

# Clinical Laboratory Improvement Advisory Committee

Summary Report

**August 30-31, 1995**



U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service



# **Clinical Laboratory Improvement Advisory Committee**

**August 30-31, 1995**

## **Summary**

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## **Record of Attendance**

The Clinical Laboratory Improvement Advisory Committee (CLIAC) met at the Swissôtel, 3391 Peachtree Street, in Atlanta, Georgia, on August 30-31, 1995. Those in attendance are listed below:

### Committee Members

Dr. J. Scott Abercrombie  
Dr. Paul Bachner  
Dr. Regina Benjamin  
Ms. Michelle Best  
Ms. Virginia Charles  
Dr. Susanne Gollin  
Dr. Stanley Inhorn  
Dr. Verlin Janzen  
Dr. J. Stephen Kroger  
Dr. Aliza Lifshitz  
Dr. Bereneice Madison  
Dr. Wendell O'Neal  
Ms. Deborah Reed  
Dr. Patricia Saigo  
Dr. Morton Schwartz  
Mr. Elliott Segal

### 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

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Ms. Nancy Anderson  
Dr. John Astles  
Ms. Rosemary Bakes-Martin  
Ms. Louise Barden  
Ms. Carol Bigelow  
Dr. Joe Boone  
Ms. Sheila Boring  
Ms. Gail Bosley  
Ms. Diane Bosse  
Ms. Genoria Bridgeman  
Ms. Cheryl Coble  
Ms. Debbie Coker  
Ms. Crystal Frazier  
Ms. MariBeth Gagnon  
Ms. Sharon Granade  
Mr. Tom Hearn

Mr. Edwin Holmes  
Dr. Adam Manasterski  
Dr. John C. Ridderhof  
Ms. Eunice Rosner  
Mr. Darshan Singh  
Ms. Elva Smith  
Mr. Gregory Smothers  
Dr. Tina Stull  
Ms. Julie Wasil  
Ms. Glennis Westbrook  
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 meeting was called to order by CLIAC Chairman Dr. Morton Schwartz. Dr. Edward Baker, Director of the Public Health Practice Program Office, CDC, and Executive Secretary of the CLIAC welcomed the committee members. Dr. Schwartz stated the role and function of CLIAC. Mr. Kevin Malone, Attorney Advisor, CDC, reviewed the conflict of interest forms and format for financial disclosure statements to be made at each CLIAC meeting. The committee members then made self-introductions and disclosure statements of their relevant financial interests as they relate to any topics to be discussed during the CLIAC meeting.

## **Presentations and Committee Discussion**

### **CLIA Update/CDC**

Dr. Carlyn Collins, Director of the Division of Laboratory Systems, CDC, stated that the waived and accurate and precise technology (APT) proposed rules are still under review, but noted that Vice President Gore indicated at a press conference that these rules would be published in the fall. [The proposed rule clarifying the waived criteria was published on September 13, 1995, and the proposed rule to create the APT subcategory was published on September 15, 1995.]

CDC has received applications for waiver of 13 test systems, including 33 analytes. Two test systems have been approved for waiver and the review of the other applications is ongoing.

CDC will host a laboratory institute entitled "Frontiers in Laboratory Practice Research" on October 1-3, 1995 in Atlanta.

### **CLIA Update/HCFA**

### **Addendum A**

Ms. Judith Yost, HCFA, presented a status report on CLIA implementation and a summary of the types of deficiencies cited in the first and the second cycle inspections. She noted that approximately 10% of the second cycle inspections have been completed and that condition level deficiencies have decreased from 14% (first cycle) to 9% (second cycle). She attributed the improvement in laboratory compliance to the educational aspects of the inspection process.

## **Committee Discussion**

One committee member asked about the denominators (total number of laboratories inspected) for the percent of laboratories with condition level deficiencies in the first and second cycle inspections. Ms. Yost stated that the denominators were essentially the same. In addition, she noted some changes in types of certificates due to the recent expansion of personnel (mid-level practitioners) allowed to perform provider-performed microscopy procedures.

