Clinical Laboratory Improvement Advisory Committee

September 11-12, 1997

Summary

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Committee Members

Dr. Regina Benjamin
Dr. Thomas Bonfiglio
Dr. Lemuel Bowie
Dr. Mary Burritt
Dr. Ronald Cada
Dr. Patricia Charache
Dr. Susanne Gollin
Dr. Verlin Janzen
Ms. Diana Mass
Ms. Deborah McHugh
Dr. Glenda Price
Ms. Sharon Radford
Dr. Patricia Saigo
Mr. Elliott Segal
Dr. Ulder Tillman

Ex Officio Members

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

Liaison Representatives

Dr. Fred Lasky (HIMA)

Centers for Disease Control and Prevention

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

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. 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 CDC, thanked the Genetics Subcommittee which met on September 10.

Presentations and Committee Discussion

CLINICAL LABORATORY IMPROVEMENT AMENDMENTS UPDATE

Centers for Disease Control and Prevention

Dr. Carlyn Collins, Director of the Division of Laboratory Systems, PHPPO, reported that CDC has waived 10 test systems since the previous CLIAC meeting. She also said that a CDC study, which compares the work performance (screening Pap smears) of cytologists to their performance on glass slide and computerized proficiency testing (PT) has been completed and the data is being analyzed. Dr. Collins will report on the CDC cytology computer-based PT model at the upcoming meeting of the College of American Pathologists (CAP) and American Society of Clinical Pathologists. In addition, CDC and Mt. Sinai Medical Center have begun a demographic study of the nation's genetic testing laboratories.

Health Care Financing Administration (HCFA) Addendum A

Ms. Judy Yost, Director of Outcomes and Improvement, HCFA, discussed the HCFA reorganization that was effective on July 6, 1997, noting that the purpose was to make the agency more customer-focused. The CLIA program is in the Division of Outcomes and Improvement, Family and Children's Health Programs Group, Center for Medicaid and State Operations.

Ms. Yost then presented a status report on CLIA implementation. She indicated that approximately 87,000 physician office laboratories (POLs) now have CLIA certificates and noted their distribution by certification type. She summarized the numbers of laboratories accredited by the six HCFA-approved organizations, and noted that HCFA validation surveys of accredited laboratories indicate good performance by the accrediting organizations. Data on the four most frequently cited deficiencies in two cycles of routine surveys indicate improved performance by all laboratories in the second cycle, which Ms. Yost attributed to HCFA's educational approach to surveys. She noted that POLs have a higher percent of deficiencies than all other types of laboratories combined. Ms. Yost said that HCFA proposed enforcement actions for approximately 1,000 of 10,000 laboratories surveyed from January through July, 1997. About 600 technical assistance actions (requiring laboratories to obtain training and technical assistance to improve performance) were proposed for initial unsuccessful proficiency testing (PT) performance. About 200 enforcement actions were imposed, including 179 technical assistance

actions for unsuccessful PT performance. Only seven actions were imposed as a result of "immediate jeopardy" situations. It was noted in discussion that although the number of laboratories in HCFA Region IX with proposed and imposed actions is high, this region has a large number of laboratories, and the proportion of laboratories with proposed and imposed actions is only slightly higher than other regions. The Laboratory Registry for calendar year 1996 listing the enforcement actions taken against approximately 107 laboratories (includes 50 POLs) is now available. Ms. Yost noted that laboratories with multiple actions may be counted more than once and the number of actions taken for POLs is not disproportionate.

In 1996, about 1700 laboratories completed the alternative quality assessment survey (AQAS), a self-survey process designed for laboratories with acceptable on-site survey performance and successful PT performance for the previous year. Laboratories performed well on the AQAS which was verified through on-site surveys.

Outcome-oriented on-site surveys were implemented by HCFA in 1996 to focus on the laboratory's quality assurance instead of using the CLIA requirements as a checklist. Surveyors look at outcomes, primarily the laboratory's results, but also the potential risk of harm to a patient. A pilot survey of participant laboratories indicated that most laboratories appreciated the educational approach to the survey process.

To receive Medicare and Medicaid payments, laboratories must meet CLIA requirements, be certified appropriately, and pay their CLIA fees. In July 1997, HCFA initiated denial of Medicare and Medicaid payment for POLs that bill beyond the scope of their CLIA certificate (e.g. seek reimbursement for moderate complexity testing but are certified to perform only waived testing) or do not meet CLIA requirements. Incorrect coding of tests for billing was a frequent occurrence. Most laboratories agreed to correct problems; only laboratories that refused to correct problems were denied payment.

