Clinical

Laboratory

Improvement

Advisory

Committee

Summary Report

<u>February 16-17, 2005</u>
Doubletree Atlanta/Buckhead Hotel
Atlanta, Georgia

U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES

Clinical Laboratory Improvement Advisory Committee
February 16-17, 2005, Summary Report
Table of Contents

Record of Attendance

Committee Members Present

Dr. David Sundwall, Chair
Dr. Kimberle Chapin
Ms. Joeline Davidson
Dr. Kathryn Foucar
Dr. Peter Gomatos
Dr. Cyril M. (Kim) Hetsko
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
Mr. Albert Stahmer
Dr. Lou Turner
Dr. Thomas Williams
Dr. Jean Amos Wilson

Committee Member(s) Absent

Ms. Paula Garrott
Dr. Margaret McGovern

Executive Secretary

Dr. Robert Martin

Ex Officio Members

Dr. Thomas Hearn, CDC
Ms. Judith Yost, CMS
Dr. Jean Cooper (for 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. Joe Boone
Ms. Diane Bosse
Dr. Roberta Carey
Ms. Debbie Coker
Ms. Carol Cook
Ms. Stacey Cooke
Ms. Maribeth Gagnon
Ms. Sharon Granade
Dr. Harvey Holmes
Ms. Jerri Holmes
Dr. Devery Howerton
Dr. Harvey Lipman
Mr. David Lonsway
Mr. Kevin Malone
Dr. Adam Manasterski
Ms. Leslie McDonald
Ms. Andrea Scott
Mr. Darshan Singh
Dr. Julie Taylor
Mr. Howard Thompson
Ms. Pam Thompson
Ms. Glennis Westbrook
Ms. Rhonda Whalen
Ms. Darlyne Wright

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

Ms. Carol Benson (FDA)
Ms. Minnie Christian (CMS)
Ms. Valerie Coppola (FDA)
Dr. Elliott Cowan (FDA)
Ms. Sandra Farragut (CMS)
Ms. Daralyn Hassan (CMS)
Ms. Cecilia Hinkel (CMS)
Ms. Penny Mattingly (CMS)
Ms. Donna McCallum (CMS)
Ms. Freddie M. Poole (CMS)
Ms. Raelene Perfetto (CMS)
Mr. Don St. Pierre (FDA)
Ms. Kathy Todd (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. David Sundwall, CLIAC Chair, welcomed the Committee members and called the meeting to order. He informed the Committee his CLIAC term ends June 2005 and announced his new position as Executive Director of the Utah State Health Department. He briefly explained the requirements and process for public disclosures, including those for conflict of interest. All members then made self-introductions and financial disclosure statements relevant to the meeting topics.

AGENCY UPDATES AND COMMITTEE DISCUSSION

Food and Drug Administration (FDA)

CLIA Initiatives and Status of FDA Waiver Guidance Document ***Addendum A***

Dr. Jean Cooper, Director, Division of Chemistry and Toxicology Devices, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD), Center for Devices and Radiological Health (CDRH), FDA, reviewed the history of OIVD, its functions, initiatives, and role in the Clinical Laboratory Improvement Amendments of 1988 (CLIA) program. She stated that the consolidation of FDA's regulatory activities for in vitro diagnostic devices (IVD) into one office improves oversight using a common technical base for pre-market review, post-market monitoring, and compliance/enforcement actions. She emphasized the benefit of a multi-tasking workforce covering all aspects of product regulation from device development through obsolescence. Dr. Cooper then addressed OIVD's CLIA initiatives, which primarily include development of waiver guidance and test categorization (including waiver approvals). She informed the Committee that the FDA waiver guidance is expected to be released for public comment in the summer of 2005 and acknowledged the lack of clear criteria and a process for waiver approvals is problematic. She explained CLIAC's recommendations are being considered as FDA develops the guidance, with input from the Centers for Medicare & Medicaid Services (CMS) and the Centers for Disease Control and Prevention (CDC). Efforts are being made to create guidance that will satisfy the needs of test system manufacturers, be consistent with the CLIA criteria for waiver, and ensure patient safety.

Dr. Cooper updated the Committee on another FDA initiative, OIVD's website (www.fda.gov/cdrh/oivd). OIVD will post a standardized template for entering/submitting product review data on the site, with stated goals of transparency and ease of use. The website will also provide a wide range of information on OIVD's programs, laboratory safety tips, news items and databases relevant to CLIA test categorization and over-the-counter approved devices. Dr. Cooper next highlighted additional OIVD accomplishments that have resulted in more rapid introduction of new technologies (e.g., West Nile virus antibody testing). She also pointed out unresolved issues and processes such as those related to analyte specific reagents (ASR), home-brew tests, and informed consent. She discussed FDA's "Critical Path" initiative, designed to help streamline product approvals to keep pace with innovation, explaining it is directed more toward drug development based on biomedical markers than toward IVDs. She stated FDA

recognizes regulation may not be the only obstacle to effectively addressing rapidly advancing technology; science, economics, legal and social issues play a role. Dr. Cooper concluded by summarizing OIVD's goals, concerns, and commitment to regulate based on good science with a clear public health vision.