## **CLIA Update/FDA**

## **Addendum B**

### **Comparison of CDC Review for Waiver and FDA Clearance for Over the Counter (OTC) Products**

In response to a previous request from CLIAC, Dr. Steve Gutman, FDA, presented a comparison of the FDA review process for clearance of OTC (home use) products and the CDC review process for determining waiver. While the processes are quite similar with respect to labeling and data requirements, he noted that it would be very difficult to harmonize the technical requirements, and somewhat difficult to harmonize the informational requirements. The two agencies operate under different statutes, serve slightly different constituencies, and have regulatory requirements which are parallel but not identical. Although some progress has been made in harmonizing the requirements, Dr. Gutman stated that there continue to be statutory differences in the charges to the two agencies.

## **Committee Discussion**

One committee member asked why the FDA cannot accept a submission that meets the CDC guidelines for waiver approval. Dr. Gutman stated that the FDA **can accept** a submission based on the guidelines for waiver but that the FDA **cannot require** that type of submission. The committee member noted that since the CLIA law requires waiver approval (if application for waiver is made) of all devices cleared for home use by the FDA, it would seem reasonable for the FDA to consult with the CDC to determine whether the FDA could clear for home use any test system waived under CLIA by the CDC. Dr. Gutman indicated that this would not be possible due to FDA's workload and limited resources.

### **Status of FDA Approval of Cytology Instruments**

External consultant review panels have recommended FDA approval of two instruments designed to assist laboratories in improving or enhancing the quality control (QC) procedures associated with PAP smear examinations.

The **Papnet** provides an adjunct test to the laboratory's routine examination of slides and rescreen of 10% of negative cases, which includes random rescreen and high risk cases. Following the initial manual screen of all slides by cytotechnologists and the mandatory rescreening of 10% of the negative cases, all negative slides are sent for review by **Papnet**, an automated computerized system which identifies by video the most suspicious 64 cells and 64 clusters of cells. The video and slides are then returned to the laboratory for cytotechnologist review to determine which of these slides should be rescreened.

The **AutoPap** instrument is intended for use as an alternative to the random rescreen QC procedure. Laboratories would continue to have cytology personnel perform the primary manual screen of all slides, but, in lieu of the random rescreen, the instrument, through computer algorithms, would select a 10% (or higher percent) subpopulation of negative slides which are more likely to be positive. The laboratory would still be responsible for review of high risk cases.

Both instruments were designed to reduce the false negative rate of Pap smears, but each instrument has different claims or functions supported by different research studies. The FDA expects timely approval of both instruments, and Dr. Gutman noted that PAP smear CLIA QC requirements may need to be reviewed for applicability to these and future systems.

### **Committee Discussion**

Several members commented on the use of these systems. Some committee members expressed concerns about delays in reporting results and the increased cost, but Dr. Gutman responded that the FDA does not consider cost effectiveness or compare the systems to one another. Another committee member was concerned about the potential for "off-label" use of the instruments. Dr. Gutman said that the products must have specific labeling that indicates the instruments are not to be used as primary screening devices. Another member was concerned about publicity or media control. She said that, due to media coverage, the public's concept is that false negative results are due to errors in reading PAP smears, when in fact many errors are due to inadequate specimen collection. Dr. Gutman stated that the FDA has clear authority to regulate promotion and advertising, but not television specials. Another member wanted to know the time frame for approval by the FDA. Dr. Gutman anticipated that, although plant inspections need to be performed, approval will occur in the next fiscal year. [*AutoPap received FDA approval on September 29, 1995; Papnet was approved on November 8, 1995.*] Another member asked if the data presented to the FDA is available to the public. Dr. Gutman replied that a transcript of the proceedings can be purchased.

Ms. Rhonda Whalen of the CDC set the stage for the Committee's deliberations on the framework, format and content of the final regulations. First, she reviewed the guiding principles of the CLIA regulations which are to assure quality testing, specify minimum standards, assure physician and patient access to testing and accommodate new technology. The most challenging task in developing regulations is accommodating emerging technology. Laboratory testing is constantly changing and the regulations should not be a barrier to innovation.

Provisions of the CLIA law provided the basis of the 1992 regulations. Standards were developed based on test complexity. The provisions in the law are broad and not specific with regard to the content of the standards for personnel, proficiency testing (PT) and QC. The CLIA regulations for personnel, PT and QC are considered to be interrelated, with quality monitoring activities incorporated into the quality assurance (QA) requirements.