Ms. Yost reported that the Fee Schedule Revision Notice was published in the Federal Register on August 29, 1997. Effective January 1, 1998, certificate fees for laboratories will increase in proportion to the number of tests performed. Ms. Yost explained that CLIA requires user-fees to support the total cost of the CLIA program which is $38 million/year; currently HCFA collects only $25 million/year. Ms. Yost provided reasons for the shortfall: (1) fewer total laboratories (less than 150,000) than projected; (2) more laboratories perform only waived testing (49%) than projected; and (3) no start-up money appropriated for CLIA.

Prior to increasing fees, CLIA program costs were decreased by reducing administrative costs, limiting or delaying studies and a personnel hiring freeze. An attempt was made to increase income by prebilling for surveys, but has been abandoned. To eliminate the shortfall in revenues and comply with the CLIA statute requiring that the program be self-funded, the certificate fees for laboratories are being increased. Ms. Yost noted that this is the first fee increase since CLIA implementation in 1992 and is consistent with the intent to equitably distribute the cost of CLIA

among laboratories and maintain site-neutrality. Many laboratories have recently paid their certificate fees and will not be affected by the increase until the next billing cycle (almost two years).

Commenting on the delay of publication of the Final, Final Regulation, Ms. Yost said HCFA and CDC are focusing on genetic testing, proficiency testing, and quality control issues that need to be resolved.

Committee Discussion:

One CLIAC member asked how many POLs had been denied payment since HCFA initiated denial of Medicare/Medicaid in 1997, and Ms. Yost replied 400.

Most of the discussion focused on the costs related to CLIA program administration. Ms. Yost and Dr. Baker explained that the fee increase was an attempt to balance CLIA revenue and costs. Ms. Yost noted the $38 million annual cost of the CLIA program, which includes 150,000 laboratories is comparable to the $160 million annual cost for HCFA to regulate 30,000-40,000 other healthcare providers and suppliers. She indicated that HCFA is sensitive to the impact on small laboratories and stated that for waived and provider-performed microscopy laboratories, the certificate fee increase means an additional cost of $ 0.07 per day. Certificate fees from these laboratories are used to cover ongoing program expenses, such as registration of laboratories, review of tests for waiver, and designing and maintaining a comprehensive data system. Noting that 50% of the cost of CLIA can be attributed to performing surveys, one committee member asked how the remaining 50% is allocated. Ms. Yost said that it is split equally between HCFA and CDC and covers all remaining CLIA costs, including: test categorization; regulations development; data system support; approval of PT programs, exempt states and accreditation organizations; and development of survey processes.

Ms. Yost clarified that accredited laboratories are issued CLIA certificates, while laboratories in exempt states are not. Accreditation organizations are not assessed a fee; certificate fees from accredited laboratories cover CLIA administrative costs associated with accredited laboratories. In CLIA-exempt states, the laboratories are not assessed a fee, but administrative costs are paid to HCFA by the states. One committee member commented that fees paid by laboratories to one accreditation organization are about 1/3 of the cost of a CLIA certificate.

GENETIC TESTING

Dr. Claire Broome, Deputy Director of CDC, welcomed the CLIAC members and thanked them for their consultation and advice. She then announced that, according to newspaper reports,Dr. David Satcher, Director of CDC, will be nominated by President Clinton to become the Surgeon General and Assistant Secretary for Health.

Noting that CLIAC has provided consultation and recommendations to improve the quality of laboratory testing while preserving access to testing, Dr. Broome said that genetic testing will be very challenging for CLIAC. She commented that, although medical researchers understand statistical concepts such as accuracy and precision, we need advice from CLIAC on converting genetic testing results into clinical information that is meaningful to physicians, legislators and others who may not be familiar with these laboratory measurements. In conclusion, she said that the Department will need and welcome advice on regulating genetic testing and methods of monitoring performance.

Overview of Genetic Testing **Addenda B-C**

Dr. Muin J. Khoury, Chairperson of the CDC Task Force on Genetics in Disease Prevention, presented an overview of genetics in human disease (See Addendum B). He referred to the Online Mendelian Inheritance in Man (a catalogue of human genes), noting that many genes are associated with each clinical condition, and the HELIX database (contains DNA-based genetic tests used in medical practice). He presented the definition of genetic testing developed by the National Institutes of Health (NIH)-Department of Energy (DOE) Task Force and noted that the definition excludes tests performed for research, somatic mutations, and forensic purposes.

Dr. Khoury presented reasons that genetics is a public health issue, and specifically a CDC issue. He said that the biggest public health concern in genetics is inappropriate use of genetic information in medical and public health practices without validation. A major role of CDC is to prevent the inappropriate use of genetic testing as this testing is integrated into medical practice. Dr. Khoury explained the scope and underlying assumptions for the CDC Strategic Plan for Genetics and Disease Prevention, which is currently in the Agency's clearance process. The focus was that certain diseases result from genotype-interaction. In people with certain genotypes (e.g. PKU), disease, death, and disability can be prevented by the use of medical, behavioral, and/or environmental interventions. However, genetic testing is moving ahead of intervention (e.g. no intervention known to prevent development of breast and ovarian cancer).