Committee Discussion

- Dr. Sundwall expressed concern over the delay in publication of the FDA waiver guidance. Dr. Cooper acknowledged his concern and assured the Committee waiver guidance is a very high priority.
- A member asked how the definition of "informed consent" varied between the FDA and the Department of Health and Human Services (HHS). Dr. Cooper responded that most HHS agencies follow what is known as the "Common Rule," where informed consent is required if samples are linked to patients (i.e., if there is risk of discovering a patient's identity). Conversely, the FDA requires manufacturers to obtain informed consent, regardless of whether a sample can be traced to the individual.
- A member requested a timeline for FDA guidance providing clarity on ASR and home brew tests. Dr. Cooper stated that providing a timeline is not possible, since in many cases guidance is developed as a product progresses through the regulatory process, and may be based on discussions with scientists who are developing the product. She detailed FDA's efforts to keep OIVD staff informed on evolving technologies by inviting companies and academics to present in-house and by hiring staff with current expertise in these areas to anticipate new product applications and develop guidance beforehand.
- Another member asked how OIVD implements guidance. Dr. Cooper replied that FDA guidance documents indicate what criteria need to be met, but FDA does not specify how a manufacturer can meet the criteria, thus allowing for innovation.

Centers for Medicare & Medicaid Services (CMS)

Clinical Laboratory Improvement Amendments (CLIA) Update and Certificate of Waiver (CW) Update ***Addenda B, C***

Ms. Judy Yost, Director, and Ms. Daralyn Hassan, Medical Technologist, both from DLS, CMS, gave a comprehensive update discussing several important past, ongoing, and future activities. Ms. Yost began by informing the Committee of CMS's involvement with the Clinical Laboratory Standards Institute's (CLSI) "Quality Control for the Future" meeting planned for March 18, 2005. *(Addendum C)* The meeting will be a collaboration of representatives from industry, laboratories, and government agencies to address issues and concerns regarding equivalent quality control (EQC); to discuss alternative quality control (QC) approaches; and to take the first steps toward developing a plan to ensure QC requirements are updated, appropriate, and least burdensome for laboratories.

Ms. Yost informed the Committee that "Partners for Laboratory Oversight" meetings were convened in November 2004 and February 2005 to improve information sharing and develop more effective survey protocols among the CLIA-approved accrediting organizations and CLIA-exempt states (WA, NY), federal agencies (CDC, CMS, Veterans Health Administration),

and other state agencies with laboratory regulatory programs. These partners drafted a guidance document, "Critical Situation Response," outlining joint responses for situations where CMS, states and accrediting organizations may take different actions. Follow-up meetings will occur to share best practices and resolve differences. Ms. Yost informed the Committee that the Government Accountability Office (GAO) is conducting a CLIA audit to evaluate laboratory quality, effectiveness of laboratory inspections, and CMS oversight of accrediting organizations and state agencies. She stated this audit may also investigate concerns about the quality of waived testing.

Ms. Daralyn Hassan continued the CMS update, presenting a revised summary of data collected from Certificate of Waiver (CW) surveys completed by CMS over the past three years. Her updated report included verified data for 2002-2004, but she emphasized CMS is still in the process of evaluating these data. She noted CMS hopes to improve the quality of the 2005 data through CMS database enhancements and a revised data verification process now requiring State Agency and Regional Office review before finalization. In addition, Ms. Hassan informed the Committee CMS is providing continuous surveyor training and periodic updates to surveyors via e-mails, newsletters, and conference calls.

Ms. Judy Yost completed the CMS update with a brief background and description of the implementation of a national cytology proficiency testing (PT) program, Midwest Institute for Medical Education, Inc. (MIME), approved in 2004. She stated that the 1988 CLIA law and the resultant 1992 regulations were very prescriptive for cytology. Ms. Yost explained that no organization was interested in developing a national PT program at that time because of startup costs, the physical and logistical burden of on-site testing requiring thousands of glass slides, recordkeeping requirements, and medical liability issues. She noted that since 1992, CDC has made numerous efforts to encourage the private sector to develop a national cytology PT program by hosting meetings and by following a 1993 CLIAC recommendation to explore use of computer-based testing to solve logistical problems associated with testing using glass slides. In conclusion, Ms. Yost listed the two current CLIA-approved cytology PT programs: the State of Maryland program and the newly approved national MIME program.

Committee Discussion

- A few members requested clarification of the CW laboratory survey data from 2002-2004, observing it did not appear to demonstrate improvement in waived testing over time. Ms. Hassan responded that different CW sites were surveyed each year, with only a small percentage of follow-up surveys. Ms. Yost added that improvement data will be calculated after surveyors revisit a statistically significant percentage of laboratories. She elaborated further, stating the anticipated publication of practice guidelines for waived testing, coupled with the FDA waiver guidance to assure robustness of waived tests, should effect improvement in the waived test performance.
- A member expressed concern over the immediate jeopardy (IJ) data and extrapolated the data to show there could be 166 cases of IJ occurring in waived testing sites each year. Ms. Yost acknowledged the member's concern and noted, while CMS has no authority under the CLIA statute to routinely oversee waived testing, surveyors are required to take action when problems are identified during CW surveys. She explained surveyors provide guidance to correct problems noted at the time the surveys are conducted. On preliminary review of

information from follow-up visits, surveyors have found CW sites are following CMS's recommendations and improving their testing practices. She also noted CW sites face several challenges affecting quality of practice, such as 40% annual staff turnover.

