Clinical

Laboratory

Improvement

Advisory

Committee

<u>February 8-9, 2006</u>
Doubletree Atlanta/Buckhead Hotel
Atlanta, Georgia

U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES

Clinical Laboratory Improvement Advisory Committee
February 8-9, 2006, Summary Report
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Ms. Joeline Davidson
Dr. Kathy Foucar
Ms. Merilyn Frances
Ms. Paula Garrott
Dr. Peter Gomatos
Dr. Carol Greene
Dr. Lee Hilborne
Dr. Anthony Hui
Mr. Kevin Kandalaft
Dr. Patrick Keenan
Dr. Michael Laposata
Dr. Dina Mody
Dr. Valerie Ng
Dr. Barbara Robinson-Dunn
Dr. Jared Schwartz
Dr. David Smalley
Dr. Thomas Williams
Dr. Jean Amos Wilson

Executive Secretary

Dr. Robert Martin

Ex Officio Members

Dr. Thomas Hearn, CDC
Ms. Judith Yost, CMS
Dr. Steven Gutman, FDA

Liaison Representative - AdvaMed

Ms. Luann Ochs, Roche Diagnostics Corporation

Record of Attendance, continued

Centers for Disease Control and Prevention

Ms. Nancy Anderson
Dr. Rex Astles
Ms. Pam Ayers
Ms. Carol Bigelow
Dr. D. Joe Boone
Ms. Diane Bosse
Dr. Roberta Carey
Dr. Bin Chen
Ms. Debbie Coker
Ms. Carol Cook
Ms. Stacey Cooke
Mr. David Cross
Ms. Christine Ford
Ms. MariBeth Gagnon
Ms. Sharon Granade
Mr. James Handsfield
Dr. Devery Howerton
Dr. Dan Jernigan
Dr. Lisa Kalman
Dr. Rima Khabbaz
Dr. Harvey Holmes
Dr. John Krolak
Dr. James Lange
Dr. Ira Lubin
Mr. Kevin Malone
Dr. Adam Manasterski
Ms. Leslie McDonald
Dr. James Pirkle
Ms. Anne Pollock
Dr. Eunice Rosner
Ms. Andrea Scott
Dr. Shahram Shahangian
Mr. Darshan Singh
Dr. Balasubr Swaminathan
Dr. Julie Taylor
Mr. Howard Thompson
Ms. Pam Thompson
Ms. Leigh Vaughan
Ms. Glennis Westbrook
Mr. Mark White
Dr. Laurina Williams
Ms. Joyce Witt
Ms. Darlyne Wright

Record of Attendance, continued

Department of Health and Human Services (Agencies other than CDC)

Ms. Minnie Christian (CMS)
Mr. James Cometa (CMS)
Dr. Elliot Cowan (FDA)
Ms. Sandra Farragut (CMS)
Ms. Daralyn Hassan (CMS)
Ms. Cecilia Hinkel (CMS)
Ms. Fran Lehr (CMS)
Ms. Raelene Perfetto (CMS)
Mr. Cornell Prodan (CMS)
Mr. Benjamin Snyder (CMS)
Ms. Kathy Todd (CMS)
Ms. Harriet Walsh (CMS)
Ms. Gwendolyn Williams (CMS)
Ms. Cheryl Wiseman (CMS)
Mr. Gary Yamamoto (CMS)

In accordance with the provisions of Public Law 92-463, the meeting was open to the public. Approximately 30 public citizens attended one or both days of the meeting.

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, Centers for Medicare & Medicaid Services; 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 also includes a non-voting liaison representative who is a member of AdvaMed 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 regulations, the reader should not infer that all of the Committee's recommendations will be automatically accepted and acted upon by the Secretary.

CALL TO ORDER – INTRODUCTIONS/FINANCIAL DISCLOSURES

Dr. Lou Turner, Chair, Clinical Laboratory Improvement Advisory Committee (CLIAC), welcomed the Committee members and called the meeting to order. Dr. Robert Martin, Director, Division of Public Health Partnerships (DPHP), National Center for Health Marketing (NCHM), Coordinating Center for Health Information and Service (CoCHIS), Centers for Disease Control and Prevention (CDC), and Executive Secretary, CLIAC, thanked the members for their dedication of time and expertise. All members then made self-introductions and financial disclosure statements relevant to the meeting topics.

AGENDA UPDATES AND COMMITTEE DISCUSSION

Centers for Disease Control and Prevention (CDC) Update

Coordinating Center for Infectious Diseases (CCID) Reorganization, including Division of Laboratory Systems (DLS) ***Addendum A***

Dr. Robert Martin, Director, DPHP, NCHM, CDC, announced the Division has returned to its original name (Division of Laboratory Systems [DLS]) and is transitioning from CoCHIS to CCID. In the proposed realignment of CCID, DLS will be in a newly created center within CCID, National Center 4 (NC-4), which is not yet named. This move will bring DLS in closer alignment with laboratories at CDC. Dr. Martin introduced Dr. Rima Khabbaz, currently the Director of the National Center for Infectious Diseases (NCID) and the future director of the proposed NC-4. She explained the proposed realignment of CCID, briefly discussed the focus of

each center, and gave short biographies of the new center directors.

Committee Discussion

- A Committee member asked if marketing would still be aligned with DLS in the agency's reorganization. Dr. Martin explained, while NCHM is the component of CDC's organizational structure emphasizing communication and partnership between the private and public health sectors, the alignment of DLS with CCID, and its crosscutting activities, will allow interaction between DLS and other CDC laboratories, infectious disease or otherwise.
- One member inquired if the bioterrorism laboratory was in the same area as DLS, which seemed like an excellent move. Dr. Martin replied the Bioterrorism Preparedness and Response Program is also part of the proposed NC-4.
- A member requested clarification on how DLS will bring in expertise for the diverse areas of concern to CLIAC since the focus of CCID is on infectious diseases. Dr. Martin answered there is no organizational structure at CDC that is broad enough to accommodate all laboratory specialties. Therefore, that has always been an issue regardless of where DLS has been located at CDC. However, DLS has the ability to bring in needed expertise when areas of a particular discipline are being discussed. Dr. Khabbaz added other programs that span the healthcare system are also housed in the proposed NC-4 with DLS and part of the commitment to the reorganization is to work across CDC on such programs.