In deliberating the role of public health in genetic testing, the CDC Task Force on Genetics in Disease Prevention developed a framework of program functions and issues critical to the success of each function and seven goals for the strategic plan. Dr. Khoury said that new genetic tests must be subjected to analytical and clinical validation studies, and data must be collected and examined for clinical utility. The NIH-DOE Task Force recommended that CDC, in collaboration with other State and Federal Agencies and private organizations, should play a coordinating role in data gathering. In addition, the newly created CLIAC Genetics Subcommittee should consider the creation of a genetic specialty or subspecialty under CLIA.

Then Dr. Khoury described the objectives under Goal 4, "Ensure the appropriateness and quality of population-based genetic testing," and presented recommendations from the NIH-DOE Task

Force and the CDC Task Force to expand activities to ensure the quality of genetic testing, which included the establishment of a Genetics Subcommittee to advise CLIAC.
[Note: See Addendum C for draft of CDC Task Force report.]

Genetics Subcommittee Report **Addendum D**

Dr. Wendell O'Neal summarized the activities of the first meeting of the Genetics 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. Richard Jackson(CDC); Dr. Steve Goodman, (American College of Medical Genetics); Dr. Ann Willey (State of New York); Dr. Pat Murphy (GYNEWISE); and Dr. Henry Travers (College of American Pathologists). The presentations included suggestions to the Subcommittee for topics of discussion, which varied from "testing is testing", i.e. genetic testing is like any other clinical testing and should be included under the existing CLIA regulations, to genetic testing is so unique (based on the implications of testing) that a new subset of regulations should be developed. Dr. O'Neal then presented to CLIAC the issues that the Subcommittee felt should be discussed at future meetings (See Addendum D).

Committee Discussion:

The Committee noted the following:

1. Defining genetic testing and what tests to regulate is a challenge. A single test may or may not be a used exclusively as a genetic test. Tests for gene DNA and messenger RNA would be considered genetic tests.
2. Genetic testing is different because it can impact the rest of one's life. Societal implications are great.
3. Many geneticists don't think CLIA covers genetic testing appropriately.
4. Some metabolites, already regulated under CLIA, have genetic implications.
5. Regulations must have the flexibility to address future testing.
6. The physician may not know what tests to order or how to interpret the results.
7. There must be sufficient resources to educate medical professionals and the public.
8. Patient test management should include pre- and post-analytical phases to address privacy and archiving of samples.
9. Many laboratories use "home-brew" reagents, probes, and primers that are not cleared by the FDA.

Several committee members asked about the applicability of CLIA to genetic testing. Dr. Collins responded that testing on human specimens for diagnosis and treatment falls under CLIA. She also pointed out that under the statute, we don't have the authority to treat a test differently based on context or utility, e.g. diagnosis vs. screening.

Several CLIAC members noted that sometimes it is difficult to determine whether genetic testing is being performed. Drs. Schwartz and O'Neal noted that billing may be a mechanism. Ms. Yost

responded that some laboratories may perform genetic testing and provide test results to clinicians and not bill even though these laboratories are subject to CLIA.

Committee members noted that it would be advisable to collaborate with other groups, agencies, etc. that have some role in genetic testing.

Public Comments on Genetic Testing **Addenda E-F**

The following individuals made public presentations:

1. Russel K. Enns, Vice-President of Regulatory Affairs at VYSIS, Inc. (See Addendum E).
2. Barbara Beninato, Laboratory Manager at the Family Practice Center in Rome, GA, and Technical Consultant for Centrex, a physician management company, presenting on behalf of American Society of Clinical Pathologists (See Addendum F).

WAIVER OF FDA-APPROVED HOME TESTS

Background Information **Addendum G**

Dr. Schwartz explained that the presentation on prescription home use was for information only and no recommendations would be accepted.

Dr. Collins reviewed the waiver criteria in the law and the 1992 CLIA regulation pertaining to waived testing (See Addendum G). She said that one example given in the law as a type of test that could be considered for waiver was FDA-approved home use tests. She noted that the preamble to the 1992 regulation clarifies that FDA home use clearance "cannot be a sole criterion for qualifying as a waived test, since all home use tests may not meet the criteria for a waived test." She reviewed the involvement of CLIAC in the waiver process, noting that CLIAC recommended: (1) clarification of the criteria for waiver; (2) a moratorium on approving tests for waiver until waiver guidelines were established; and (3) harmonization of the CDC waiver approval and the FDA home use clearance processes.