- Dr. Hearn asked if CMS had data showing a positive association between CW sites located in states with laboratory regulations and overall performance in CW surveys. Ms. Yost recounted that the initial data showed CW sites in states with laboratory licensure, PT, and QC requirements performed very well compared to those in states with no oversight.
- A member inquired if there was funding available to CMS to conduct similar surveys of provider-performed microscopy (PPM) certified laboratories. Ms. Yost replied that PPM laboratories are subject to CLIA regulations, as applicable. PPM laboratories are not routinely inspected, but surveyors of facilities performing non-waived testing are encouraged to examine PPM procedures during inspections. She pointed out the scope and severity of problems in PPM laboratories is less than in CW sites, but this does not preclude the possibility of combining them or doing separate PPM surveys.
- Dr. Sundwall asked if CMS and the College of American Pathologists (CAP) have initiated unannounced inspections of facilities. Ms. Yost replied CMS is not doing routine unannounced inspections. A Committee member noted CAP is not currently doing unannounced inspections but may be moving toward this practice. This member also stated the term "unannounced inspections" is not yet clearly defined. A second member conveyed concern regarding the effect of unannounced inspections on physician office laboratories, explaining they can cause cancellation of appointments with attendant negative consequences to patients. Another member observed it is typically testing personnel being interviewed during inspections, not the laboratory director.
- Dr. Sundwall inquired about the timeline for completion of the GAO audit and asked for the status of the genetic testing rule. Ms. Yost replied GAO would not disclose an audit timeline. She informed the Committee the proposed rule for genetic testing is on the CMS regulatory schedule and efforts are underway to publish the proposed rule in the *Federal Register* late this year.
- A member expressed enthusiasm for Partners for Laboratory Oversight and asked if there was a forum for input from the laboratory community on the Occupational Safety and Health Administration's (OSHA) interpretations and mandates affecting the laboratory. Ms. Yost said she could not speak for OSHA, but noted CLIA requires the laboratory director to ensure a safe environment for employees and patients. She stated that accrediting organizations have specific safety standards to address the OSHA requirements and added if a surveyor finds a severe safety/biohazard offense, the case will be referred to OSHA.
- Several members shared their concerns about the apparent disconnect between OSHA and the laboratory community. A few members asked if it would be feasible to have an OSHA representative attend the CLIAC meetings or serve as a liaison with the Committee. Dr. Martin replied the structure of the Committee was well established; however, the issue would be considered, and the scope and appropriateness of this request determined.

Implementation of Cytology PT ***Addendum D***

Ms. Cheryl Wiseman, Health Insurance Specialist, CMS, presented and discussed the implementation of cytology PT. Expanding on Ms. Yost's introductory overview, she explained that the CLIA law and regulations both specify "periodic" and "on site" PT for each individual

cytologist who screens/interprets gynecologic cytology specimens (Pap tests), and that cytology PT must be carried out "to the extent practicable, under normal working conditions." As a result, the CLIA regulations contain specific requirements for annual cytology PT that assign responsibility to the laboratory director for ensuring annual PT enrollment and testing of individuals and for taking prescribed remedial actions in the event of PT failure. The regulations also require PT programs to submit applications for approval/re-approval by July 1 in order to administer PT the next calendar year, to be a private, non-profit organization, and to provide annual testing with retesting for failures. Ms. Wiseman described the diagnosis categories and the test scoring grid and explained the differences in grading for pathologists and cytotechnologists. (Charts of the scoring grid, the challenge categories, result-notification deadlines, and retest deadlines are included in the CLIA regulations found at http://www.phppo.cdc.gov/clia/regs/toc.aspx. She emphasized all testing results will be confidential and distributed by PT programs only to individual participants and their laboratory director(s) after each examination or repeat examination. Results will be sent to CMS only after an individual passes one of the annual testing opportunities or after failing all testing events. She explained CLIA requires validation of each glass slide PT challenge by consensus of diagnosis of a minimum of three pathologists certified in anatomic pathology. Ms. Wiseman gave a brief outline of the newly developed CMS Cytology Personnel Record System (CYPERS) database, designed to monitor enrollment and participation and maintain records of individual scores. She emphasized each laboratory must remain in one testing program for one calendar year before changing to another approved program.

Committee Discussion

- The Chair noted cytology PT would affect about 4,000 laboratories and 20,000 cytologists.
- Several Committee members expressed concerns about portions of the 1992 cytology regulations. To help frame the discussion, CMS and CDC representatives first explained which aspects of the regulations were prescribed by law and changeable only by Congressional amendment (e.g., cytology PT must test the performance of individuals rather than laboratories). Next, those portions of the regulations that could be revised were identified. The Committee focused on the latter, especially the PT categories and scoring grid; members expressed these reflected outdated practice standards in cytology and requested the regulations be revised to reflect current practice. Ms. Yost replied CMS would work with the currently approved PT providers to monitor and interpret data and with cytology professional organizations to determine if there is a solid basis to support the need for revising and updating the CLIA regulations. Ms. Yost and Ms. Whalen agreed accomplishing such revisions could take three to five years.
- Committee members raised questions about the approval of only one national PT program for 2005. Ms. Whalen emphasized HHS has not solicited applications from potential PT providers since a 1993 Request For Proposal resulted in no applications, with professional organizations offering numerous reasons why there would be none forthcoming. She went on to explain when an application was received in 2004, the program was approved based on submission of credible evidence it met the CLIA requirements. No other applications were received in time to be approved for 2005. Ms. Whalen noted HHS has never ceased efforts to implement cytology PT. Since 1993, CDC has pursued development and validation of computer-based PT and consideration was being given to revising the CLIA regulations to allow alternatives to glass slide testing.

