee's relationship to the CLIAC. He noted that presentations were made to the Subcommittee by: Dr. Margaret McGovern (Mount Sinai School of Medicine); Dr. Michael Watson (American College of Medical Genetics); and Dr. William Raub (Office of the Secretary, Department of Health and Human Services - HHS). The presentations included, respectively, the results of a survey on quality assurance practices in molecular genetics testing laboratories in the United States; a summary of the issues addressed and recommendations made by the National Institutes of Health - Department of Energy (NIH/DOE) Task Force on Genetic Testing; and a report on the activities of an HHS workgroup created to address regulatory and advisory issues related to genetic testing. Dr. O'Neal then presented to the CLIAC for consideration a summary of the issues discussed by the Subcommittee pertaining to the definition of genetic testing; unique aspects of genetic tests;

and issues specific to the pre-analytic, analytic, and post-analytic phases of genetic testing. The Subcommittee suggested to the CLIAC that these topics be considered by workgroups, which will bring recommendations to future Subcommittee and CLIAC meetings.

Committee Discussion:

Definition of Genetic Testing

The Genetic Testing Subcommittee recommended that the CLIAC consider the definition of genetic testing developed by the Subcommittee as a proposed working definition, which may be revised. Dr. Schwartz added that in developing this definition, the Subcommittee suggested beginning with a broad definition, which could be more narrowly defined later. However, he indicated that the Subcommittee had agreed that the definition should clearly exclude microbial genetic material, and thus the word "human" was used twice in describing what is being tested. Some CLIAC members shared their thoughts about terms in the definition that are flagged as being subject to further discussion, and the Committee agreed that the proposed working definition as written is sufficient at this point (phrases in italics are subject to further discussion and potential revision).

- Genetic Test - The analysis of materials derived from the human body, including human DNA, RNA, chromosomes, *proteins, and certain metabolites* 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 in individuals, families, or populations.

Pre-analytic Genetic Testing Issues

Dr. Pat Charache reviewed the list of work topics for all phases of genetic testing. She began with the pre-analytic phase of genetic testing, explaining that each workgroup will address these issues to make recommendations to the CLIAC regarding the applicability and appropriateness of CLIA. Several CLIAC members questioned whether the pre-analytic issues are beyond the scope of CLIA and "quality laboratory testing". One member noted that additional expertise would be required to address the issues sufficiently. Dr. O'Neal and other Subcommittee members agreed that some of the areas of concern may go beyond what CLIA can or should address, but that they need to be considered from a broad policy point of view. The workgroup should consider where the line of responsibility for the laboratory should be drawn, especially for the issues of providing consultation to physicians and appropriateness of testing, genetic counseling, and specimen preparation and handling. From a regulatory (CLIA) standpoint, the workgroup may determine that some of the issues are already adequately addressed. When asked if any additional items should be included for consideration, suggestions were made to add the following: communication between the laboratory and the healthcare provider community; and ordering of tests by a laboratory, patient (self-ordering) or public health agency.

Analytic Genetic Testing Issues

In discussing the work topics for the analytic phase of genetic testing, members stated that many of the current CLIA standards for high complexity testing (especially chemistry, cytogenetics, and

histocompatibility) are most likely adequate and appropriate. The two biggest areas of concern were personnel requirements and proficiency testing. Dr. Collins raised the issue of validation for "home-brew" genetic tests, and noted that while CLIA has a requirement for laboratories to establish performance characteristics for "in house" methods, there is a gap between FDA/CLIA oversight. CLIAC members added the issues of control of contamination, workflow, and the laboratory environment to the list of concerns to be addressed by the workgroup for the analytic phase of testing.

Post-analytic Genetic Testing Issues

No additions were made to the work topics for the post-analytic phase of genetic testing. One CLIAC member asked for clarification as to the term "non-geneticist care givers". It was explained that these are professional healthcare providers with no expertise in genetics. Two members stressed that it is important that genetic test results not be reported directly to patients, but that these be given to a provider who can appropriately explain the results and counsel the patient (or family) if needed. Genetic test results were compared to surgical pathology reports, which always go through a physician, who explains them to the patient.

Public Comments on Genetic Testing

There were no public comments on genetic testing.

PROFICIENCY TESTING

Overview of CLIA Proficiency Testing **Addendum C-4**

Dr. Joe Boone, Assistant Director for Science for DLS, PHPPO, presented a brief overview of the Federal PT program, including a historical perspective, the current CLIA program, and goals for PT in the year 2000 and beyond. In looking towards the future, Dr. Boone stated that goals include updating and clarifying PT requirements; bringing the CLIA requirements into alignment with international standards to the extent possible; and making the program relevant by expanding the required PT menu.