Marketing Good Laboratory Practices for Waived Testing – Update ***Addendum B***

Ms. Sharon Granade, Health Scientist, Laboratory Practice Standards Branch (LPSB), DPHP, NCHM, CDC, presented an update of the Division's activities surrounding marketing CLIAC's recommended Good Laboratory Practices (GLP) for Waived Testing Sites. She gave a brief background of the development of the recommendations, which were published in the *Morbidity and Mortality Weekly Report (MMWR): Reports and Recommendations*. Reviewing CLIAC's suggestions for marketing, she noted the importance of disseminating the GLP to a wide audience using a variety of channels. Immediately after publication in the *MMWR*, CDC sent announcements with links to the full document via e-mails and listservs to laboratories, laboratory and medical professional organizations, and colleagues. By asking these associations to share the information, large numbers of waived test users can be reached. Ms. Granade named the websites and professional publications where the GLP have been referenced to date and mentioned potential new channels for distribution. Future marketing considerations include customizing materials for target audiences, using focus groups or surveys for feedback, and collaborating with target groups to provide information at their professional meetings and develop training materials.

Committee Discussion

- One member asked if the CMS Certificate of Waiver (CW) studies could be used to measure the success of the GLP recommendations and if the CW studies or implementation of the GLP have been tied to any of the major payers' reimbursement to laboratories. Ms. Yost

replied CMS follows up with laboratories where issues have been found to determine whether education, including the GLP recommendations, has led to sustained improvement. She stated she was not the right person to answer the payment question.

- Several members complimented the *MMWR* GLP document and commented on the positive impact such recommendations will have on improving the skills of those performing waived testing, particularly in the point of care setting, rapid HIV testing sites, and healthcare training programs. They emphasized the need for the recommendations to focus on and be written for various targeted audiences.

Food and Drug Administration (FDA) ***Addendum C***

Waiver Guidance Update

Dr. Steven Gutman, Director, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD), Center for Devices and Radiological Health (CDRH), FDA, provided an update on the status of the "Draft Guidance for Industry and FDA Staff: Recommendations for Clinical Laboratory Improvement Amendments of 1988 (CLIA) Waiver Applications." The 40 comments received during the public comment period are being analyzed and the guidance modified. The document is a high priority with the end of 2006 as the target date for issuance of the Final Draft and moving forward with the Proposed Rule. Dr. Gutman also commented on OIVD's current work including reviewing CDC's polymerase chain reaction (PCR) assay for influenza A/H5, a series of glucose meter recalls, and publication of notice, not guidance, of informed consent paperwork reduction.

Committee Discussion

- No questions or comments

Summary of 11/30/05 Blood Products Advisory Committee (BPAC) Session: Approaches to Validation of Over-the-Counter (OTC) Home-Use HIV Test Kits

Addendum D

Dr. Elliot Cowan, Chief, Product Review Branch, Division of Emerging and Transfusion Transmitted Diseases, Office of Blood Research and Review, Center for Biologics Evaluation and Research, FDA, summarized the November 2005 meeting of FDA's Blood Products Advisory Committee (BPAC) on validation approaches for OTC home-use HIV test kits. He gave an overview of FDA's considerations from the beginning of home-use blood collection kits in 1986 to the 1995 *Federal Register* notice revising FDA guidance for specimen collection kits for HIV antibody testing. The 1995 notice pertained only to specimen collection and did not address kits for home-use testing of specimens for evidence of HIV infection. Dr. Cowan then reviewed the changes since 1995 in HIV testing including approval of rapid HIV tests. He discussed the approval requirements, standards, and sales restrictions for rapid HIV tests and emphasized sales restrictions apply to rapid HIV tests. Noting the recurring themes in benefits and risks associated with OTC home-use HIV test kits, he pointed out additional issues of obtaining a test result without a supplemental test, the cost factor for those who need the test most, and potential conflict with state and/or federal health reporting requirements.

Dr. Cowan reviewed highlights of the speakers' presentations at the November 2005 BPAC meeting. Topics included the proposal for an OTC rapid HIV antibody test using oral fluids, suggested changes in HIV testing practices and counseling recommendations, and an explanation of the role of quality systems in diagnostic testing. Dr. Cowan also detailed the discussion of the psychological and social issues associated with HIV testing and OTC home-use tests and presented an overview of FDA's OTC review process including human factors considerations. In addition, he described the open public hearing comments regarding home-use HIV test kits. Three issues were presented to BPAC for discussion: the appropriateness of FDA's previously established rapid HIV test sensitivity and specificity criteria for rapid OTC home–use HIV tests, the clinical studies necessary to validate the safety and effectiveness of these OTC tests, and the proposed content and adequacy of informational materials. Dr. Cowan commented BPAC did not express opposition to the concept of an OTC home-use HIV test kit; rather the BPAC discussion centered on what conditions would be needed to validate a home-use kit approval. He reviewed the next steps for evaluating the proposed studies to support the approval of OTC home-use HIV tests and the status of reports of reduced specificity with OraQuick oral fluid testing, noting the latest information on this issue from CDC's February 6, 2006, webcast, "Investigation of Reports of Excessive False-Positive Oral Fluid Rapid HIV Tests" at www.retroconference.org/2006. In conclusion, Dr. Cowan encouraged the audience to attend and participate in the next BPAC meeting on March 10, 2006, and reminded those planning to make public comments to register to speak. He assured the Committee FDA would consider all comments and recommendations.