- Committee members requested clarification regarding specific PT logistics, field validation of glass slides, and confidentiality/discoverability of PT failures. Ms. Wiseman stated cytotechnologists working at more than one facility must identify the facility where they will be tested and explained other specific logistics questions will need to be answered by the PT provider. She stressed slides selected for PT will not represent ambiguous cases, and emphasized an individual is not considered to have failed PT until he/she has failed all testing opportunities for the calendar year. Ms. Wiseman reiterated all results will be confidential and sent only to individuals, laboratory directors and CMS. Further, no results will be sent to CMS until an individual either passes a testing event, or fails all testing opportunities offered for the calendar year.
- Dr. Martin reminded the Committee to consider its recommendations in the context of the Government being required to implement cytology PT, but not bound to act on CLIAC recommendations. Dr. Sundwall suggested CMS provide a progress report on cytology PT implementation at the next CLIAC meeting.
- CLIAC unanimously passed a motion requesting consideration be given to revising the cytology PT regulations, basing the revisions on updated comments from the professional organizations and the public to reflect current practice, evidence-based guidelines, and anticipated changes in technology.

Centers for Disease Control and Prevention (CDC) Update

Futures Initiative Update ***Addendum E***

Dr. Robert Martin, Executive Secretary, CLIAC, and Acting Director, Division of Public Health Partnerships (DPHP), National Center for Health Marketing (NCHM), Coordinating Center for Health Information and Service (CoCHIS), CDC, gave a broad overview of how CDC is structured to accomplish its mission and goals. He contrasted CDC's last major reorganization 24 years ago—a hierarchical approach resulting in organizational silos—with the current Futures Initiative, where a more "outside-in" method identified the agency's customers and their public health concerns as the driving forces for change. He stated the CDC budget would be aligned with these same public health issues. In proceeding with its public health mission, Dr. Martin explained CDC will work toward fulfillment of two overarching goals: (1) Health promotion and prevention of disease, injury, and disability—so all people can achieve their optimal lifespan with the best quality of health in every stage of life; and (2) Preparedness—the protection of people from infectious, occupational, environmental, and terrorist threats. He listed CDC's new strategic imperatives: health impact, customer focus, public health research, leadership, global health impact, and performance improvement, and emphasized the Futures Initiative has changed CDC from an organization responding to outbreaks to an organization doing ongoing, capacity-building work. Dr. Martin said the Center-level goals and objectives will be implemented through the CDC's Coordinating Centers and concluded by briefly describing the functions of the new entities (CoCHIS, NCHM, DPHP and Laboratory Systems) in relation to CDC's mission and goals.

Public Health and Public/Private Partnerships ***Addendum F****

Dr. Thomas L. Hearn, Associate Director for Laboratory Systems, DPHP, NCHM, CoCHIS, CDC, provided an overview of CDC's numerous public health and private partnerships. He illustrated these with charts of the Division of Public and Private Partnerships and DPHP, new NCHM divisions, and focused on several partnerships developed by DPHP. Dr. Hearn explained the importance of public and private partnerships, emphasizing CDC can most effectively address current and anticipated public health challenges by recognizing existing and potential public health problems, identifying stakeholders in those issues, and forming partnerships with defined roles and responsibilities. He stressed the importance of measuring outcomes and effectiveness and communicating this information to partners. Dr. Hearn identified the Institute for Quality in Laboratory Medicine (IQLM) as a venue for such communication in laboratory medicine. He compared successful partnerships to good teams**:** both require an understanding of what motivates participants and a development of trust and commitment to common goals. Dr. Hearn characterized current Laboratory Systems' partnerships as ranging from simple exchanges of information to non-funded and funded collaborations and provided the Committee with examples in each category. He concluded by pointing out the necessity for ongoing strategic thinking to identify and form appropriate partnerships to further improve laboratory testing for public health.

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

Development of Public-Private Laboratory Systems ***Addendum G****

Dr. Rex Astles, Senior Health Scientist, Laboratory Systems Development Branch, DPHP, NCHM, CoCHIS, CDC, addressed challenges to roles and communication for both CDC and private health laboratories and emphasized the importance of strengthening their connection. He detailed the National Laboratory System (NLS) development process and stated the purpose of NLS is to strengthen relationships between state public health laboratories and clinical (private) laboratories by establishing a collaborative network of federal/state/local public health laboratories, hospital and independent/reference laboratories, and physician office laboratories. Dr. Astles stated NLS seeks input from professional organizations, federal partners and federally funded state projects, and noted recent public health issues (e.g., bioterrorism, the threat of chemical terrorism, West Nile Virus, vaccine shortages) have highlighted the importance of this national system. He said the effectiveness of NLS and public/private laboratory partnerships will be measured by goals already established, such as the "Healthy People 2010" goal to improve comprehensive laboratory testing capabilities by 80%, and by performance standards currently in development by CDC and the Association of Public Health Laboratories (APHL). Dr. Astles discussed various tools available through NLS and described lessons learned from states participating in the Public-Private Laboratory Integration Project. He concluded with a description of the National Laboratory Database, which is based on CMS's Online Survey Certification and Reporting System and available to all state laboratories online.

***Note:** The addendum was revised from material provided in the Committee's notebooks to

reflect last minute updates by the presenter.

