Clinical

Laboratory

Improvement

Advisory

Committee

Draft Summary Report

February 14-15, 2007
Omni Hotel at CNN Center
Atlanta, Georgia

U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES

Clinical Laboratory Improvement Advisory Committee
February 14-15, 2007, Draft Summary Report
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Record of Attendance

Committee Members Present

Dr. Lou Turner, Chair	Dr. Kevin Mills McNeill
Ms. Joeline Davidson	Dr. Dina Mody
Dr. Nancy Elder	Dr. Valerie Ng
Ms. Marilyn Francis	Dr. James Nichols
Ms. Paula Garrott	Dr. Gary Overturf
Dr. Carol Greene	Dr. Barbara Robinson-Dunn
Dr. Lee Hilborne	Dr. Thomas Williams
Mr. Kevin Kandalaft	Dr. Jean Amos Wilson

Committee Members Absent

Dr. Jared Schwartz
Dr. Gerri Hall
Dr. David Smalley
Ms. Luann Ochs, Roche Diagnostics Corporation (Liaison Representative – AdvaMed)

Executive Secretary

Dr. Thomas Hearn

Ex Officio Members

Dr. Devery Howerton, CDC
Ms. Judith Yost, CMS
Dr. Steven Gutman, FDA

Record of Attendance, continued

Centers for Disease Control and Prevention

Ms. Nancy Anderson
Ms. Carol Bigelow
Dr. Joe Boone
Ms. Diane Bosse
Dr. Bin Chen
Ms. Deborah Coker
Ms. Stacey Cooke
Mr. David Cross
Ms. Joanne Eissler
Ms. Christine Ford
Ms. MariBeth Gagnon
Ms. Sharon Granade
Mr. James Handsfield
Dr. Lisa Kalman
Dr. John Krolak
Dr. Ira Lubin
Mr. Duncan MacKellar
Ms. Leslie McDonald
Ms. Andrea Scott Murphy
Ms. Anne Pollock
Ms. Emily Reese
Ms. Diane Ricotta
Dr. Shahram Shahangian
Ms. Colleen Shaw
Mr. Darshan Singh
Ms. Shuenae Smith
Dr. Susan Snyder
Mr. Steve Steindel
Dr. Julie Taylor
Mr. Eric Thompson
Ms. Pam Thompson
Ms. Leigh Vaughan
Ms. Glennis Westbrook
Ms. Irene Williams

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

Ms. Carol Benson (FDA)
Dr. Elliot Cowan (FDA)
Ms. Penny Mattingly (CMS)
Ms. Harriet Walsh (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. All members then made self-introductions and financial disclosure statements relevant to the meeting topics.
Dr. Thomas Hearn, Acting Director, Division of Laboratory Systems (DLS), National Center for Preparedness, Detection, and Control of Infectious Diseases (NCPDCID), Coordinating Center for Infectious Diseases (CCID), Centers for Disease Control and Prevention (CDC), and Executive Secretary, CLIAC, also welcomed the members.

AGENCY UPDATES AND COMMITTEE DISCUSSION

Centers for Disease Control and Prevention (CDC) ***Addendum A***

Julie Taylor, Ph.D.
Senior Service Fellow
Division of Laboratory Systems
National Center for Preparedness, Detection, and Control of Infectious Diseases
Centers for Disease Control and Prevention

Dr. Taylor began her presentation with a discussion of plans for the upcoming CDC 2007 Institute – "Managing for Better Health," the fifth in a series of Institutes addressing critical issues in medical laboratory practice. She explained the Institute's provisional vision and

purpose and described the processes currently underway to develop the agenda, workgroup sessions, and program content through use of both an Institute Committee and a Content Workgroup. In concluding her overview of plans for the Institute, Dr. Taylor enumerated next steps toward launching it and outcomes expected from it. Dr. Taylor then introduced a CDC project entitled "Defining Best Practices in Laboratory Medicine" and stated the overall goal of the project is to enhance the practice of laboratory medicine by identifying ways to improve laboratory testing and services. She discussed the status of and next steps for the project's three tasks:

- development of a report describing the current state of the field of laboratory medicine;
- development of a process to define, identify, categorize, and evaluate best practices and policies in laboratory medicine; and
- evaluation of the effectiveness of proficiency testing (PT) programs in the United States to meet quality improvement, educational, and regulatory goals for clinical laboratories.

In concluding her presentation, Dr. Taylor identified and thanked team members associated with the 2007 Institute and the best practices project and emphasized that these initiatives represent the framework for a significant body of work intended to engage partners and stakeholders well into the future. Dr. Taylor provided a web link for additional information on the CDC projects, http://www.phppo.cdc.gov/dls/bestpractices/. This site will be updated periodically as the projects move forward.

Committee Discussion

The Committee expressed their overwhelming support for CDC's projects and provided the

following suggestions and comments:

- Request input from the leading United States' academic laboratory medicine departments on the CDC tasks and projects.
- Involve a geneticist in workgroup planning for both the Institute and the best practices project.
- Include a discussion in the laboratory medicine report on maximizing the integration of laboratory medicine into the whole of medicine.
- Consider use of the term "promising practices" instead of the potentially more limiting term "best practices."
- Implement a process to measure the impact and effectiveness of identified best practices in laboratory medicine.
- Consider using pre- and post-analytical issues of genetic testing as a demonstration project addressing how to "drive" best practices.