Committee Discussion

- A Committee member inquired about efforts to avert false positives in low-prevalence areas. Dr. Cowan replied part of FDA's challenge in clinical trials will be to show that any risks are mitigated.
- Members discussed manufacturers need to carefully design the test performance criteria, emphasizing the importance of valid positive predictive values and inclusion of this information in the package insert. One member asked if there is existing evidence showing that intended users read the package insert; is there a way to ensure that the user understands what is meant by a "preliminary positive" result. Dr. Cowan responded that predictive values vary greatly depending on the population and emphasized that it is the manufacturer's responsibility to address this. Based on studies, FDA would ascertain whether the test is designed appropriately.
- Another member expressed psychosocial concerns when HIV testing does not include face-to-face counseling. The member also had concerns about the validity of clinical trials since they would most likely not reach the population for which the tests were intended. Another member questioned whether current gaps in HIV testing needs are sufficient to warrant the challenges of OTC home-use testing, such as the ramifications of false positive results, lack of counseling, and loss of public health reporting. The member also expressed concern over the possibility of additional infectious disease testing outside of a controlled environment. In contrast, a CLIAC member made statements in support of OTC home-use HIV testing related to test performance, reduction of perinatal transmission, anonymous access to counseling,

and destigmatization of the disease. This member's only concern was for possible off-label use of tests approved for OTC home-use HIV testing in the professional (healthcare) setting, e.g., physician offices.

- A Committee member, noting that the percentage of HIV-positive persons who are unaware of their status has remained constant over the past five years, questioned whether OTC HIV testing would decrease this percentage. Dr. Cowan responded the key to address this concern is to determine why people do not know they are infected.
- The CLIAC Chair concluded the discussion by noting the potential difficulty in guiding individuals into the healthcare system to receive treatment if home testing is offered. She also questioned if the test kits would be affordable to the population most likely to use home testing.

Centers for Medicare & Medicaid Services (CMS) ***Addendum E***

Ms. Judy Yost, Director, Division of Laboratory Services (DLS), Survey and Certification Group (SCG), CMS, updated the Committee on the Partners in Laboratory Oversight's membership, accomplishments, and current and future projects. These projects include efforts to improve the consistency of quality policies among the accreditation organizations, exempt states, and CMS; and to clarify the laboratory director's responsibilities. She discussed the Quality Control (QC) for the Future activities, including the Clinical and Laboratory Standards Institute (CLSI) manufacturers' guidance document on risk management (anticipated publication by end of 2006) and the CLSI guidance to laboratories for developing and customizing QC protocols based on

the manufacturer's risk management information and the laboratory's unique environmental factors. Ms. Yost also reviewed the status of the Government Accountability Office's (GAO) audit and the new CLIA Automated Complaint Tracking System (ACTS) that CMS is initiating at the end of March.

Ms. Yost continued by updating the Committee on CLIA statistics and the status of the proposed rule for genetic testing. Commenting on Certificate of Waiver (CW) studies, Ms. Yost stated although this is the final year of the current approval, CMS has submitted a proposal to continue the studies indefinitely. She noted the number of CW laboratories continues to grow and education facilitates improved performance.

In conclusion, Ms. Yost introduced the topic of cytology proficiency testing (PT). In 2005, the first year of national cytology PT, 98% of laboratories enrolled and 91% of individuals taking the test passed. No one will fail this year and no action will be taken unless the laboratory does not enroll in the PT program. Failure of the laboratory to enroll in a PT program will result in fines, revocation of the laboratory's cytology certificate, and/or denial of cytology Medicare payments.

Committee Discussion

- Ms. Luann Ochs, AdvaMed Liaison to CLIAC, congratulated CMS on providing more information for laboratory directors and inquired as to the types of complaints CMS was compiling in their complaint-tracking database. Ms. Yost replied the complaints vary and

come from physicians, employees, and others. She explained CMS considers everything and all complaints will go into the tracking system to be counted. Breakdowns will be provided according to complaint source, resolutions, and whether the complaint was verified.

- A Committee member inquired about how the system would work if CMS received a complaint concerning an accredited laboratory. Ms. Yost explained CMS would notify the accrediting agency immediately and the decision would be made as to whether CMS, the accrediting organization, or both would follow up with a survey. The new tracking system will improve the coordination between CMS and the accrediting agencies.
- Another member asked if CMS was considering creating a type of patient safety organization where issues that did not reach the complaint level could be reported. Ms. Yost stated CMS has preliminarily discussed working with the Institute for Quality in Laboratory Medicine (IQLM) to combine quality requirements into the broader scope of patient safety. She noted the Veterans' Administration (VA) and accrediting organizations are considering other patient safety initiatives.
- One member congratulated CMS on the progress made towards publication of the proposed rule for genetic testing, and commented that the 2003 changes in CLIA regulations pertaining to genetic testing have been very useful to the genetics community. The member welcomed the opportunity to comment on the proposed rule when it was published, particularly with the increased migration of esoteric testing with complex interpretations into more routine laboratory environments.
- A member asked what follows if a laboratory fails to enroll in cytology PT or if an individual fails the testing. Two members asked for more specifics regarding laboratories that had not

signed up for the cytology PT program and if some were no longer offering gynecological cytology services. Ms. Yost replied that no one will fail the test this year while CMS evaluates the ramifications and effects of the PT program. She stated CMS has identified laboratories that have not yet signed up, but has not yet identified the reasons why they have not done so. Ms. Yost explained CMS has encouraged consolidation of laboratories that perform small numbers of gynecologic testing. She added cytology PT applies only to gynecological testing sites and original CMS data for laboratories that conduct cytology testing did not distinguish between laboratories performing gynecological cytology testing and non-gynecological testing. CMS has now culled those doing only non-gynecological testing from their list of laboratories subject to cytology PT.