Dr. Collins reported that a moratorium was imposed and then lifted when the waiver guidelines were developed, and the CDC and FDA processes have become more congruent. The guidelines CDC has been using to approve tests for waiver were published in a proposed rule in September 1995. Under the guidelines, FDA-approved home use tests are being approved for waiver. In March 1997, the FDA cleared two devices for "home use with prescription."

"Prescription Home Use"

Dr. Steve Gutman, of the FDA, said that more than 300 in vitro diagnostic (IVD) tests have been cleared for over-the-counter (OTC) use since the passage of the Medical Device Amendments to the Food, Drug and Cosmetic Act in 1976. According to an OTC guidance document published by the FDA in 1988, manufacturers must: (1) perform field studies that demonstrate that lay

users of an OTC device produces results equivalent to those produced by laboratory professionals; (2) perform clinical evaluations which demonstrate that test results are interpretable by the lay user; and (3) demonstrate that the benefits of home use outweigh the risks of testing. A major issue in the FDA's review of OTC devices is whether labeling information can be clearly communicated to lay users and would be expected to lead to actions which promote personal or public health and minimize harm.

Prior to 1997, the 300 OTC devices cleared by the FDA included only seven categories of tests: blood glucose, cholesterol, fecal occult blood, pregnancy, fertilization, various dipstick urine analytes, and certain collection devices. In early 1997, after review panel meetings and extensive evaluation of analytical and clinical data, the FDA cleared for home use two tests for new analytes: one test system for fructosamine and two test systems for prothrombin time. Home use approval of the prothrombin tests is considered a milestone, since these tests are believed to provide unique benefits (improved anticoagulant status and patient outcomes) and pose some risks (testing and dosing errors). Clinical experience with home prothrombin time testing in Europe has demonstrated the benefits, and the American manufacturers of these tests will perform post-market studies to assess the performance of these devices over time. Because of the potential for unique benefits and risks, the FDA proposed, the FDA review panel supported, and the device sponsors accepted the designation of this category as "prescription home use" (instead of OTC home use). This designation of the prothrombin tests as "prescription home use" is the first application of this home use restriction specifically for in vitro diagnostic products. For tests designated as prescription home use, the physician is responsible for: (1) selecting patients who are appropriate candidates for home use testing; (2) appropriate training of the patient and oversight of the home testing system; and (3) dosing changes which might occur due to home test results. The FDA anticipates an increase in the number of products submitted for home use approval and expects that this new application of prescription home use to IVD products will allow clearance of a wider variety of devices for patient use.

Dr. Gutman said that although progress has been made in harmonizing the requirements for home use clearance with approval of waived tests, there are still differences. The FDA uses an equivalency determination to clear devices for marketing while the CDC uses a standards-based approach in determining that waived tests are both simple and accurate. The agencies are continuing to address the differences in the processes.

Dr Collins then reemphasized that Dr. Gutman's presentation was informational and that no recommendations are currently solicited from CLIAC. She anticipates bringing additional information about the home use with prescription category to a future CLIAC meeting and requesting input from the Committee at that time.

Committee Discussion:

Committee members raised a number of concerns about the potential waiver of prescription home use tests:

1. The need for educational information to be attached to the product and a mechanism to assure that the labeling is read by the patient.
2. Responsibility for safety issues, e.g. needle disposal.
3. Prescription home use testing places considerable responsibility on the physician, but some aspects of testing are out of the physician's control, e.g. one patient might use another person's device/test kit.
4. If a patient changes physicians, whether patients should return the prescription home use device to the prescribing physician.
5. The impact of the prescription home use devices on the required reporting of infectious agents by the physician.
6. If a prescription home use test were not waived, a physician would be required to perform the test in his office laboratory under the CLIA requirements for moderate or high complexity testing.
7. The FDA's definition of clinical equivalency.
8. Whether CDC accepts less imprecision in the waiver approval process than FDA accepts in the OTC clearance process.
9. The status of the final waiver rule.

A major concern of CLIAC members was the extent of a physician's liability if a patient suffered an adverse event as a result of using a prescription home use IVD device. Members wanted assurance that the Committee would have an opportunity for future in-depth discussions on prescription home use and other waiver issues. Dr. Schwartz agreed that CLIAC should consider these issues and noted that lengthy discussions on the difference between a patient's use of an IVD product at home and professional use of the device in an institutional setting occurred when CLIAC discussed glucose meters. Dr. Baker commented that CLIAC has previously used the test categorization subcommittee to have in-depth discussions on similar issues.