Committee Discussion

- Dr. Sundwall recognized CDC's efforts to promote and develop relationships between public and private laboratories. He expressed concern about the disconnect between clinical and public laboratories and the difficulty in facilitating cooperation between them. A member suggested continued efforts to demonstrate that state and clinical laboratories are necessary parts of a team working to improve public health and respond effectively to emergencies.
- CLIAC members identified poor communication between state public health laboratories and clinical laboratories and between neighboring state public health laboratories as a major problem. Dr. Martin stated the members' experiences reflect the reasons CDC initiated efforts to integrate the work of clinical and public health laboratories.
- A Committee member observed state public health laboratories have varying missions, visions, and leadership. Elaborating, this member stated APHL's National Center for Public Health Laboratory Leadership has developed an assessment tool to try to bring these elements to the same level and APHL spent ten years developing core functions that established a baseline of services for all state laboratories.

Institute for Quality in Laboratory Medicine (IQLM) ***Addendum H***

Dr. Joe Boone, Associate Director for Science, DPHP, NCHM, CoCHIS, CDC, updated the Committee on two recent IQLM partnerships meetings. The IQLM Professional Partners Meeting in October 2004 marked the beginning of collaboration; more than 40 health-related associations, professional societies, and government agencies gathered to address laboratory services issues. The professional partners identified several high priorities for IQLM and developed broad and specific goals relative to these priorities. More recently, IQLM Technology Partners met in February 2005. Over 25 IVD corporations, information technology companies, independent laboratories, and biotechnology firms likewise identified priorities for IQLM. Dr. Boone said workgroup reports will be presented at the upcoming IQLM Conference in April 2005. The conference will address quality indicators for laboratory processes and services, results of a pilot survey of laboratory quality practices, and an outline for a national report on laboratory quality. He told the Committee IQLM hopes to announce incorporation at this conference; a board of directors can then be nominated and bylaws adopted. He stated IQLM is currently operating with CDC startup funds and dues are yet to be requested. A primary goal is to make the Institute self-supporting by obtaining reliable funding. In closing, Dr. Boone informed the Committee that IQLM now has a newsletter and encouraged members to visit the website at http://www.iqlm.org.

Committee Discussion

- A member applauded the IQLM goals but noted the absence of reimbursement mechanisms to pay for creation, dissemination, and use of a patient-specific interpretative report or risk assessment. Dr. Sundwall pointed out the barriers in effecting changes in payment policy especially in the current environment and suggested that in conjunction with IQLM, cooperative efforts among accrediting and professional organizations will be needed to influence payment policy.

- A member emphasized that most errors in laboratory testing occur in the pre- and post-analytic phases, then suggested IQLM focus on appropriate test ordering and integration of results into an evidence-based patient care program. The member suggested laboratory reports are often lost or not used appropriately in patient treatment and identified development of information technology (e.g., electronic medical records) as a key step toward solving these problems.
- Another member said the laboratory could track pre-analytic errors but does not have the ability to control post-analytic errors once they leave the laboratory's computer system. Dr. Sundwall acknowledged this, but commented laboratories still have a responsibility for post-analytic data utilization and follow-up.
- Dr. Boone announced that Dr. Michael Laposata, a current CLIAC member, would be honored at the upcoming IQLM Conference in April with an award in recognition of his contributions to improving clinical integration activities. Dr. Boone also noted about 60 posters would be presented at the meeting, many addressing best practices for laboratory medicine.

PRESENTATIONS AND COMMITTEE DISCUSSION

Good Laboratory Practices for Waived Testing Workgroup Report

Addendum I

Dr. Jared Schwartz, Chair, CLIAC Good Laboratory Practices for Waived Testing Workgroup, presented the Workgroup's report. In September 2004, CLIAC recommended formation of a workgroup comprised of key stakeholders and charged to consider practices associated with the total testing process, evaluate the impact of these practices on the quality of waived testing, and recommend guidelines for "good laboratory practice" for waived testing. CLIAC further recommended publication of waived testing survey findings along with the good laboratory practice guidelines. Dr. Schwartz reviewed the specifics of the CLIA law pertaining to waived testing and the requirements for a CLIA Certificate of Waiver (CW). He explained the Workgroup addressed management considerations before testing, activities or practices to promote quality throughout the total testing process, personnel training/continuing education, and various mechanisms for broad and effective dissemination of the guidelines. He detailed additional Workgroup comments, including the concept that over time "recommendations" can become a standard of care. In conclusion, Dr. Schwartz discussed numerous Workgroup recommendations for dissemination of the "good laboratory practice" guidelines, including identifying and distributing a "Top 10" list of the most readily implemented and affordable laboratory practices that could achieve the greatest impact on quality and patient safety.

Committee Discussion ***Addendum J***

Dr Sundwall and the Committee commended Dr. Schwartz and the Workgroup members for their efforts in providing a comprehensive list of suggestions for good laboratory practices for waived testing. He explained that CLIAC recommendations formulated from this report would serve as the basis for a publication in *MMWR Recommendations and Reports* along with a summary of the findings from CMS's CW surveys and CDC's Laboratory Medicine Sentinel Monitoring Network. Committee members discussed the report and recommended adopting the Good Laboratory Practices for Waived Testing Workgroup proposals. In doing so, they

provided clarification in some areas and made additional recommendations as follows:

CONSIDERATIONS BEFORE TESTING

Certificate of Waiver (CW)

CLIAC Recommendations:

- Clarify the term "testing site," to include non-traditional sites (e.g., nursing homes, mobile laboratories, field sites) covered by a CW
- Stress that testing personnel should know the location where the waiver certificate is maintained
- Provide specific examples of the responsibilities of the director or responsible person, such as signing the CW application, receiving product notifications and recalls, and taking appropriate action
- Avoid use of the acronym "COW" in publications; it may give a negative impression