National Cytology Proficiency Testing (PT) Update ***Addendum F***

Ms. Cheryl Wiseman, Health Insurance Specialist, DLS, SCG, CMS, updated the Committee on national cytology proficiency testing (PT) through 2005. She briefly reviewed the cytology-specific language of the 1988 CLIA statute, listed the approved cytology PT providers for 2005 and 2006, and outlined the testing format before discussing preliminary results of the 2005 testing. The results as of January 31, 2006, included both the national Midwest Institute for Medical Education (MIME) program and the State of Maryland program. She compared the year-end statistics with those of August 2005, noting their similarity. She added that the four locum tenens failures included two cytotechnologists and two primary screening pathologists and noted 141 individuals chose not to attempt a second test after failing the initial test. The data included comparison of the pass rates of primary screening cytotechnologists with primary

screening pathologists. She also compared the initial statistics from MIME to the State of Maryland's figures in 1990 and 1995.

Ms. Wiseman then described a comparison of test scores broken down by slide preparation type, and reviewed the automatic failure rates. She advised CLIAC of proposed legislation, H.R.4568, which has passed the House and is now in a Senate subcommittee and could influence cytology PT. Ms. Wiseman concluded by discussing current CMS activities, including convening a CLIAC cytology PT workgroup. Additionally, CLIAC will convene for an interim 2006 meeting for the Committee to consider the workgroup's findings and formulate recommendations to the Secretary, Department of Health and Human Services, to facilitate rule making.

Committee Discussion

- Commenting on the reduction in numbers of primary screening pathologists since 1995, one member asked if CMS had information on what kind of practices the primary screening pathologists were in. The member stated an organization was recommending against such practice by pathologists. Ms. Wiseman replied CMS has the names and locations of these pathologists, but all the information regarding the reduction in numbers has not yet been analyzed. She assured the Committee CMS would make every effort to get the information to them when it is available.
- The same member inquired about the outcomes of challenges made by examinees of their PT results, specifically about notifying those who may have failed due to problematic slides and about correcting any possible wrongful test failures. Ms. Wiseman said these data were

among five or six data sets that have been requested but not yet received. The member commented on how important such matters are to examinees, both economically and professionally, adding that confidentiality in the event of failures is not assured with on-site testing in small laboratory situations. Ms. Wiseman replied the testing programs were required to have procedures in place to manage any technical or scientific issues that arise. Further, CMS has made confidentiality a high priority but there are cases where individuals have voluntarily announced their test failure. She reassured the Committee that CMS was in the process of working to provide them with data related to cytology PT.

- Another member asked if there were objections to persons with multiple failures having to stop reviewing slides. No CLIAC members stated objections, but a member expressed concern at the possibility of failure being linked to improperly validated slides. Ms. Yost noted slides associated with testing failures are closely monitored and this information is recorded. The Chair noted that in-house mandatory monitoring of technologist screening competency is required, stating laboratories should be detecting weak performance prior to a PT failure. She added the current CLIA review process does not, however, require similar performance review, i.e., 10% random rescreen, for pathologist screeners.
- A member asked if examinees should contact CMS directly when procedural problems are not addressed by testing proctors. Ms. Wiseman agreed they should and added CMS is investigating such complaints.
- A member questioned whether 100% slide review is instituted if an examinee fails the PT or withdraws before attempting the third retest. The Chair noted her laboratory would institute 100% reviews before reaching that point.

Process for Revising Regulations for Cytology Proficiency Testing ***Addendum G***

Dr. Devery Howerton, Chief, Laboratory Practice Evaluation and Genomics Branch, and Acting Chief, LPSB, DPHP, NCHM, CDC, provided an overview and discussion of the process for revising the CLIA cytology proficiency testing regulations. She described the process being used to solicit comments and defined expectations for appropriate input. She discussed both general and cytology-specific proficiency testing requirements, detailed the necessary steps for publication of a proposed rule, and provided a timeline for revising the regulations and developing a final rule. Dr. Howerton concluded by announcing the CLIAC Cytology Workgroup would meet in Atlanta March 28-29, 2006. In addition, she suggested potential dates for an interim CLIAC meeting in 2006.

Committee Discussion:

- In response to a question regarding the workgroup membership, Dr. Howerton provided the following details and preliminary agenda for the two-day meeting:
  - Workgroup Chair: Diane Solomon
  - Workgroup Members: Pathologists – George Birdsong, Diane Davey, William Frable, Ronald Luff, Dina Mody, and Stephen Raab; Cytotechnologists – Gwen Brown, William Crabtree, Paul Elgert, Deanna Iverson, Jacalyn Papillo, and Thomas Scheberl

- Process for Invited Consultants and Comments: On day one, invited representatives from proficiency testing providers and new technology manufacturers will participate as consultants to provide information and comments for workgroup consideration. Additionally, invitations will be sent to the professional organizations for distribution to their memberships, allowing an opportunity for individual comment.

Update on American Society for Microbiology (ASM) Survey of QC Failures with Microorganism Identification Systems ***Addendum H***

Dr. David Sewell, Pathology and Laboratory Medicine Service, Veterans Affairs Medical Center, and Department of Pathology, Oregon Health Sciences University, provided an update on ASM's final survey results of QC failures experienced by users of microbiology identification (ID) systems. He reminded CLIAC that CLIA requires laboratories test each substrate or reagent in microbial ID panels for positive and negative reactivity with each batch, lot number, and shipment. He stated ASM was asked to collect QC data from microbiology laboratories to assist CLIAC in substantiating the need for a change in the CLIA QC requirements for microbial ID systems. Explaining the survey instrument, Dr. Sewell reviewed the general and QC related questions; discussed the number of surveys sent, response rate, and demographics of the responding laboratories; summarized the survey results; and thanked the CLIAC and CDC staff who helped with the survey instrument. Dr. Sewell concluded by recommending use of the Clinical and Laboratory Standards Institute (CLSI) consensus process to determine appropriate

QC for these systems, indicating ASM is currently in discussion with CLSI to develop a QC protocol.