In developing the 1992 CLIA regulations, experience with previous regulations and inspections was considered. In addition, the regulations incorporated input from the 50,000 comment letters and consultation received during the CLIA rulemaking.

In the CLIA regulations, QC is defined as the processes necessary to prevent and detect laboratory errors, and the function of QC is to monitor the **total testing process**, i.e. all the laboratory's activities in producing a test result, not just the analytical phase (test performance). The total testing process includes the environmental conditions involved in testing in the laboratory, as well as specimen manipulation, processing and handling.

In the QC regulations, there is a phase-in period for certain requirements applicable to unmodified, moderate complexity test systems cleared by the FDA through the 510K or PMA process. For these systems, basic minimum requirements were applicable for the first two years of regulation, which included provisions for laboratories to follow manufacturers' test system instructions and, in addition, perform some simple QC procedures. During this phase-in period, previously unregulated laboratories would gain experience with QC procedures and the FDA would develop the process for review of test system QC instructions for CLIA compliance. At the end of the phase-in period, the QC requirements would be the same for moderate complexity and high complexity testing. The phase-in, which was to end September 1, 1994, was extended in December 1994 to September 1, 1996 (59 FR 62606).



Ms. Whalen then compared the current QC requirements for moderate and high complexity tests. She described the relatively simple, basic requirements for laboratories performing unmodified, moderate complexity tests cleared by the FDA 510K or PMA process.

The next step in CLIA regulation development is to complete the rulemaking process initiated in 1992. In developing revisions to the CLIA regulations, the basic tenets (presented previously) used in developing the 1992 regulations would be considered, as well as the following:

- September 1, 1996 expiration of the QC phase-in for unmodified commercial, moderate complexity test systems.
- Comments to the February 28, 1992 regulations.
- Experience with inspections, training, review of accreditation and state program requirements, and public communication and correspondence. (For example, in July 1995 CDC convened a meeting of QC consultants to address many of the topics under discussion at this meeting.)
- Regulatory reform mandate to ensure that regulations are simple, understandable, cost effective and ensure quality, while imposing the least amount of burden.

Ms. Whalen then presented the CDC approach for revising the QC section of the CLIA regulations. The basic concept of monitoring the total testing process would be maintained. Changes would be made to the regulatory framework to simplify the structure and language of the regulation. A core set of requirements, which applies to all test systems, and a mechanism to deal with exceptions and alternatives would be established. In addition, improving the organization and names of the subparts and eliminating redundant requirements, where possible, would make the regulations more understandable. As an example, Ms. Whalen noted that some parts of the testing process (specimen handling, processing and manipulation) are included in the Patient Test Management subpart, which causes confusion, since the same topics are addressed under the procedure manual requirements in the Quality Control subpart. Also, some activities are inappropriately included in the Quality Assurance subpart.

### **Committee Discussion**

The Chairman asked how CLIAC could assist in regulations development. Dr. Baker said that CLIAC could provide suggestions and examples of regulatory approaches that have been effective, as well as ideas about how to reduce the

regulatory burden of the requirements. One committee member thought that the concept of monitoring the total testing process has been lost due to the structure of the regulation. She noted that the organization is confusing and said that QA is really quality improvement. She said that the parts of the regulation should be organized in a manner consistent with the testing sequence, beginning with the test requisition and ending with reporting test results. Another member agreed with this approach, but emphasized that the intent of the regulations should not be changed if the structure and wording are changed. He felt that test complexity is no longer an issue, but laboratories need to know what to do to comply with the regulations. He encouraged efforts to simplify the regulations. One member noted that most confusion about the regulations occurs in the low volume, moderate complexity laboratories and suggested that a “tier approach” would make the regulations more understandable. Similarly, another member commented that although the regulations should be “site neutral,” for ease of understanding, all requirements for physicians’ office laboratories (POLs) should be located in one section of the regulations. Another member stated that laboratories having the most difficulty understanding the regulations are the previously unregulated labs, which may have untrained personnel. He felt that educating personnel on how to comply with the regulations may be more important than changing the language in the regulations.