Several CLIAC members were confused about why there could be no discussion on this issue. Gene Matthews, CDC legal advisor, explained that because there was inadequate time to give the required notice and have a full discussion of the issues, the Committee must not engage in deliberations at this time.

Dr. Schwartz commented that, because prescription home use is different from the usual home use category, the Committee needs to reassess the waiver process.

Public Comments on Prescription Home Use Presentation **Addendum H**

The following individuals made public presentations:

1. Frank M. LaDuca, Ph.D., Vice-President of Clinical and Regulatory Affairs, International Technidyne Corporation (See Addendum H)

2. Brad Thompson, partner in Indianapolis law firm Baker & Daniels

Mr. Thompson was concerned that any discussion of prescription home use had occurred. He had understood that the presentation would be for information only, since the Federal Register Notice was not published 15 days prior to the meeting as required by law to allow all interested parties to participate. Because of the short notice, it was impossible for several interested physician groups and manufacturers to attend the meeting. Mr. Thompson felt the views presented by Dr. Gutman were very important, but cautioned CLIAC members not to form opinions on the prescription home use category until the views of all interested parties could be presented.

At the conclusion of Mr. Thompson's presentation, several Committee members expressed concern about not being able to discuss the prescription home use category and one Committee member said that CLIAC should have been informed in the beginning about the need to preclude discussion.

MEASURING CLIA EFFECTIVENESS

CLIA Research Update **Addendum I**

Dr. Thomas L. Hearn, Chief of the Laboratory Practice Assessment Branch in the Division of Laboratory Systems at CDC, discussed three projects which were nearing completion: the Cytology Study evaluating computer and glass slide proficiency testing (PT) and comparing this PT performance to cytology work performance (screening patient slides); Quality Assurance Practices in Molecular Genetics Laboratories; and a National Laboratory Inventory Study which collects information on a sample of laboratories nationwide, on-site, to document the type of tests, the test methods and the volume of tests that are currently being performed. Demographic data were shown to provide a perspective on the different populations of laboratories being studied. Other reported research findings include: PT results and their correlation with routine performance; PT performance improves with experience; external quality control (QC) improves performance; the testing process is not error free and laboratory problems do have negative consequences. The issues of quality and access were addressed relative to the question, "Have improvements in health care occurred as a result of CLIA?" in the National Ambulatory Medical Care Survey (NAMCS) carried out from 1989-1994. NAMCS is a national random sample of physicians who were interviewed regarding on-site laboratory testing within their practices. Evaluation of the survey indicated the type of practice (solo vs. joint), the specialty of the

physician, the volume of testing being performed within this random sample group as a whole as well as looking at volume of testing in solo vs. joint practices. Laboratory quality indicators were assessed relative to: PT enrollment, QC being used each day of testing, and written instructions used if QC exceeds the limits of acceptable results. The NAMCS provided data regarding the percentage of physicians performing one or more of 19 tests. This survey, between 1989 and 1994, indicated little if any change in on-site testing for a select set of tests. Results since 1989 showed that there has been a steady increase in enrollment in PT. There has been a slight increase in the use of quality control and written instructions, if the QC suggests an error, by individuals performing laboratory testing in physician office laboratories (POL's) since 1989. It was concluded that access, cost and quality are important and that multiple approaches are required for CLIA impact measurements while confounding variables must be controlled. Additionally, since 1989 there has been a decrease in POLs performing on-site testing, while improvements in quality are documented through increased use of PT and QC. Finally, the surveillance of the laboratory practice is critical for effectively responding to changes in the health system.

HCFA Surveys

Ms. Yost commented on improved laboratory performance in the second cycle surveys, which she attributed to HCFA's educational approach to inspections. The low number of HCFA enforcement actions has had no effect on the access to laboratory testing. Although some laboratories may have decreased testing when problems were found in on-site surveys, HCFA data since the implementation of CLIA indicate no net change in the number of laboratories or the number of tests performed. Also since 1993, the number of tests billed to Medicare by physicians and Medicare payments to physicians have increased by at least 10%. There has been an increase in the number of waived laboratories and the number of waived test systems; many tests performed in POLs are waived. Ms. Yost then noted that DHHS has made and will continue to make changes in the CLIA regulations to accommodate changes in laboratory practice. The Department will continue to respond to changes and will solicit the input of organized medicine and private and professional laboratory groups in order to develop the best standards possible. HCFA intends to increase the use of quality indicators and performance improvement measures to determine laboratory quality.

Noting that the survey is critical to the CLIA process, Ms. Yost introduced two HCFA regional laboratory consultants who reported on some of their experiences as surveyors.