Committee Discussion

- A member inquired about a timeline for specific QC recommendations. Dr. Sewell said a proposal will be presented to CLSI at their April meeting and CLSI will then form a committee if document development is deemed feasible. Dr. Hearn added that once a proposal is accepted by CLSI, the timeline should be 22 months at maximum.
- A member expressed concern this issue would extend to affect multiplex genetic analysis, cautioning a large number of controls would be expensive; synthetic supercontrols are used in multiplex genetic testing to assure effective QC while using fewer wells. The member wondered if synthetic supercontrols might also be effective in future multiplex microbiologic testing development.
- In response to the question of the study design permitting evaluation of using fewer organisms to detect QC failures effectively, Dr. Sewell responded affirmatively, saying the tests failing QC were attributable to either an organism or substrate failure. Additionally, he noted that of the seven lots failing QC, six were from different systems, indicating no one test system was identified to be a problem.
- Discussion among several members focused on requiring manufacturers to include appropriate data on the performance of individual lots and /or certain biochemicals to help reduce the amount and frequency of QC. Dr Sewell agreed and pointed out requiring

manufacturers to provide specific performance data with media had resulted in reduced QC requirements for media.

- In answer to a question regarding reduced QC requirements affecting new test systems entering the market, Dr. Sewell acknowledged this as an important concern that is not being addressed. He stated that data is available for only 52 of the 72 microbiology test systems on the market, questioned whether sampling of new and infrequently used systems was adequate, and suggested this issue needs to be examined by a consensus group. Another member pointed out manufacturers, through Good Manufacturing Practices (GMP), must guarantee test system quality, and GMP should be continued with new systems entering the market.
- CLIAC members agreed a consensus group including manufacturers, users, and regulatory agencies should address many of the issues raised, and the next step should be to present a proposal to develop QC protocol for microbiology ID test systems to CLSI at their April meeting.

Coordinating Council for the Clinical Laboratory Workforce (CCCLW) ***Addendum I***

In response to the Committee's request for a report on workforce issues, Ms. Joeline Davidson, Administrative Director, Laboratory Services, West Georgia Health Systems, and CLIAC representative to the CCCLW, updated the Committee on CCCLW activities. She prefaced her presentation by reviewing a list of the Council's participants and acknowledging their

contribution to the Council's activities. She went on to provide an overview of the four major elements of the strategic plan, the CCCLW participant lead for each element, and the continuing and future activities of CCCLW advocating for the laboratory profession and targeting laboratory workforce issues and shortages. Ms. Davidson concluded by presenting the U.S. Bureau of Labor and Statistic's Laboratory Workforce projections for 2012, emphasizing the need for new insights to address recognized issues that continue to contribute to the growing shortages in the laboratory workforce.

Committee Discussion

CLIAC members agreed the CCCLW's strategic plan targeting retention and recruitment was correctly focused and long overdue. Several members recounted their experiences with workforce shortages and others provided examples of how their institutions were trying to address workforce shortages. Views expressed by the Committee members included the following:

- Laboratorians must be promoted within their institutions and their professional image must be improved
- Skills and competencies of existing personnel need to be better managed to include better utilization of the associate degree technician
- Workforce shortages in all areas of healthcare are much higher in the underserved populations and worse than the recent studies seem to indicate

- Medical technologists in some areas of the country are seeing pay increases but this needs to occur nationally and include all laboratory personnel
- Higher work loads and fewer staff to perform the work is resulting in increased "burn out"
- Better technologies and the development of molecular testing is increasing automation and reducing personnel needs even in the more complex testing areas
- Laboratory education programs and curricula must be more flexible and more structurally diverse
- Diverse, poorly monitored on-the-job training programs are increasing the number of under-qualified individuals performing high complexity testing
- More incentives (scholarships, grants, stipends, sign-on bonuses) are required to recruit and retain laboratory personnel
- Graduates from laboratory science programs are going into more lucrative fields instead of practicing in hospitals and clinical settings
- Younger professionals want more flexible work schedules and are less willing to seek employment that requires weekend/holiday commitment
- Colleges are not attracting students into the science fields

Ms. Davidson concurred, indicating that the existing data as well as her experience support the Committee's views. She also pointed out recent graduates often feel over-qualified for routine bench testing and quickly become bored. She suggested more challenging, higher educational levels, e.g., clinical doctorate as proposed by several organizations to fill consultative and other high-level laboratory roles, might revitalize the profession. She emphasized the National

Accrediting Agency for Clinical Laboratory Science (NAACLS) is now addressing changes in educational levels and curriculum requirements for laboratory training programs in an effort to narrow the gap with a quality laboratory workforce. She agreed with several members that, without required licensure, it is difficult to attract quality candidates and to promote the laboratory profession. In addressing retention in laboratories, Ms. Davidson cautioned that laboratory science programs marketing their programs as "stepping stones" to other areas could be detrimental to the profession's retention efforts. In a final comment, one member referred to a recent article listing medical technology among the growing healthcare career opportunities for college graduates as a "ray of hope" amidst other work force issues.

Diagnostic Detectives Toolkit ***Addendum J***

Dr. Robert Martin, Director, DPHP, NCHM, CDC, provided CLIAC with a snapshot of a resource tool developed by the Michigan Association of Laboratory Science Educators with support from a CDC/Michigan Department of Community Health grant and available on medtech@msu.edu for teachers and students. He cited the CD ROM tool kit as an example of the outcome of a public/private collaboration addressing the laboratory workforce shortage. The tool kit uses "day in the life" presentations, case studies, interactive web links, games, and other activities to promote careers in laboratory sciences to pre-college/college audiences. He recognized other collaborative efforts addressing workforce shortage issues, emphasizing there is no single solution to the complex issues associated with laboratory workforce shortages.
Dr. Martin concurred with Ms. Davidson that innovative approaches to both retention and

recruitment issues must be developed and implemented to stem the increasing vacancy rates observed in the laboratory science professions.