One committee member said that making the regulations more understandable was not the issue. He felt that CLIAC should challenge the rules instead of reworking them; he favored having as few rules as possible. Another member asked whether the regulations are working, and if the desired accuracy and reliability have been achieved. He said that studies are needed to determine this. In his view, through studies and data, it would be possible to determine which areas of the regulations should be less stringent and which should be strengthened. The data could show whether fewer or more controls are needed. There was some agreement that definitive studies are needed to support a change to less stringent requirements, and that it would be appropriate for manufacturers to financially support such studies. However, one member disagreed that data were needed to support a change to less stringent requirements. Another member commented that compliance with the regulations, i.e. fewer citations in the second cycle of inspections, does not necessarily correlate with laboratory improvement. The HCFA representative, Ms. Yost, responded that the survey process has identified some significant laboratory problems and that there appears to be a relationship between improved quality in laboratories that have fewer citations in their second cycle inspections. She also stated that PT data indicates improvement in laboratory performance in PT over time. A committee member noted that PT measures a process, not an outcome. Dr. Baker noted that CDC has research studies in

progress which measure outcomes. The Chairman suggested that a presentation of data illustrating whether there has been improvement in laboratory performance since CLIA implementation, would be a good topic for a laboratory institute or a future CLIAC meeting.

## **Public Presentations on Quality Control**

### **American Society for Microbiology (ASM)**

### **Addendum D**

Dr. Alice Weissfeld presented data from a recent survey of microbiology laboratories documenting the incidence of QC failures of some commercial reagents. Based on the survey results, the ASM recommended decreasing the frequency of QC testing for these reagents.

### **Committee Discussion**

Two committee members agreed that the ASM survey is valuable in collecting data, and such surveys could be used in areas other than microbiology. The chairman asked if a 22% response rate was considered an acceptable rate of return.

Dr. Weissfeld said yes, based on information received from marketing people since the survey was completed. She anticipated better returns on future surveys if CLIAC supports this type of data collection. She also noted that, if CLIAC supports the ASM recommendations to decrease the QC frequency of those reagents with low failure rates, the ASM would be willing to expand the survey to include additional reagents.

Dr. Baker commended the ASM on the data presented and asked the Committee for feedback on the utility of the data and whether the CDC should consider the ASM's recommendations for decreasing the QC frequency of these reagents. The Committee supported the ASM recommendations and was in general agreement that the regulations should be revised to reflect QC testing of microbiology reagents in accordance with frequencies suggested by the ASM. The Chairman concluded the discussion, stating that CLIAC encourages the ASM to conduct additional surveys as planned.

### **Bayer Corporation**

### **Addendum E**

Dr. Donald Parker reviewed the CLIA requirements related to the QC phase in for commercial, moderate complexity test systems (cleared by the FDA through the 510(k) or PMA process) and noted that the FDA will not be able to review manufacturers' QC instructions for CLIA compliance. Dr. Parker stated that the

Bayer Corporation believes that, if the FDA had been able to implement the CLIA review process, QC procedures acceptable for FDA clearance would also be acceptable under CLIA.

Dr. Parker explained that for some test systems, less frequent control testing is appropriate. He stated that the FDA has cleared moderate complexity test systems that have a QC frequency different from the CLIA requirements. In such cases, Dr. Parker outlined the Bayer proposal to allow laboratories to meet the CLIA requirements by following the manufacturers' QC instructions. Under the Bayer proposal, those laboratories performing tests not cleared by the FDA would be required to meet the current CLIA requirements (perform and document control procedures using at least two levels of control materials each day of testing). Dr. Parker stressed that today's technology supports the suggested change and presented arguments for Bayer's position using the DCA 2000 system as an example of alternative QC that should be acceptable under CLIA.

### **Committee Discussion**

Committee members questioned how laboratories would know about test system failures if QC checks were not performed. Dr. Parker responded that internal checks are included in systems to notify operators of test system failures. Several members were concerned about manufacturers determining the frequency of laboratory QC testing. Dr. Parker noted that manufacturers have data to support performance claims for testing QC at less frequent intervals than required under the current regulations and, in his view, laboratories should be allowed to follow manufacturer recommendations. One member expressed concern about relying totally on the manufacturer, stating that many laboratories would not be able to evaluate the manufacturer's data and make appropriate decisions regarding QC frequency. The same committee member asked Dr. Gutman if the FDA reviews, or will evaluate, the manufacturer's data supporting QC recommendations as part of the FDA clearance process. Dr. Gutman stated that the FDA review process has changed in the last few years, but the FDA does not review the manufacturer's data for CLIA QC compliance. He also noted that the FDA lacks resources to review manufacturers' data for QC compliance. He indicated that plant inspections by the FDA may be more important than the premarket review process, as FDA has observed that many failures occur when the manufacturer begins production. One committee member noted that ultimately the reliability of instruments must be determined by the user. Another member said he would not be comfortable with relying on QC procedures recommended by the test system manufacturer, if the test system was cleared by the FDA five to ten years ago.

