Clinical

Laboratory

Improvement

Advisory

Committee

Summary Report

May 29-30, 1996

U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

Clinical Laboratory Improvement Advisory Committee

May 29-30, 1996

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Record of Attendance

The Clinical Laboratory Improvement Advisory Committee (CLIAC) met at the Centers for Disease Control and Prevention (CDC), Auditorium B, in Atlanta, Georgia, on May 29-30, 1996. There were approximately 114 people in attendance. The Committee members, CDC staff and presenters in attendance are listed below:

Committee Members

Dr. J. Scott Abercrombie
Dr. David Baines
Dr. Regina Benjamin
Ms. Michele Best
Dr. Thomas Bonfiglio
Dr. Ronald Cada
Dr. Susanne Gollin
Dr. Verlin Janzen
Ms. Sandra Johnson
Dr. J. Stephen Kroger
Dr. Bereneice Madison
Ms. Deborah McHugh
Dr. Wendell O'Neal
Dr. Glenda Price
Dr. Sharon Radford
Dr. Patricia Saigo
Dr. Morton Schwartz
Dr. Ulder Tillman

Ex Officio Members

Dr. Carlyn Collins, CDC
Dr. Steve Gutman, FDA
Ms. Judith Yost, HCFA

Executive Secretary

Dr. Edward Baker

Liaison Representatives

Dr. Fred Lasky (HIMA)

Centers for Disease Control and Prevention

Ms. Nancy Anderson
Ms. Rosemary Bakes-Martin
Ms. Carol Bigelow
Dr. Joe Boone
Ms. Cheryl Coble
Ms. Carol Cook
Ms. Crystal Frazier
Ms. Sharon Granade
Dr. Tom Hearn
Dr. Edwin Holmes
Dr. John Krolak
Dr. Anne O'Connor
Dr. John C. Ridderhof
Dr. Eunice Rosner
Dr. Shahram Shahangian
Mr. Darshan Singh
Mr. Gregory Smothers
Ms. Julie Wasil
Ms. Rhonda Whalen

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 Announcements

The CLIAC meeting was called to order and committee members were welcomed by Chairman Dr. Morton Schwartz. The committee members made self-introductions and disclosure statements of their relevant financial interests as they relate to any topics to be discussed during the CLIAC meeting. Dr. Schwartz then stated the role and function of CLIAC.

Presentations and Committee Discussion

Clinical Laboratory Improvement Amendments (CLIA) Update/CDC

Dr. Carlyn Collins, Director of the Division of Laboratory Systems, reviewed the status of three regulations in progress: (1) the final rule for criteria for waiver; (2) the final rule that extends the phase-in period for the quality control (QC) requirement applicable to moderate complexity testing which expires September 1, 1996; and (3) the regulatory reform final regulation which simplifies the CLIA regulations pertaining to proficiency testing (PT), inspections, and accreditation and exemption. Because these regulations have been given high priority and may be published by the end of the year, the publication of the final, final regulations has been delayed. Responding to a CLIAC member, Dr. Collins noted that the requirements for APT (accurate and precise technology) testing will be considered as we develop the final, final regulations.

Dr. Collins also reported that the U.S. Court of Appeals for the District of Columbia has reversed the district court's decision in the lawsuit of Consumer Federation of America and Public Citizen vs. the Department of Health and Human Services (HHS). The Court of Appeals ruled that:

- The CLIA regulations for categorizing tests and personnel qualifications were established in accordance with the law. The higher court agreed with the Department's position that the current regulation takes risk of harm into account and that test categorization based on the potential consequences of erroneous results would be too subjective and unworkable.

- HHS must publish an official explanation justifying the current cytology PT regulations allowing individuals to examine PT slides at a rate lower than normal workload rate. In the mean time, the current cytology PT regulations remain in effect.

Dr. Collins (and later Dr. Ed Baker, Director of the Public Health Practice Program Office, CDC, and Executive Secretary of CLIAC) noted that HHS has received considerable correspondence on genetics testing. CDC is participating in a genetics

task force established by the National Institutes of Health and Dr. Collins said that CLIAC advice would be sought in addressing some of the genetics testing issues. Dr. Schwartz suggested that CLIAC should provide input on DNA and RNA testing but not the ethical and legal aspects of genetics testing.