Committee Discussion

CLIAC applauded the CD ROM, seeing it as an excellent recruitment tool for pre-college audiences and a creative vehicle for promoting the diverse career paths open to laboratory science program graduates. Several members voiced concern that too much focus was on recruitment tools and too little on innovations to address the more difficult issues contributing to low retention rates. CLIAC concurred as follows:

- Funding is needed to support successful, large scale marketing and public relations efforts
- Strengthening public school science curricula and promoting well-trained science teachers is critical
- Retention issues, e.g., pay and professional recognition, must be addressed
- Healthcare institutions and professional organizations need to develop and support local programs promoting careers in laboratory science, e.g., shadowing and internships, and educational workshops for teachers and students
- Studies correlating quality laboratory practice with improved patient outcomes could effectively promote recognition and give value to the profession
- Quality laboratory medicine can be promoted though patient testimonials
- Expanding healthcare institution and college/university partnerships will support and promote laboratory training curricula

Enhancing Connectivity Between Public Health and Clinical Laboratories

Addendum K*

Dr. Robert Martin, Director, DPHP, NCHM, CDC, introduced the topic of enhancing connectivity between federal laboratories, public health laboratories, and clinical laboratories. He described CDC's strong, long-time partnership with the Association of Public Health Laboratories (APHL), whose mission is to promote the role of public health laboratories in support of national and global objectives. In addressing the need for strengthening connectivity between public health and clinical laboratories, Dr. Martin provided examples of how CDC's realigned goals and strategic imperatives necessitate and encourage stronger partnership between federal, public, and private laboratories. He gave a conceptual overview of a national laboratory system, describing it as a link between federal laboratories, state and local public health laboratories, and hospital, independent and physician office laboratories. Dr. Martin explained that four states were involved initially in helping to articulate what state public health laboratories could do to increase connectivity with clinical laboratories. He went on to provide a detailed explanation of the formative evaluation conducted to determine the process required to expand the national laboratory system concept to all 50 states, which included case studies of the initial four state demonstration sites, a survey of state public health laboratory directors, and a survey of a sample of clinical laboratories. Dr. Martin discussed factors identified in the survey of clinical laboratory directors and managers that would increase reliance by clinical laboratories on state public health laboratories as a source of information and thus improve their connection. He recounted recent natural disasters and the emergence of a virulent influenza A strain that

have highlighted the importance of coordinating efforts among all laboratory constituents. Dr. Martin concluded by introducing the Laboratory Outreach Communication System (LOCS), intended to build a volunteer communications infrastructure for the exchange of laboratory-related information between CDC and the broad laboratory community. LOCS will utilize multiple routes of communication to focus on dynamic issues such as changes in regulations, standards or practices, urgent public health issues, and disaster relief and will help enhance CDC's existing communication structures to reach various audiences.

***Note:** The addendum was revised from material provided in the Committee's notebooks to reflect last minute updates by the presenter.

The Role of Public Health Laboratories ***Addendum L***

Dr. Katherine Kelley, Director of Public Health Laboratories, Connecticut Department of Public Health (CPHL), and President, Association of Public Health Laboratories, used the CPHL's customers, services, and performance standards as an example of the role of public health laboratories. She indicated the primary customers of state public health laboratories are communities consisting of other state agencies, local public health departments, clinical laboratories, federal agencies, and many public health partners. Dr. Kelley explained how public health laboratories support numerous programs and provide a wide scope of services, both clinical and environmental, and stressed that the expanding role of public health laboratories requires implementation of an integrated data management system for information sharing in real

time. Dr. Kelly stated the priority for public health is development of performance standards and accreditation of public health laboratories through processes encompassing laboratory improvement and regulations, policy development, emergency preparedness, public health research, management and leadership skills, strategic planning, and stronger communications. Dr. Kelly emphasized the future must include improved collaboration among clinical and public health laboratories with real-time information sharing to achieve positive health outcomes.

Committee discussion:

The discussion following Dr. Martin's and Dr. Kelly's presentations covered examples of problems experienced by Committee members in their relationships with public health laboratories as well as examples of successful collaborations that improved laboratory services. Major issues identified included the variability of public health resources allocated by states, lack of standardization of services, communications between the public health and clinical laboratory communities, and workforce issues.

- Committee members gave examples of their experiences with successful collaborations such as an agreement for management services of a public health laboratory using independent and university laboratories. This resulted in the formation of a workgroup consisting of regional hospitals, independent laboratories, and physician office laboratories to create manuals, compile contact information, and recruit volunteers for the strategic national stockpile. The LOCS was also cited as an example of a successful communications network within the laboratory community.
- One member asked Dr. Kelly about the crucial roles and interactions of public health

laboratories and agricultural and veterinary laboratories. Dr. Kelley acknowledged these as critical relationships and described CPHL's partnerships with other state agencies (environmental protection, agriculture), including barriers to be addressed. Other members mentioned the collaborative efforts of public health, universities, and government agencies, such as that between a Michigan state university and several state agencies to produce a web site on emerging infectious diseases for public and laboratory use.

- Suggestions from Committee members included incorporating more expertise when addressing prevention-based genetic testing and contacting medical programs to incorporate public health system education into the core curriculum to address variability among medical schools, residencies, and state public health programs.
- Regarding barriers to standardization efforts, Dr. Martin summarized that leadership is needed at the federal, state, public, and private levels to encourage collaboration among the states, and recommendations from CLIAC would be helpful both now and in the future.