Karalou Eastmo, from the Denver regional office, related observations about failures in proficiency testing and corresponding incorrect reporting of patient results in chemistry, bacteriology, and hematology. Ms. Eastmo observed that such problems often occurred in laboratories where the laboratory director lacks actual testing experience and the testing personnel lack technical knowledge and experience, or there are continual changes in the staff. The Denver region includes about 5,000 laboratories in six western states. Although the region is primarily rural, access to testing does not seem to be a problem. Responses to a State of Colorado post-CLIA survey questionnaire indicate: (1) satisfaction with the conduct of the survey, the quality of

information from the surveyors, and the quality of reports to the laboratory after the survey; and (2) the educational survey approach is beneficial.

Ruth McArthur made some observations from CLIA inspections in the Atlanta Region. This region is composed of eight southeastern states, and contains a large number of rural, urban, and medical center laboratories. She agreed with the Denver regional consultant that laboratory problems are often due to personnel turnover. She noted that in Georgia, State regulations and CLIA regulations are fairly congruent and one inspection is adequate for both sets of requirements. In addition, Ms. McArthur reported an increase in calls from physicians requesting information on test methods and establishing laboratories, and from consumers reporting potential laboratory problems. She felt this indicated increased awareness of the services provided by the HCFA regional offices.

Committee Discussion:

A committee member asked what percent of laboratories had the problems reported, and Ms. McArthur replied about five percent. Several committee members expressed concern about problems with personnel turnover and training. One CLIAC member felt that the CLIA personnel standards are too lenient. Another noted that laboratory education is needed for directors, in addition to testing personnel. Dr. Schwartz commented that professional organizations are promoting laboratory education for physicians. Commenting on the impact of managed care, one CLIAC member indicated that some data is available on the proportion of laboratory tests performed in POLs, and the impact of managed care on the number of POLs performing laboratory testing.

One CLIAC member felt that access to testing is still a problem in rural areas in the Denver region, and another asked how it was determined that the availability of testing is adequate. Ms. Eastmo replied that the number of laboratories under CLIA had remained constant. Another CLIAC member reported that, since the advent of managed care, 15-18% of physicians no longer perform their own laboratory tests.

Impact of CLIA in California **Addenda J-K**

Dr. Paul Kimsey, Assistant Director for Laboratory Science in California, presented inspection data on condition-level deficiencies compiled by California (See Addendum J). For POLs and non-POLs inspected by the State (accredited laboratories are not included), the number of condition-level deficiencies has declined yearly from 1993 through the first half of 1997.

Dr. Lee Hilbourne, Chairman of the California Clinical Laboratory Technology Advisory Committee, presented the background and preliminary results (See addendum K) from the first of a three-part POL study mandated by the California legislature in 1995. Statistically significant differences exist in proficiency testing (PT) performance in 1996 between POLs which did not employ licensed clinical laboratory scientists (CLS) for laboratory testing, POLs which employed

licensed CLS, and non-POLs which employed licensed CLS. The results are similar to those of a CDC study using 1994 PT data, and suggest that further revisions in laboratory personnel requirements might best await the results of additional definitive studies.

Committee Discussion:

In discussion, several parameters of the POL studies were clarified. California defines POLs as physicians or physician groups (five or fewer physicians) performing tests on their own patients. The non-POL category may contain laboratories operated by more than five physicians. PT data for 1996 in the California study looks worse than the CDC study using 1994 PT data, but the 1996 data might indicate improved performance if it were compared to pre-1996 data. When CLIA standards were accepted by California in 1995, personnel requirements for POLs became less stringent, prompting the California legislature to require POL studies. PT data was from only one provider; the trends observed may vary with other PT providers; and criteria for some analytes varies with the PT provider. Performance on PT samples may not accurately reflect performance on patient samples. Ms. Yost commented that laboratories with more years of participation in PT tend to improve and maintain good performance, and therefore the year of enrollment in PT may be a significant issue. She also noted that education is always available from the state survey agencies.

American Medical Association (AMA) Analysis of CLIA **Addendum L**

Dr. Palma Formica, a member of the Board of Trustees of the AMA, presented preliminary analysis of data from a recently completed AMA-developed electronic mail survey of physicians regarding the impact of CLIA on their practices and the quality of patient care. The AMA participated in two CLIA impact surveys published in 1992 and 1995, and Dr. Formica reported that the results of the third survey confirm results from the earlier surveys. In response to CLIA, physicians have reduced office testing and as a result the cost of testing and patient inconvenience have increased. She said that the common theme, the perception of physicians that quality of care has not improved under CLIA, appearing in all of these studies should be of interest to CLIAC.