CLIA Update/Health Care Financing Administration (HCFA) Addendum A

Ms. Judith Yost, Director of the Division of Laboratory, presented a status report on CLIA implementation. She summarized CLIA laboratory enrollment data by certificate type and by laboratory type, enrollment data from accreditation organizations, and noted the category of CLIA-exempt laboratories.

Ms. Yost then reviewed data from surveys. She said that HCFA surveys more than 34,000 laboratories every two years [approximately two-thirds are physicians office laboratories (POLs)] and that second cycle surveys of about 10,700 laboratories have been completed. She noted a large increase in the percentage of laboratories with no deficiencies and a decrease in the percentage of laboratories with condition level deficiencies. The most frequent condition level deficiency continues to be failure to enroll in a PT program. Ms. Yost reported that POLs have shown dramatic improvement on surveys, which she attributed to HCFA's educational approach to inspections.

Ms. Yost reported that about 1,700 laboratories have participated in the Alternate Quality Assessment Survey, a paper self-survey for laboratories that have no deficiencies in their first inspection and that demonstrate satisfactory PT performance for one year. HCFA has recently implemented an outcome-oriented, on-site inspection process which it considers to be more efficient and more effective than earlier surveys. The new inspection process focuses on how the laboratory identifies, corrects, and prevents the recurrence of problems.

One committee member expressed surprise that 30% of the laboratories surveyed by HCFA for the second time have no deficiencies. He reported that the Commission on Office Laboratory Accreditation has experienced an increase in laboratories with no deficiencies, but that the numbers were lower than HCFA figures.

QC Issues

Background

Introduction **Addendum B**

Ms. Rosemary Bakes-Martin briefly reviewed issues discussed at previous CLIAC meetings concerning the revision of the CLIA QC requirements to address new

technology. Previous discussions centered on the phase-in of the QC requirements for unmodified, moderate complexity testing, the manufacturer's role in QC, whether traditional QC concepts are applicable to new technology, the establishment of a core set of QC requirements, and simplification of the regulatory structure and language. Ms. Bakes-Martin then introduced the speakers who would give background information for discussion of QC issues.

Evolution of QC Practices in Health Care Laboratories **Addendum C**

James Westgard, Ph.D., reviewed the current status of laboratory and statistical QC practices and noted that the Food and Drug Administration CLIA QC clearance process has not been implemented due to budget constraints. He observed that current QC practices are based on QC rules used ten years ago and are arbitrary because we have not defined the quality we want to achieve. Reviewing the evolution of laboratory statistical QC practices, Dr. Westgard noted that the development of QC systems significantly lags behind the development of test systems and commented that it is impossible to design control procedures to achieve a zero error rate. He said that historically the laboratory focus shifts between quality and cost control, and that currently the emphasis is on cost control. Because of the focus on cost control, the laboratory employment of skilled personnel, who could detect many errors, has decreased. In addition, laboratories have not defined the amount of error they are willing to tolerate; thus they can't define the level of quality they want to achieve.

Dr. Westgard stated that laboratories currently have the tools to design a quality monitoring system and suggested that laboratories use the PT requirements (criteria for acceptable performance) as a benchmark for defining test quality. In establishing QC procedures, he noted that laboratorians must consider the stability of the testing process and the frequency of problems encountered using the test system. Because the employment of skilled personnel has decreased, Dr. Westgard stressed that instrument design should incorporate quality systems to assure that test results meet quality requirements.

In the discussion that followed Dr. Westgard's presentation, Dr. Schwartz noted that the laboratory is responsible for the analytical phase of the total testing process and asked for input on developing quality requirements. Dr. Westgard suggested that the development of requirements should be data driven. He also noted that electronic controls only monitor the instrument and indicated that traditional controls may be the most efficient way to monitor a multi-step testing process. Alternatively, he said that for unit test measurement devices, monitoring those steps in the test system's testing process which could cause enough variation in the test result to impact the diagnosis or treatment might be appropriate.