Summarizing, the Chairman noted that the FDA does not have a process for review of manufacturers' QC procedures for CLIA purposes and suggested that CDC might consider the possibility of establishing some type of provision to allow alternative QC procedures when supported by manufacturers' data. Dr. Collins stated that reviewing QC procedures for each test system would be very labor-intensive and require resources not currently available at the CDC. However, she pointed out that many of the test systems might meet the requirements for the proposed APT subcategory, and QC review would be part of the evaluation for APT categorization.

## **PT, QA AND QC Subcommittee Report**

## **Addendum F**

Dr. Wendell O'Neal distributed and summarized the subcommittee report on the two issues considered and presented the following recommendations of the Subcommittee:

### **Requirements for test method verification**

- *The regulations should be descriptive, but not proscriptive. Requirements should be included in the regulations, but not protocols.*
- *Prior to reporting results on patient specimens, laboratories should, at a minimum, verify the accuracy, reproducibility and reportable range of the test method.*

### **Appropriate materials for QC testing**

- *Maintain the current requirement that two controls be tested per run, and that the regulations not specify the analyte levels in QC samples.*

### **Committee Discussion on Method Verification**

Dr. O'Neal noted the Subcommittee's concern about the definition of "accuracy" as it applies to verifying the performance of a test method and pointed out that a mechanism exists for including definitions in the regulations. A few CLIAC members suggested deleting from the test system verification section, the requirement to verify "(G) Any other performance characteristic required for test system performance" (42 CFR 493.1213). One member felt that it should be clarified that the verification requirements apply to the user, not the manufacturer. One committee member was under the impression that the test system verification requirements apply only to quantitative procedures. Another member thought that sensitivity and specificity should be verified. The CLIAC Chairman clarified the subcommittee recommendation that, in general, for moderate complexity test

systems, only accuracy, precision and reportable range, as stated on the manufacturer's label, need to be verified. He also stated that reportable range meant linear range as stated by the manufacturer. One committee member said that there are ambiguities in the requirements for verifying accuracy, precision, and reportable range and laboratories are receiving conflicting interpretations of the requirements from HCFA, CDC, accreditation organizations and State agencies. The Subcommittee's recommendation was intended to provide relief for the small laboratory by specifying the minimal user performance verification required for new test systems. The Chairman noted that CLIAC's recommendations are intended to provide guidance to CDC on the requirements to include in the final regulations, and emphasized that the Subcommittee does not recommend specifying in the regulations "how to" comply with the requirements.

Dr. Collins noted that the regulations were written to allow maximum flexibility, but that many labs, especially previously unregulated labs, want specific guidance that would include verification protocols. The Committee acknowledged that previously unregulated laboratories need assistance and was in support of providing guidance to laboratories for determining appropriate protocols to verify test method performance. In general, the Committee agreed that the regulations should specify what is required, with one member suggesting that the regulations include examples of protocols. Other members thought there should be a mechanism external to the regulations, for providing suggested protocols for verifying test systems. One member suggested including protocols in the HCFA State Operations Manual, while other members felt that PT providers, professional organizations or manufacturers should distribute guidelines or suggested procedures for test system verification.

#### **CLIAC Recommendation:**

- Accept the Subcommittee's recommendation to include in regulations the descriptive requirements but not specific protocols for meeting the requirements.
- Prior to reporting patient results, the laboratory should, at a minimum, verify the accuracy, reproducibility and reportable range of the test method.