Committee Discussion:

One CLIAC member, who had reviewed the 1992 and 1995 impact studies, felt strongly that all three studies are severely biased (especially in the area of patients referred elsewhere for laboratory tests) and are contrary to the AMA's desire to produce reliable data. She suggested that the AMA should collaborate with CDC and the state health departments in formulating an unbiased physician questionnaire to generate reliable data to be shared with policy makers and the community. Dr. Formica responded that the AMA is dedicated to scientifically valid information, could certainly reevaluate the most recent study, and would be willing to consider working with CDC or other organizations in future surveys. Dr. Baker said that CDC would welcome the opportunity to collaborate with the AMA.

Other CLIAC members questioned the AMA's statement that CLIA is a barrier to quality care. One committee member asked if there is documentation to show that the testing eliminated is quality testing. Several members felt that the report should state more clearly that the results are preliminary. Noting that managed care has mandated that tests be referred, another CLIAC member said that the report seems to imply that laboratories would resume tested if CLIA goes away. Dr. Formica agreed that this would probably not occur. Another committee member said that many POLs have eliminated the QC and PT costs associated with on site testing by referring testing off site, and noted the expenses associated with referring specimens for testing. Drs. Baker and Schwartz asked the AMA to provide a dollar figure for the perceived additional costs due to CLIA quality requirements. Another committee member felt that CLIAC has failed to educate physicians about the value of CLIA. Dr. Schwartz noted that COLA has been effective in educating physicians and CLIAC needs data on costs. Emphasizing the preliminary nature of the report and the AMA's offer of collaboration, Dr. Schwartz concluded that in the future there should be a survey of physicians that provides reliable data on the impact of CLIA.

Impact of CLIA in Washington State **Addendum M**

Ms. Martha Simon, Director of the Office of Laboratory Quality Assurance, presented results from two studies of Washington's medical test site licensing program and from a Washington/CDC cooperative agreement study. She noted that Studies I and II include survey data only from previously unregulated laboratories. She also indicated that the increase in the percent of serious deficiencies observed in the second cycle of surveys was due to a change in medical test site rules which brought previously waived tests under regulation. She said that the number of uncorrected deficiencies and problems with PT enrollment observed in second cycle surveys indicate a need for continued on-site surveys and educational programs.

Ms. Simon also presented examples of serious deficiencies observed during surveys, emphasizing those related to inadequate staff training. She noted that Washington has an on-going training program and that surveyors also serve as consultants.

Ms. Simon presented results from the Washington/CDC cooperative agreement study, which includes data from 1/3 of all laboratories inspected in Washington. She note that the percent of serious deficiencies did not decrease significantly between the first and second cycles. Ms. Simon explained that the plateau in the percent of serious deficiencies observed in the second cycle surveys is due to the number of new laboratories coming under regulation and to laboratories that have added new tests.

Ms. Simon also reported on the percent of discontinued tests and changes in test volume between first and second cycle inspections and the reasons for the changes, noting that laboratories in the cooperative agreement study ranked "regulations" as the third most common reason for discontinuing tests and the fifth most common primary reason for decreases in test volume.

Overall since 1993, the number of medical test sites in Washington has increased about 10%, and the number of sites performing waived/physician performed microscopy testing has increased, while the sites performing moderate and high complexity testing has decreased. Ms. Simon considered this an indication that CLIA has not resulted in decreased access to laboratory testing.

Committee Discussion:

In response to a previous question, Ms. Simon presented some information on fees for various laboratory categories and noted that the single fee for each category includes the inspection fee and the certificate fee. In discussion, it was noted that Washington physicians are updated on waived tests via a monthly newsletter.

Update on Waiver Approval and Test Categorization **Addenda N-P**

Dr. Schwartz noted that the update on the waiver process was being presented in response to a CLIAC request.

Ms. Rhonda Whalen of the CDC presented background for the test categorization and waiver processes (See Addendum N). She first reviewed the CLIA law and the criteria in the regulations for categorizing moderate and high complexity tests. She noted that CDC has categorized (moderate or high complexity) about 20,000 test systems, test complexity is determined concurrently with FDA clearance, and that categorizations are available on the Internet (See Addendum O).

She then reviewed the provisions in the CLIA law regarding waived tests (noting difficulty interpreting the phrase "insignificant risk of erroneous result"), the criteria for and the list of waived tests in the 1992 CLIA regulations. She noted the similarities between the waived analytes and the types of tests cleared by the FDA for home use. In response to the concerns about the waiver criteria and the limited number of waived tests, CLIAC recommended that CDC clarify the statutory criteria for waiver and declare a moratorium on waiving additional tests.