Referring to the impossibility of designing control procedures to detect a zero error rate, Dr. Schwartz asked Dr. Westgard to comment on acceptable error rates. Dr. Westgard suggested that a "worst case" error rate of 1 in 1,000 might be acceptable, but 1 in 10,000 would be better. One committee member said that the acceptable defect rate should be defined in the context of the use of the test result.

Dr. Westgard reemphasized that defining and monitoring quality is important in spite of economic constraints. Formerly we depended on experienced laboratory personnel to monitor quality; now we depend on monitoring processes. In addition, because of the changes in health care practices, Dr. Westgard said that a standard process should be developed for monitoring quality that guides people, allows for different input sources, can be managed quantitatively, and can be passed on to others.

Point-of-Care (POC)Testing **Addendum D**

Barbara Goldsmith, Ph.D., discussed the type of technology used for POC testing in various types of institutions. She described the proposed National Committee for Clinical Laboratory Standards (NCCLS) guidelines for POC testing and focused on the QC aspects of the new technology being used in POC testing. The guidelines were produced as a resource to establish uniformity in POC testing, are oriented toward non-laboratory trained personnel, and should become an approved NCCLS standard by January 1997.

Following Dr. Goldsmith's presentation, CLIAC members discussed the following issues concerning POC testing and the technology used in that testing:

- Electronic controls may check the performance of the instrument but not the operator; operator performance must be adequately controlled.

- Whole blood controls and proficiency testing materials are not available for many instruments.

- POC testing in hospitals may differ from POC testing in other environments (for example, testing personnel training).

- Positive screening test results are often confirmed by additional tests. Negative screening results usually are not confirmed and might cause a diagnostic error.

- Expense associated with POC testing may limit its use.

- The definition of test turn-around-time (the starting point and the ending point) and its impact on patient care need clarification.

- Various accrediting agencies have different QC requirements.

QC Concepts for Revision of Regulations **Addenda E-G**

Ms. Bakes-Martin presented a progress report from the CDC QC Workgroup and referred CLIAC members to an internal reference document (see addendum E) that summarizes the results of a literature search on ten pertinent QC topics. The document served as a resource for developing the following concepts for consideration in revising the CLIA QC requirements:

- Consolidate the regulations on Patient Test Management (PTM), QC, and Quality Assurance (QA) into one section to be named "Quality Monitoring" (see addendum F).

- QC protocols should consider two issues: potential for error and monitoring over time (see addendum G).

- The analytical phase of the testing process primarily has three potential sources for error: test system, environment, and operator (see addendum G).

Ms. Bakes-Martin noted that one of the QC issues to be resolved is defining levels of control and types of controls needed to monitor new technology, specifically POC testing. Ms. Bakes-Martin stated that traditional QC was designed to monitor all three components (test system, environment, and operator) and then gave examples of how each component can be monitored for error using alternative approaches. She noted that there is less operator intervention in some of the new test systems. Ms. Bakes-Martin commented that traditional controls would still be important in evaluating operator performance and in monitoring over time. However, the current requirement for testing traditional QC during each run of patient samples may be too restrictive for test systems with internal controls. For test systems having internal QC monitors, CDC recommended consideration of an approach that could include running traditional QC a minimum of once per week in order to monitor the entire analytical phase of the testing process over time.

QC Issues for Committee Discussion **Addendum H**

Regarding the concepts presented, CDC asked the Committee to consider the following issues:

Issue #1: Does the reorganization of "Patient Test Management," "Quality Control," and "Quality Assurance" into one section called "Quality Monitoring" reflect present day clinical laboratory practice?

Issue #2: Does the CDC proposal for revising the minimum standards for Quality Control make adequate allowances for new technology?

Issue #3: Does the CDC proposal adequately address the potential for error in test performance?

Issue #4: Does the CDC proposal adequately address the concept of monitoring over time to ensure quality?

Committee Discussion

The Committee agreed with the concept of reorganizing PTM, QC, and QA into one section, but recommended naming the section "Quality Assurance" or "Quality Systems," instead of "Quality Monitoring." In a lengthy discussion of Issues #2-4, committee members expressed the following concerns:

- Non-traditional (internal) controls may not monitor operator competency. Changes in operator may need to be monitored.