International Guidelines for Proficiency Testing **Addendum C-5**

Mr. Dan Tholen, a statistical consultant with extensive expertise in PT, described national and international standards and guidelines for PT providers and compared the CLIA standards with these guidelines. He indicated that international standards emphasize the educational value of PT. Several areas in which international standards for PT providers are more stringent than CLIA are in requirements for an advisory group with technical knowledge and expertise; methods of determining traceability of assigned values; procedures to establish accuracy of consensus values; standardization of participant reports, to include information regarding target values and summary results; and methods of ensuring the homogeneity of samples. International PT standards also require an oversight body with knowledge of the guidelines to monitor compliance with PT programs by performing on-site audits and statistical reviews of the data.

Committee Discussion:

The industry liaison commented on manufacturers' concerns about the increased costs of PT that would result from compliance with more stringent standards. He questioned the need for higher PT standards, in light of the fact that United States manufacturers are operating under the FDA Good Manufacturing Practices requirements. A CLIAC member noted that there are reasons for higher stringency in PT for environmental testing, or when operating in the global economy, for which the international standards are intended. Several Committee members raised the issue of the numbers of ungradable PT samples determined by various providers under CLIA, and emphasized the need for standardization of the PT programs. Dr. Schwartz ended the discussion by asking for comments from any of the CLIA-approved PT providers in the audience. The following providers responded:

- Bill Donohue (Accutest) - Mr. Donohue commented on the ungradable PT samples, noting that Accutest is a small PT program. He stated that Accutest attempts to grade small peer groups by using comparable methods, and provides reason codes for ungraded samples to HCFA and the CDC. He felt that Accutest could comply with international PT standards.
- Diedre Astin (New York State - NYS, Clinical Laboratory Evaluation program) - Ms. Astin reported that although NYS is a CLIA-exempt program, physician offices are not regulated under New York law. NYS gathers PT data for physician office laboratories. She was concerned about the numbers of ungraded samples, and nonparticipation in PT. She added that NYS could probably comply with international PT standards.
- Nick Serafy, Jr. (American Association of Bioanalysts) - Mr. Serafy commented on the international PT standards, and indicated his concern that compliance with these standards would increase the costs of PT significantly. He did not see a need for increased stringency to improve sample quality, and noted that PT for clinical laboratory testing is not required globally at this time.

Criteria for Adding Analytes to CLIA PT **Addendum C-6**

Ms. Nancy Anderson, a Health Scientist in DLS, PHPPO, discussed the current PT requirements under CLIA, and asked the CLIAC for recommendations regarding expanding the PT program content and options for implementation of changes to PT. She explained that when the 1992 final CLIA regulations were published, the PT program requirements were gradually phased-in. In addition, the number of analytes or tests for which PT is currently required is limited compared to the number of analytes for which PT is available on a voluntary basis. Ms. Anderson asked the Committee for input on criteria to be used if additional analytes are to be included in the required PT program, and for suggestions as to whether an expanded program should be implemented in a single step or through a phase-in process.

Committee Discussion:

Several CLIAC members asked for clarification as to which analytes are "regulated", and one member referenced the CLIA statute which says that PT is required for all analytes for which it can be developed. Members asked if required PT analytes could be removed from the list, and

whether the law states that analytes must be added. Dr. Collins agreed that the law does require PT for all analytes (except when HHS has determined that a PT program can not reasonably be developed), and noted that the preamble to the 1992 final regulations explained that although required PT was limited at that time, analytes would be added to those that are required. She indicated that the law may not allow removal of regulated analytes. Although there was disagreement among Committee members as to which criteria for adding analytes be given the highest priority, they did suggest that all of the criteria mentioned by Ms. Anderson are important to consider. The Committee also recommended that a PT Subcommittee be re-established to look at the issues presented by Ms. Anderson.

Public Comments

There were no public comments for the CLIAC.

Concluding Remarks

Dr. Schwartz announced that the date for the next CLIAC meeting would be May 29, 1998, preceded by a meeting of the Genetic Testing Subcommittee on May 27 - 28. Dr. Schwartz then adjourned the CLIAC meeting.

I certify that this summary report of the January 29 - 30, 1998, meeting of the Clinical Laboratory Improvement Advisory Committee is an accurate and correct representation of the meeting.

Addendum C-1

Addendum C-2

Addendum C-3

Addendum C-4

Addendum C-5

Addendum C-6