In response to the CLIAC recommendation, a moratorium on approving tests for waiver was imposed. In December 1994, interim waiver guidelines clarifying the waiver criteria were distributed to manufacturers of moderate complexity tests (See Addendum P). A proposed rule was published in September 1995 which included the waiver guidelines. Under the guidelines, FDA approved home use tests are granted waiver (CLIAC had recommended harmonization of the CDC waiver and the FDA clearance processes). Under the interim guidelines, studies are required to demonstrate that the waiver criteria for simplicity and accuracy are met. Highly accurate tests are considered to have an "insignificant risk of erroneous result". Ms. Whalen reviewed the steps in the waiver process and noted that the average time for CDC to make a waiver determination is three to six months and the average time from receipt of application to waiver decision is nine to twelve months. She also noted that, since the implementation of the interim waiver approval test, the number of waived test systems has tripled, and the number of

waived analytes has doubled. In addition, nine of 10 most commonly performed POL tests are waived. Currently there are 475 waived test systems which include 16 analytes; there are 14 test systems that have not been approved for waiver and 16 test systems are pending a waiver decision. Ms. Whalen noted that CDC is continuing efforts to make the waiver process more efficient, and the final waiver regulation is under development.

Committee Discussion:

One CLIAC member asked why the 14 test systems were not approved for waiver and Ms. Whalen responded that they failed to meet the waiver criteria for simplicity and accuracy. Another CLIAC member was concerned about ensuring that the users of certain glucose meters follow the instructions in the labeling for the interpretation of results. Ms. Whalen replied that, for waived tests, CLIA requires the user to follow the manufacturers instructions, but the requirement is not generally enforced because waived tests are not routinely inspected.

Responding to a question about costs, Dr. Collins clarified that manufacturers pay for the studies required to meet the waiver criteria, while the cost of data analysis by CDC is covered by CLIA user fees. The importance of harmonizing the requirements for CDC waiver approval and FDA home use clearance was emphasized by the Health Industry Manufacturers Association liaison, who commented that a labeling change required by CDC might require a resubmission to the FDA. He also said that manufacturers are anxious for publication of the final waiver rule and noted that controversy about the waiver approval process has decreased because manufacturers are now aware of the waiver requirements while test systems are in the design phase.

Health Industry Manufacturers Association (HIMA) Analysis of CLIA Addendum Q

Ms. Carolyn Jones, representing HIMA, presented a summary of information gathered in an informal survey of HIMA members and non-members and reported results about the negative impact of CLIA on POL testing from a study conducted by the Wilkerson Group. HIMA recommended that: (1) CDC develop review criteria for waived status that are clearly articulated and reasonable and do not change the intent of CLIA; (2) the waiver process not duplicate FDA's premarket review requirements; and (3) CDC establish a clear-cut process for handling recategorization requests. In addition, there must be constructive dialogue between CDC, FDA, manufacturers and healthcare providers to accomplish these goals.

Committee Discussion:

The CLIAC Chairman asked if HIMA has data on the cost for a laboratory performing only waived tests to initiate moderate complexity testing. Ms. Jones replied that HIMA does not have this information. Dr. Schwartz commented that the cost per test has decreased in a large healthcare institution. The CLIAC manufacturers' liaison clarified that the information in the HIMA report applies only to small test sites, and said that costs in large institutions has not

increased due to CLIA because these laboratories were already meeting requirements equivalent to CLIA.

Public Comments **Addenda R-S**

The following individuals made public presentations:

1. Alice Weissfeld, Director of Microbiology Specialists Incorporated, on behalf of the Coalition to Preserve Safe Patient Testing (See Addendum R).

2. John A. Boffa, American Association of Bioanalysts, suggested that a change should be made in the CLIA regulations so that a patient could order his/her own laboratory test, i.e. would be included in the "persons authorized by law." He thought that "self-referral" should be available for waived, home use or prescription home use tests.

3. Judy Davis, Chair of the Government Affairs Committee, the American Society for Clinical Laboratory Science (See Addendum S).

Summary of Quality, Cost, And Access Issues From Presentations

Dr. Schwartz briefly summarized the viewpoints of the presenters on the impact of CLIA on laboratory testing quality, cost and access. Noting the variety of viewpoints and that some were based on strictly anecdotal data, he said that it was impossible for CLIAC to draw conclusions on the impact of CLIA. He said that CDC should proceed to design and implement scientifically valid studies on the impact of CLIA, and the results should be presented to CLIAC for evaluation.

CONCLUDING REMARKS:

Dr. Schwartz announced that the dates for the next CLIAC meeting would be January 29-30, 1998, preceded by a meeting of the Genetics Subcommittee on January 27-28. The 1998 fall CLIAC meeting was scheduled for September 17-18, with a possible Genetics Subcommittee meeting on September 16. Dr. Schwartz then adjourned the CLIAC meeting.

I certify that this summary report of the September 11-12, 1997, meeting of the Clinical Laboratory Improvement Advisory Committee is an accurate and correct representation of the meeting.

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