- Non-traditional (internal) controls may require monitoring to ensure their effectiveness.

- PT assists in monitoring quality, but PT samples are not available for many of the new technology instruments.

- For test systems having internal monitors, running traditional QC a minimum of once per week seems arbitrary. A QC frequency requirement should be based on data. Clarification is needed as to whether the laboratory director would be required to determine the frequency of QC testing. Definitions of traditional controls (liquid materials vs. other options) are needed.

- Traditional QC may not be appropriate for many instruments that have non-traditional (internal) controls.

- Manufacturers may have data to show that non-traditional (internal) controls adequately monitor the test system, the environment, and the operator and to suggest whether (or how frequently) traditional controls should be tested.

- For new technology, specific QC requirements for individual test systems could be incorporated into HCFA surveyor guidelines.

- Regulations must be flexible to accommodate changes in technology. The concept presented appears flexible, but lacks detail.

- Definitions of quality, error, and accuracy are needed, as well as a better understanding of the concept of "monitoring over time."

- Operator monitoring could be accomplished through on-going education and training.

In general, the Committee agreed that the test system, the environment, and the operator are the main sources of error. Several CLIAC members felt that testing traditional controls weekly may be sufficient for monitoring, but others felt that this type of testing would not make adequate allowance for new technology and noted that options other than testing traditional QC might be used. To allow flexibility, some members suggested that the frequency of testing controls might be "as appropriate for technology," rather than "at least once per week." The committee members, however, wanted additional information before making any recommendations concerning frequency and type of controls, and asked that specific data on QC performance be presented at a future CLIAC meeting.

Additional Committee Concerns

One committee member asked about the status of the ASM recommendations on microbiology QC. Dr. Collins acknowledged that the data presented by ASM indicated that some revisions may be needed to the QC requirements for microbiology reagents and said that CDC plans to focus on microbiology QC once the general QC issues are resolved. Committee members raised additional concerns about (1) the variation among accreditation agencies' requirements and differences between accreditation agency requirements and the CLIA requirements, e.g. frequency of QC testing, and (2) the possible need for reconsideration of laboratory specialty/subspecialty classification as new technologies develop.

Public Comments **Addendum I**

1. Frank LaDuca, Ph.D., Vice-President, International Technidyn Corporation, noted that with POC testing (single use test devices), the entire testing unit is consumed each time a test is performed. In his opinion, the manufacturer should

be responsible for demonstrating that all potential sources of error except operator error are monitored. Dr. LaDuca felt encouraged by the CLIAC discussion and said that he would be willing to share information/data on coagulation instruments.

2. William Moffitt, President and Chief Executive Officer of i-STAT Corporation, said that no single monitoring system is appropriate for all technology and that regulations should assure quality rather than requiring a particular QC system (see addendum I). He suggested that the FDA's Good Manufacturing Practice (GMP) standards be considered in CLIAC discussions about QC procedures, noting that "laboratory" could be substituted for "manufacturer" and the standards would be appropriate regulations for laboratories. Regulations which parallel the GMP standards would acknowledge the variety of technology and environment-specific applications and allow manufacturers to develop appropriate quality systems to be validated by the laboratory director.

Noting the Committee's discomfort with assumptions and opinions, Mr. Moffitt said that numerous manufacturers have data supporting their alternative quality systems. He suggested that CLIAC should have manufacturers make presentations and share data on the newer technologies.

Concluding Remarks

Dr. Schwartz expressed appreciation to CLIAC members whose official terms expire on June 30, 1996 (Dr. Scott Abercrombie, Ms. Michele Best, Ms. Sandra Johnson, Dr. Stephen Kroger, and Dr. Wendell O'Neal). He announced that the dates for upcoming CLIAC meetings will be September 25-26, 1996, and January 8-9, 1997, and then adjourned the meeting.

I certify that this summary report of the May 29-39, 1996, meeting of the Clinical Laboratory Improvement Advisory Committee is an accurate and correct representation of the meeting.

/S/ Morton K. Schwartz, Ph.D.
Chairman