Management Responsibility for Safety

CLIAC Recommendations:

- Designate and maintain a "clean area" and the appropriate physical environment for testing
- Emphasize the importance of following Universal Precautions
- Provide resource information (e.g., FDA, CMS, MedWatch)

Diagnostic and Patient Benefits

CLIAC Recommendations:

- Emphasize decision-makers should understand and abide by intended use as described in the product insert
- Balance patient benefits of waived testing, including immediate accessibility for patient care and treatment, with cost considerations

Physical Requirements for Testing

CLIAC Recommendations:

- Explain that, for many test systems, manufacturers' instructions indicate the acceptable environmental temperature range for testing and/or test system/reagent storage
- Ensure staff access to sinks for hand washing or antiseptic gels for "dry" cleaning

TEST PERFORMANCE

Pre-testing Phase

CLIAC Recommendations:

- Acknowledge anonymous testing considerations
- Acknowledge Health Insurance Portability and Accountability Act of 1996 (HIPAA) applicability to waived testing
- Include examples to illustrate how to confirm and document patient identification

Testing Phase

CLIAC Recommendations:

- Emphasize "do not mix components of different manufacturers' kits, lots, or tests"
- Include precautions for batch testing and for performing a variety of different tests simultaneously (e.g., labeling, identification, timing)
- Stress the importance of not altering test components (e.g., cutting test cards, strips)
- Inform manufacturers or distributors to either supply QC materials with test kits, when possible, and include instructions for use, or provide information for user to purchase appropriate controls

Post-Testing Phase

CLIAC Recommendations:

- Confirm and document verbal communications. Emphasize and explain read-back of critical results to confirm verbal report
- Emphasize the importance of following initial waived test results with confirmatory/supplemental testing, when needed, since many waived tests are screening tests. Stress whenever confirmatory testing is necessary, it should be stated in the product insert
- Provide specific information about the sample type and identification and test(s) ordered when referring samples for confirmatory/supplemental testing
- Clarify that laboratories performing confirmatory/supplemental testing must be CLIA-certified. Note: If results of testing performed in a research facility are used to treat patients, the facility must be CLIA-certified

PERSONNEL TRAINING AND CONTINUING EDUCATION

CLIAC Recommendations:

- Emphasize the need for patient confidentiality, and give examples of circumstances where breaches of confidentiality could occur
- Include a thorough explanation of Universal Precautions—for example, the need for changing gloves between patients may not be obvious to non-laboratorians

- Emphasize safety and QC procedures as two major components requiring training
- Stress the HIPAA law applies to waived testing and include the HIPAA website (http://www.hhs.gov/ocr/hipaa)
- Define and give examples of how to provide on-the-job training
- Define "competency" in a glossary, as it is a difficult concept to convey

DISSEMINATING GOOD LABORATORY PRACTICE GUIDELINES

CLIAC Recommendations:

- Consider *MMWR Recommendations and Reports* as the comprehensive source document
- Post guidelines on the CMS website
- Request State Survey Agencies to mail a copy of the guidelines to CW applicants
- Mail a copy of the *MMWR Recommendations and Reports* publication to professional organizations and encourage dissemination to their members
- Include Medical Group Management Association and HIV/AIDS educators when disseminating the guidelines
- Collaborate (Health Industry Distributors Association [HIDA] with CDC) to devise a one-page tool to be provided at no charge to customers and posted on the HIDA website. The HIDA website will have a CLIA Resource Center
- Recommend manufacturers and distributors post links to the guidelines on their websites
- Provide a web cast via the Public Health Training Network

ADDITIONAL GENERAL COMMENTS

CLIAC Recommendations:

- Ensure the publication is accessible, understandable, and simple enough to be useful
- Vary reading level according to targeted audience
- Provide an acronym table to explain CLIA, OSHA, HIPAA
- Include the following terms in the glossary: clean area, screening test, confirmatory test, competency, manufacturer, distributor
- Emphasize the importance of documentation (e.g. control results, verbal reports) throughout the publication
- If feasible, include a list of analytes for which waived test systems are available. Include a link to the FDA waived test website
- Provide a section or table for HIV testing and other infectious disease special considerations
- Provide a generic template of a product insert to identify key points/information
- Caution laboratories to abide by manufacturer's intended use of test systems
- Provide checklists or table of key waived testing concepts and/or steps for the laboratory director ("responsible party") and testing personnel
- Reference the Joint Commission on Accreditation of Healthcare Organizations National Patient Safety Goals

- Use CLSI documents as reference

A complete list of the CLIAC Recommendations for Good Laboratory Practices for Waived Testing can be viewed in ***Addendum J-1***