#### **Committee Discussion on QC Samples**

Noting that the subcommittee members were not unanimous in the recommendation to maintain the current requirement to test two QC samples per analytical run, Dr. O'Neal agreed with another member's observation that probably all five subcommittee members voted as they did for different reasons. He stated that the Subcommittee's decision to maintain the current number of QC samples

was really a “default vote,” i.e. the Subcommittee did not have a reason or basis to justify a change. He noted that those who voted in favor of no change probably did so because they could not suggest a more appropriate number of QC samples, and were not in favor of deleting the requirement. He stated that perhaps a more appropriate alternative would evolve from the CLIAC discussion.

The Chairman began the discussion by asking for a vote on whether CLIAC would accept the Subcommittee’s recommendation to maintain the number of QC samples per run at two. The Committee voted **against** accepting the Subcommittee’s recommendation.

CLIAC members then discussed two alternative proposals to the subcommittee’s recommendation:

- The regulations should not specify the number of QC samples required; QC samples of appropriate number and frequency should be run to assure the detection of laboratory errors. The laboratory director is responsible for ensuring that appropriate QC is performed, and the laboratory must be able to demonstrate the basis for testing less than [or more than] two QC samples per run.
- Regulations should require laboratories, at a minimum, to follow the manufacturer’s QC recommendations. The number of controls needed to monitor test performance varies with circumstance and instrument, and the manufacturer can best determine appropriate QC procedures for each device. The laboratory director must be able to justify the reasons for **not** following the manufacturer’s QC instructions.

Discussion focused on whether the minimum number of QC samples per run should continue to be two, or be changed to require more or fewer QC samples. One member commented that QC activities cost money and that laboratories may be reluctant to increase the cost per test by performing QC. He noted that manufacturers have a financial incentive to reduce laboratory costs by eliminating or reducing QC. Another member stated that the number of QC samples should not be “zero.” Dr. Collins reminded the Committee that CDC had only asked CLIAC for input on whether the requirement to test two controls per analytical run, should be changed. One member asked about the definition of a “run.” Dr. Collins responded that according to the regulations, a run cannot be greater than 24 hours. The Chairman noted that in both proposals the laboratory director is responsible for the QC policy. There was general agreement that the two proposals could be reworded and combined as follows:

- QC of appropriate number and frequency must be run to assure the detection of laboratory errors.

One member wanted to add the phrase “in a timely manner,” but the idea was rejected due to the difficulty in defining timeliness. Another member wanted to change the phrase “laboratory errors” to “analytical errors,” but another member thought that would imply monitoring only the analytical phase, not the total testing process. One member pointed out that the purpose of running QC samples is to evaluate patient results and determine whether the test values are correct. Another member referring to a statement in the regulations, “control procedures are performed on a routine basis to monitor the stability of a test system,” noted that performing QC may not ensure the detection of laboratory errors.

Ms. Yost expressed concern about making the requirement less stringent and less specific when 35% of the laboratories surveyed by HCFA did not run two levels of QC or follow the manufacturer’s test system instructions. One member asked if these laboratories had established QC policies. Ms. Yost responded that most of the laboratories did not have policies, while some did not follow the established policies.

The discussion on the number of QC samples was tabled; it was suggested that CDC consider the points discussed by the Committee and, at a future meeting, present this issue along with supporting data reflecting the impact on manufacturers, laboratories and the public.

In a brief discussion about specifying analyte levels in QC samples, the Committee was in general agreement that producing this type of QC material would be expensive and difficult, if not impossible.

#### **CLIAC Recommendation:**

- Analyte levels for QC samples should **not** be specified in the regulations.

#### **Quality Control Limits**

#### **Addendum G**

Dr. Joe Boone, of the CDC, in discussing the requirements pertaining to QC limits, noted that although laboratories must assess test system accuracy and reproducibility or precision, there is no requirement for a laboratory to document the appropriateness of its QC limits. As determined during inspections, some laboratories have no criteria for establishing appropriate QC limits. In which case, the QC procedures of these laboratories may not be providing adequate patient protection. Dr. Boone presented the following issues for CLIAC consideration:



- Should laboratories be required to use acceptable protocols to document the basis upon which the QC limits are established?
- Should laboratories be required to periodically verify that their QC limits are comparable to other laboratories that use comparable test methodologies?