Emergency Preparedness Connectivity ***Addendum M***

Dr. Harvey Holmes, Deputy Chief, Laboratory Response Branch, Bioterrorism Preparedness and Response Program, NCID, CDC, presented an overview of the Laboratory Response Network (LRN) and its activities relative to communicating with state public health laboratories. He discussed a 2004 report from the Office of the Inspector General, "States' Laboratory Response Programs for Bioterrorism: Level A Laboratory Participation," that cited three key vulnerabilities and made recommendations to improve communications on resources and policies, improve emergency

communications, enhance training for Sentinel laboratories, and provide criteria that define Sentinel laboratories. Dr. Holmes reported a committee consisting of the APHL, CDC, National Laboratory Training Network, and state public health laboratories developed definitions for both the Sentinel laboratory and the basic capacity clinical laboratory classifications. Additionally an American Society for Microbiology Sentinel Guideline Workgroup produced criteria for the basic and advanced Sentinel laboratories. Clear identification of these laboratories provides opportunities for better training and communications with the LRN.

Outbreaks and Public Health Responses ***Addendum N***

Dr. Daniel Jernigan, Acting Associate Director for Epidemiologic Science, Division of Healthcare Quality Promotion, NCID, CDC, presented the components of outbreak investigations (detect, confirm, characterize, survey, intervene, prevent) as part of public health on a local and international level. He provided examples from several CDC investigations that illustrated these components and emphasized the relationships between laboratory and epidemiologic activities as part of the public health response.

The Role of the Clinical Laboratory and the Public Health Laboratory in Foodborne Diseases Surveillance, Outbreak Investigations and Prevention ***Addendum O****

Dr. Balasubr Swaminathan, Team Leader, Laboratory Units, Foodborne and Diarrheal Diseases Branch, Division of Bacterial and Mycotic Diseases, NCID, CDC, reviewed the scope of CDC's

public health surveillance for foodborne diseases and its efforts to expand the reporting of infectious agents in all 50 states and some additional countries outside of the United States. CDC programs that are important for foodborne disease surveillance, monitoring, and prevention include the National Antimicrobial Resistance Monitoring System (NARMS), FoodNet (surveillance, burden and trend monitoring), PulseNet (foodborne pathogens subtyping for outbreak detection and investigation), and Electronic Foodborne Outbreak Reporting (eFORS) for reporting foodborne outbreaks to CDC using the internet. The success of these programs depends on timely reporting of notifiable cases and timely submission of the pathogens to state or local public health laboratories for identification and control of outbreaks. Cooperation with clinical laboratories is an essential part of this process, since they supply the isolates to the public health laboratories.

Dr. Swaminathan concluded by describing challenges to surveillance activities arising from traditional laboratory isolation of foodborne pathogens being replaced by non-culture testing. The resultant absence of pathogenic isolates available for surveillance studies compromises recognition of prevalent strains and new pathogens causing foodborne diseases. Although CDC supports the use of non-culture assays, the continuation of culture and identification from positive specimens remains a critical element in disease surveillance, control, and prevention.

***Note:** The addendum was revised from material provided in the Committee's notebooks to reflect last minute updates by the presenter.

Committee Discussion

- Dr. Martin began the discussion by asking the speakers if there were new technologies that would help address the potential public health impact of having fewer isolates available for epidemiologic studies. Dr. Swaminathan indicated microarrays would be a possibility in the future. For the short term, he suggested communicating with clinical laboratories about the new molecular methods and the consequences of not culturing positive specimens. For the long term, public health should prepare for new molecular testing by having communication networks in place to share ideas, techniques, and reagents. Dr. Jernigan added monitoring some diseases is becoming more difficult without isolates for testing. He acknowledged the expansion of rapid test methodologies in response to a growing patient safety movement and suggested this could be balanced by pursuing the epidemiologic need for isolates as an equally important patient safety concern.
- Members reiterated this epidemiologic dilemma already exists because resistant organisms are not being identified by molecular tests. Another member suggested CLIAC broaden the perspective beyond infectious diseases to include issues of cancer and genetic testing, noting concerns with transferring to some new technologies and losing the ability to conduct older methods that may be more expensive and labor-intensive, yet more accurate.
- Dr. Martin requested CLIAC help develop an agenda to address and broadly examine the issues discussed (disease detection/epidemiologic surveillance/determination of antibiotic resistance in the absence of isolates, validation of technology transfers), bringing stakeholders, including manufacturers, into the discussion.

Biomonitoring ***Addendum P***

Dr. James Pirkle, Deputy Director for Science, Division of Laboratory Sciences, National Center for Environmental Health (NCEH), CDC, introduced the Division's infrastructure, instrumentation, and methodologies used in their biomonitoring (biological monitoring) program for toxic industrial chemicals. He defined the biomonitoring role as measuring the internal dose of environmental toxicants in people and explained the difficulty and assumptions made in establishing toxicant exposure information and health effects data. Dr. Pirkle used lead data from the 1970's and 1980's to demonstrate how quality human data can reduce the uncertainty in health risk assessments and how environmental modeling predictions without biomonitoring data may lead to false conclusions. He also showed how the continued biomonitoring of human blood lead levels revealed health effects at lower exposure levels than originally established, resulting in CDC considering lowering the lead exposure limits. Dr. Pirkle discussed biomonitoring of other specific toxicants, how a toxicant's metabolic pathway is used to determine the appropriate sample type, and the role NCEH has played in supplying data and assessing a toxicant's health risk to the U.S. population. He encouraged the CLIAC to view the "Third National Report on Human Exposure to Environmental Chemicals," at www.cdc.gov/exposurereport, stressing its value to public health. Dr. Pirkle closed by emphasizing the critical importance of identifying at-risk populations and reducing the health effects of exposures to environmental toxicants.