CLIA Quality Control Requirements – Present and Future ***Addendum K****

Ms. Rhonda Whalen, Chief, Laboratory Practice Standards Branch (LPSB), DPHP, NCHM, CoCHIS, CDC, discussed present and future CLIA QC requirements as a prelude to the September 2005 CLIAC meeting, where QC will be a major topic. She acknowledged requests to CLIAC for recommendations concerning appropriate QC for microbiology identification panels and explained for non-waived testing, QC requirements present the most challenging aspect of the CLIA program. She stated since the requirements became effective, there have been ongoing requests for variances or exceptions from both manufacturers and laboratories, with these requests being complex and variable, representing challenges to regulatory enforcement and uniform application of federal requirements. Ms. Whalen asked CLIAC to begin considering whether a process can be developed to evaluate requests for exceptions to the requirements for daily testing of control materials. She reviewed the CLIA QC requirements published in the 1992 final rule and changes instituted in the 2003 revised CLIA rule. She explained since regulations usually are a "one-size-fits-all" process, accommodating new and emerging technologies becomes problematic. She stated the section of the CLIA interpretive guidelines covering control procedures was developed to address new technology, provide flexibility, acknowledge the benefits of built-in QC, and accommodate stable test systems through use of alternative mechanisms (i.e., Equivalent Quality Control [EQC]). However, she said these measures are not sufficient to address manufacturers' and laboratories' concerns with several evolving technologies and myriad of test systems. Reviewing the general CLIA QC requirements, Ms. Whalen elaborated on numerous challenges to implementation in today's laboratory environment. She identified the challenge in developing a process for determining appropriate QC among all laboratories and under various testing conditions and detailed the necessary considerations. Ms. Whalen posed the question of whether focusing only on vulnerable areas of testing using risk analysis would be sufficient in determining appropriate QC. In discussing possibilities associated with collection of evidence-based performance data to aid decision-making, she proposed creation of a cooperative network of laboratories using specific test systems to accomplish the requisite data collection. She stated traditional and alternative QC schemes need to coexist and identified issues for consideration, including type of QC materials, QC procedures, control testing frequency, and data evaluation. Ms. Whalen concluded by acknowledging it is difficult to weigh all aspects of the dilemma, and the situation is complicated by the diversity of current and anticipated technology.

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

Bacterial Identification Systems – Quality Control and Regulations – An FDA Perspective

Addendum L

Ms. Freddie Poole, Team Leader, Bacteriology, Division of Microbiology Devices, OIVD, FDA, began her presentation by providing a regulatory history of bacterial identification (ID) systems. She explained that in 1982, bacterial ID systems were classified as Class I IVDs (i.e., devices requiring minimal regulatory scrutiny). She stated Class I devices were exempt from premarket notification (510(k)) procedures as of January 2000, although there are exceptions to this exemption (e.g., systems for identification or inferring identification of microorganisms directly from clinical specimens). Ms. Poole then described the FDA's regulatory oversight of exempted devices, which includes being subject to registration and listing, Quality Systems regulations, and adverse event reporting. She explained that reports of serious adverse events could result in recalls, injunctions, or seizures, and FDA would reconsider exemptions on devices involved in adverse events. Ms. Poole informed the Committee that FDA examines the clinical studies included in the premarket notification applications for data supporting intended use, validating design and software, and validating QC. She stated FDA expects QC systems to be transparent (i.e., the user should be able to understand how the QC material is to be used and what it controls). She explained, however, laboratory practice heterogeneity precludes mandating laboratory-specific practices (e.g., frequency of QC). In reviewing challenges with IVDs, Ms. Poole explained the combined challenge involves the effects of new assays on public health and infection control, how laboratories are able to use the devices, and any implications to industry and FDA. She stated all bacterial ID systems should include a package insert or operator's manual complying with regulations, and concluded by emphasizing the QC section of a package insert should indicate that laboratory performance of QC needs to conform to local, state or federal requirements.

Quality Control Requirements for Microbiology Identification Systems

Addendum M

Ms. Nancy Anderson, Senior Health Scientist, LPSB, DPHP, NCHM, CoCHIS, CDC, began her presentation by posing the question, "What are the appropriate CLIA quality control procedures for microbiology identification systems that utilize panels or cards containing multiple substrates/reagents to generate organism identification?" She first reviewed the CLIA definition of ID systems and the current QC requirements for these systems, pointing out varying numbers of control organisms must be tested to provide the required positive and negative reactivity for each substrate/reagent. After briefly detailing the scope of microbiology ID systems commercially available in the United States, she stated FDA no longer performs pre-market evaluations of these systems, nor do they review QC protocols or labeling to ensure CLIA compliance. Ms. Anderson then referenced two letters to CLIAC from individual microbiologists suggesting CLIA QC requirements for bioMérieux's Vitek ID products are excessive. The letters referred to the manufacturer's recommendation to test only one QC organism to check each shipment and lot number of ID panels or cards. In consideration of this issue of appropriate QC requirements for microbiology ID panels, she posed three critical questions: Is it necessary to check each substrate/reagent for positive/negative reactivity with

each shipment/lot number? Is there an appropriate alternative to testing each reagent/substrate? Should the CLIA requirements specify a minimum number of control organisms?
Ms. Anderson explained that determining a process for appropriate QC is difficult since CLIA requirements cannot be specific to a manufacturer or test system, and she emphasized the goals of quality care and patient safety should guide this process. She then provided a detailed description of a clinical laboratory survey conducted by the American Society for Microbiology (ASM) in 1995-1996, which resulted in a 2003 CLIA regulatory change decreasing the frequency of QC testing for commercial microbiology reagents/stains. Ms. Anderson described CDC's plans to collaborate with ASM on a survey designed to gather evidence-based QC performance data for microbiology ID systems from a full spectrum of clinical laboratories and manufacturers as a first step toward addressing the previously posed questions. In conclusion, she stated if the survey data support changes to CLIA QC requirements for microbiology ID systems, the revisions will be published in the CLIA interpretive guidelines and disseminated to laboratories.