### **Discussion on Establishment of QC Limits**

Several members, in discussing the concepts presented, pointed out that laboratories are currently required to document performance of the general QC requirements and the laboratory director is responsible for ensuring appropriate QC practices. One member was opposed to including in regulations, a definition of acceptable QC limits. Another member noted that physician feedback was one way to monitor the appropriateness of QC limits.

One member asked if the problem is philosophical or practical. Dr. Boone responded that it is a practical problem, but that the extent of the problem is unknown. He said that if a laboratory sets its limits so broadly that the QC values are always within limits, performing QC would be pointless; conversely some laboratories set their limits too narrowly. A member thought that the requirements should not be increased unless there is data to support the change. Several members were concerned about the phrase “using acceptable protocols.” Dr. Boone indicated that establishing QC limits on the basis of medical usefulness criteria would be acceptable, but using PT performance criteria would not be appropriate.

### **CLIAC Recommendation:**

- Laboratories should be required to document the basis on which they establish their QC limits. The phrase “use acceptable protocols” was not included because such protocols would need to be defined.

### **Discussion on Verification of Comparability of QC Limits**

The Chairman thought it would be very difficult for POLs to verify QC limits with other laboratories. Another member agreed, stating that the databases don't exist and questioned the benefit of such a requirement. He also questioned whether the comparison should be based on methodology or clinical context. Dr. Boone said that this would be a measure of the laboratory's reproducibility and that laboratories needs to know if their reproducibility is not comparable to that of other laboratories using the same device. Some differences in variability would be expected in different clinical contexts. One member was concerned that this would shift the laboratory efforts currently involved in ensuring accurate testing to focus on

ensuring comparability with another laboratory. Another member had concerns about which laboratory should be used to verify comparability and questioned the burden and value of determining comparability for each analyte.

**Committee Recommendation:**

- Laboratories should not be required to periodically compare their QC limits to those of other laboratories using comparable methodology.

**Public Comments at End of CLIAC Meeting**

1. Michael Zelin, Vice-President of I-STAT Corporation, addressed the issue of developing regulations that are simple, yet flexible. He suggested that CDC look at the structure of the FDA's Good Manufacturing Practices (GMP) regulations and guidelines. The GMP defines the goals but not the "how to" for manufacturers. The guidelines include examples of how manufacturers may comply with GMP.
2. See Addendum H for statement and letter to the Secretary of the Department of Health and Human Services from the American Medical Technologists (AMT). Ms. Linda Cromeans, President of AMT, noted that the minimum standards of most certifying organizations exceed the CLIA personnel standards. The AMT feels that the recognition of private-sector certifying organizations would streamline the regulations without sacrificing testing quality. The American Association for Clinical Chemistry and the American Society for Clinical Laboratory Scientists have endorsed the AMT proposal and Ms. Cromeans stated that the AMT is unaware of any opposition.
3. Mr. Robert J. Slomoff, representing HemoCue, referred to Dr. Gutman's comparison of the FDA review process of OTC products and the CDC review process for waived devices, and the problems with harmonizing the technical requirements. He suggested that FDA, HCFA and CDC ask the Department's lawyers to review the regulatory construction from a practical point of view and to determine the types of devices approved for home use which might be granted waived status.
4. Richard Naples, Director of Regulatory and Government Affairs for Boehringer Mannheim Corporation, stated that a colleague, David Phillips, has submitted to the National Committee for Clinical Laboratory Standards (NCCLS) a proposal for development of guidelines for alternative QC procedures. A group of individuals met during the meeting of the American Association for Clinical

Chemistry in July and again at the Clinical Laboratory Management Association meeting in August to discuss alternative QC. He said that CLIAC, CDC and HCFA are dealing with similar issues and invited each agency to send a representative to the group's next meeting in October.

The Chairman suggested that minutes of the group be sent to the CLIAC members. [A copy of the minutes from the July 17, 1995 meeting was received after the CLIAC meeting and is in Addendum I.]

### **Concluding Remarks**

The Chairman presented certificates and letters of recognition to Dr. Stanley Inhorn, Dr. Paul Bachner and Ms. Virginia Charles, retiring members of CLIAC.

The Chairman ended the meeting, but asked CLIAC members to remain for a group picture.

I certify that this summary report of the August 30-31, 1995, meeting of the Clinical Laboratory Improvement Advisory Committee is an accurate and correct representation of the meeting.

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