Committee Discussion

- When asked if background levels of pesticides were highest in food or water, Dr. Pirkle responded that, although not well established, it is generally thought to be higher in food because of large amounts imported from areas where pesticides are not regulated. He reminded the audience to always wash fruits and vegetables before consuming.
- Referring to the graph of cotinine levels (non-tobacco users in households with no smokers), another member asked why serum levels did not reach zero. Dr Pirkle explained that trace amounts of cotinine in foods, e.g., tomatoes and iced tea, inhibit the correlation of cotinine levels lower than .005ng/mL to tobacco smoke exposure.
- One member asked for clarification of where Dr. Pirkle's laboratory fit within the CDC organizational structure. Dr. Pirkle gave a brief description of the reorganized CDC then added an open invitation to CLIAC members to tour their new facilities at the Chamblee campus.
- A member expressed curiosity regarding the impact of the Health Insurance Portability and Accountability Act (HIPAA) on acquiring and testing human samples in a public health laboratory. Dr. Pirkle replied that HIPAA impacted their testing about 30% of the time.

Influenza Laboratory Diagnosis and Surveillance: Enhancing Connectivity Between Public Health and Clinical Laboratories ***Addendum Q***

Dr. Peter Shult, Director, Communicable Diseases Division and Emergency Laboratory Response, Wisconsin State Laboratory of Hygiene, presented "Influenza Laboratory Diagnosis

and Surveillance: Enhancing Connectivity between Public Health and Clinical Laboratories." Introducing statistics on the annual impact of influenza, he stressed pandemic influenza preparedness activities are becoming a national priority and provided the website for strategic national plans: www.pandemicflu.gov. Emphasizing surveillance is the core of preparation and response to any pandemic flu plan, he detailed the objectives of influenza surveillance and highlighted laboratory contributions to good surveillance. Acknowledging the expanding role of the clinical laboratory in the diagnosis of influenza, Dr. Shult reviewed influenza test methods and time required for results and discussed the advantages and concerns surrounding rapid test methods. He expressed concern that widespread use of rapid testing could have a negative effect on surveillance because using these methods might not allow retention of influenza isolates for strain typing, which is the cornerstone of the vaccine system. Dr. Shult encouraged public health laboratories to engage rapid test sites as key partners in an effort to encourage state public health and clinical laboratories to work together. He reviewed biosafety requirements for rapid antigen testing, suggesting clinical laboratories provide biosafety training for their satellite laboratories to ensure testing is performed safely. Dr. Shult concluded by saying all laboratories need to start prioritizing now to prevent testing capacities being overwhelmed in the event of an influenza pandemic.

Committee Discussion

- Members agreed with the issues presented by Dr. Shult, adding that staffing, supplies, and test volume capacity are also critical concerns for laboratories preparing for a pandemic response.

- One member stated rapid influenza testing has resulted in under-reporting case numbers due to lack of confirmation by other test methods and shared a sample collection method that provides sufficient sample for both a rapid test and further testing. The same member asked Dr. Shult how he encourages rapid test sites to send test results and specimens to the public health lab and agreed with his concerns regarding biosafety practices in rapid testing facilities. Dr. Shult reaffirmed the importance of encouraging rapid test sites to communicate with public health laboratories to maintain active epidemiologic surveillance. He indicated LRN coordinators in his state played an important role in improving inter-laboratory communication and in encouraging rapid testing laboratories to collect samples for confirmatory testing. He referred CLIAC to the appendix of the CDC pandemic plan for additional discussions on these issues and reemphasized the need for training clinicians and laboratorians. With respect to positive and negative predictive value in rapid influenza testing, Dr. Shult stressed the importance of educating users to the concept that a negative predictive value is more useful during the influenza "off season" than it is during the peak season.

COMMITTEE DISCUSSION/WRAP-UP

The Committee's final discussions focused on addressing information technology (IT) challenges, e.g., difficulty in data mining due to lack of compatible interfacing, as a part of improving communication between public health and clinical laboratories. It was agreed future discussions should include IT representatives and involve IT resources such as eHealth network,

the Office of the National Coordinator for Health Information Technology (ONCHIT), and APHL.

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SPECIAL PRESENTATIONS

The Committee recognized the contributions of six retiring members whose terms will end June 2006:

- Dr. Kimberle C. Chapin
- Dr. M. Kathryn Foucar
- Dr. Peter J. Gomatos
- Dr. Anthony N. Hui
- Dr. Michael Laposata
- Dr. Jared N. Schwartz

On the occasion of her recent retirement from 33 years of dedicated and exemplary federal service, Ms. Rhonda Whalen, Chief, Laboratory Practice Standards Branch, Centers for Disease Control and Prevention, was presented with a commemorative plaque from the Clinical Laboratory Improvement Advisory Committee in recognition of her outstanding contributions and commitment to the promotion of high quality laboratory testing and practices.

PUBLIC COMMENTS

Dr. David Sewell, American Society for Microbiology	***Addendum R***
Ms. Janie Robertson, American Society for Cytotechnology	***Addendum S***
Ms. Robin Stombler, Institute for Quality in Laboratory Medicine	***Addendum T***
Dr. George Birdsong, American Society of Cytopathology	***Addendum U***
Dr. Mark Stoler, American Society for Clinical Pathology	***Addendum V***

ADJOURN

Dr. Turner thanked the members and partner agencies for their support and participation. The following reflects the recommendations and outcomes from this meeting:

- A workgroup has been formed and will meet on March 28-29, 2006, to address potential changes to the cytology proficiency testing regulations
- CLIAC will convene in June 2006 to consider the Cytology Proficiency Testing Workgroup's report and make recommendations for changes in cytology proficiency testing regulations
- The Committee requested the formation of a workgroup comprised of stakeholders including epidemiologists, clinical laboratories, public health laboratories, industry, and government to examine and broadly address the myriad issues related to the impact of rapid testing technology on clinical laboratories, public health laboratories, and epidemiology

Dr. Turner announced the remaining 2006 CLIAC meetings are scheduled for June 20-21 and

September 20-21, and adjourned the Committee meeting.

I certify this summary report of the February 8-9, 2006, meeting of the Clinical Laboratory Improvement Advisory Committee is an accurate and correct representation of the meeting.

Lou Flippin Turner, Dr.P.H., CLIAC Chair Dated: 4/26/2006