Committee Discussion

- Dr. Robert Martin opened the discussion, explaining the intent to gather information necessary to make an informed decision, emphasizing the need for a process to be used to ensure appropriate changes are implemented in a timely manner, and stressing the challenge relates to determining appropriate QC measures for laboratories, given the existing CLIA laws and regulations.
- A member inquired whether there are data validating some of the quantitative aspects of the EQC approach. Ms. Whalen reiterated EQC was developed in response to public comments indicating the need for updated QC provisions addressing new technology. She explained there is experiential or anecdotal data indicating traditional QC need not always be tested at the frequency specified in the CLIA regulations. Further, reviews of data from CMS laboratory inspections typically indicate controls remain in range; in cases where problems are identified, these often relate more to control materials than to devices.
- Several members concurred that no microbiology ID system has greater than 95% accuracy and, rather than being a result of a QC failure, misidentifications could be due to an insufficient database or to organisms affected by antimicrobial agents and no longer reacting as expected.
- A member requested clarification on interim measures that can be reasonably recommended in the absence of specific data. Dr. Martin responded that in some cases manufacturers make recommendations that are inconsistent with the current regulations, but many laboratories feel they are complying with CLIA when they follow these manufacturers' recommendations, since the regulations specify that laboratories are to follow manufacturer instructions. However, if the CLIA regulations include requirements that are more stringent than the manufacturer's instructions, a laboratory must be in compliance with CLIA. He stated this is an issue for FDA, CMS, the manufacturers, and the clinical microbiology community; each must take the appropriate level of responsibility for making the right decision.
- Ms. Ochs explained the apparent conflict in some product inserts, stating manufacturers recommend the level of QC sufficient to control a device, but also instruct end-users to comply with federal, state, and local regulations since labeling for these products is generalized for a global market. She stated manufacturers expect laboratories performing

moderate and high complexity testing to know and follow the most stringent of applicable federal, state, and local requirements.

- A member inquired whether the issue of excessive QC represents a potential limitation on testing. Other members responded it did not. However, they clarified that laboratories must sometimes purchase QC organisms recommended but not provided by manufacturers, which can present a financial issue, particularly for smaller laboratories.
- Dr. Hearn asked CMS to respond to the situation in which laboratories are confronted with the dilemma of CLIA regulations conflicting with test system labeling. Ms. Yost replied laboratories must follow the current CLIA requirements. In the future, the interpretative guidelines could be changed to permit an exception to the requirements. She expressed appreciation for the efforts of ASM, other professional organizations, and individuals who are concerned about microbiology ID system QC, but emphasized CMS will enforce existing regulations unless data show that a change or exception should be specified in the interpretive guidelines.
- Ms. Ochs formally requested, on behalf of the manufacturers, that CMS use its administrative discretion to allow laboratories to follow manufacturers' QC instructions until new QC guidelines can be developed and implemented. Ms. Yost reiterated CMS's policy is to uphold the law and the implementing regulations; if a deficiency is noted during the course of an inspection, it will be cited.
- A Committee member asked for clarification of the process for data collection and evaluation. Ms. Whalen replied CDC plans to consult with ASM as they develop and conduct the survey to collect representative data, and will collaborate with CMS to develop and disseminate appropriate policies if, in fact, the data prove a change in QC for microbiology ID systems is warranted.
- Dr. Martin acknowledged the laboratory community's contention that CLIA QC requirements for microbiology ID systems are excessive and its willingness to provide data necessary to determine the appropriate level of QC. He noted similar concerns on the part of industry and expressed hope manufacturers would likewise be willing to provide data to aid in decision-making.

SPECIAL PRESENTATIONS

The Committee recognized the contributions of four retiring members whose terms will end June 2005:

- Dr. Cyril (Kim) Michael Hetsko
- Dr. Mary Margaret McGovern
- Mr. Albert H. Stahmer
- Dr. David N. Sundwall, CLIAC Chair

PUBLIC COMMENTS

Dr. George Birdsong, American Society of Cytopathology	***Addendum N***
Matthew Schulze, American Society for Clinical Pathology	***Addendum O***
Robert Eusebio, Dade Behring	***Addendum P***
Wendy Williams, BD Diagnostic Systems	***Addendum Q***

Dr. David Sewell, American Society for Microbiology ***Addendum R***
Cindy Somogye, bioMérieux, Inc ***Addendum S***

ADJOURN

Dr. Martin expressed gratitude to Dr. Sundwall for his dedicated service to the Committee and recognized his confirmation as Executive Director of the Utah State Health Department as a tribute to his professional knowledge, leadership, and management skills. Dr. Hearn then announced Dr. Lou Turner would assume the role of CLIAC Chair at the next meeting.

Dr. Sundwall concluded with a review of the outcomes from this meeting:

- The FDA should expedite publication of waiver guidance for manufacturers requesting waived status of test systems
- Consideration should be given to revising the cytology PT regulations based on updated comments from the professional organizations and the public to reflect current practice, evidence-based guidelines, and anticipated changes in technology
- CLIAC provided recommendations for good laboratory practices for waived testing based on suggestions from the Workgroup.
- ASM and CDC will collaborate on a survey to gather QC performance data for microbiology ID systems and will present a status report on the survey to CLIAC in September 2005.

Dr. Sundwall announced September 7-8, 2005, as the next CLIAC meeting and adjourned the Committee meeting.

I certify this summary report of the February 16-17, 2005, meeting of the Clinical Laboratory Improvement Advisory Committee is an accurate and correct representation of the meeting.

_____ Dated:

David Sundwall, M.D., CLIAC Chair