In concluding the discussion, Dr. Hearn responded to a question from the Chair of how the findings of the PT workgroup might affect CLIAC's prior cytology PT recommendations. He stated that cytology PT would fall under the general purview of the workgroup, which is examining PT in a broad sense.

Food and Drug Administration (FDA) Update ***Addendum B***

Dr. Steven I. Gutman, M.D.

Director, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)

Center for Devices and Radiological Health (CDRH)

Food and Drug Administration

Dr. Gutman provided updates on the status of three FDA draft guidance documents: Recommendations for Clinical Laboratory Improvement Amendments of 1988 (CLIA) Waiver Applications - Draft Guidance for Industry and FDA Staff; Draft Guidance for Industry and FDA Staff - Commercially Distributed Analyte Specific Reagents (ASRs): Frequently Asked Questions (FAQs); and Draft Guidance for Industry, Clinical Laboratories, and FDA Staff - In Vitro Diagnostic Multivariate Index Assays (IVDMIA). Regarding the latter two guidances, he informed the members that the public comment period had been extended to March 5, 2007, and stated that FDA has cleared a novel device, an expression array intended for use in breast cancer diagnosis, as an IVDMIA. He concluded his remarks with a review of current FDA critical path initiatives, emergency preparedness efforts, and flexible regulatory tools that provide a variety of techniques and approaches to maintain a short, fast critical regulatory path based on sound science.

Committee Discussion

- Using the example of the recently approved device characterized by the FDA as an expression array, a member inquired about the expected lag time between device availability and determination of reimbursement potential. Dr. Gutman opined that there is reasonable potential for reasonable reimbursement of prognostic tests that provide adjunctive information. He acknowledged, however, that there are FDA cleared products for which obtaining reimbursement remains a challenge.

- Another member identified the challenge of integrating reasonable discipline into test ordering practices. Dr. Gutman responded that, while FDA is cost-blind in the review process, the agency expends significant effort when tests are cleared to ensure sufficient information is available in the labeling and in FDA's decision memos to support informed decision making about test use.
- A Committee member thanked the FDA for granting an extended public comment period for the ASR FAQs and the IVDMIA guidance.

Centers for Medicare & Medicaid Services (CMS) ***Addenda C & D***

Judy Yost, M.A., M.T.(ASCP)

Director, Division of Laboratory Services

Survey and Certification Group

Centers for Medicare & Medicaid Services

CLIA Update 2007

Ms. Yost presented CLIAC with a comprehensive written update addressing a variety of topics: current CLIA statistics, electronic health records, state surveyor consistency training, Clinical and Laboratory Standards Institute (CLSI) Evaluation Protocol (EP) – 23, and PT policy, as well as oversight of genetic testing and the status of the cytology Notice of Proposed Rulemaking (NPRM). She confined her oral presentation to a discussion of the latter two topics.

CLIA Oversight of Genetic Testing

In response to the Committee's September 2006 request for further discussion on the CMS decision against publishing a Notice of Proposed Rulemaking (NPRM) for a genetics specialty, Ms. Yost provided an update on the status of CLIA and genetic testing oversight. She discussed the background and history of the genetics NPRM, presented a general overview of the CLIA program, identified the current CLIA requirements applicable to genetic testing, and specified the reasons for not establishing the genetics specialty at this time. In concluding her presentation, Ms. Yost detailed CMS' plan to enhance genetic testing laboratory oversight under the current regulation and expand and improve their website.

Committee Discussion: CLIA Oversight of Genetic Testing

Following Ms. Yost's presentation, the Committee expressed support for CMS' efforts to improve its website, provide technical training to surveyors on genetic testing issues, and collaborate with CDC to publish educational materials via a *Morbidity and Mortality Weekly Report (MMWR) Recommendations and Reports*. CLIAC made the following comments and suggestions regarding enhancing CLIA oversight for genetic testing:

- Several CLIAC members disagreed with the CMS decision not to establish a genetics specialty under CLIA and stated that the rationale for this decision requires further justification. It was stated that genetic testing should be recognized as a specialty under CLIA because genetics is an area of medicine recognized by the American Medical Association and a specialty approved by the American Board of Medical Specialties.

- The definition of genetic tests needs to be determined.
- Several members cited concerns of the genetic testing community regarding the quality of result interpretation and personnel qualifications in some laboratories performing genetic tests and stated that CMS survey data would not identify such deficiencies since surveyors might not specifically assess all aspects of genetic testing performance.
- There should be specific oversight for laboratories performing genetic testing (including molecular genetics) in the CLIA regulations or surveyor guidelines regarding personnel, PT, and quality control (QC).
- Since most identified problems occur in the pre- and post-analytic phases rather than the analytic phase of genetic testing, minimum training and/or experience requirements are needed for technical supervisors and laboratory directors of genetic testing laboratories.
- Genetic tests ordered for patient care should have both analytical validity and clinical validity. This could be ensured through appropriate requirements for the pre-analytic phase and through education for laboratory personnel and users of laboratory services. CLIAC recognizes, however, that clinical validity of testing is beyond the scope of CLIA.
- It is important to recognize voluntary standards developed by professional societies and use them as best practice guidelines.

At the conclusion of the discussion, the Committee acknowledged the expedience of exploring and using the current regulatory framework to attain enhanced oversight for genetic testing. CLIAC agreed that CMS and CDC should work with experts to further clarify the critical issues and subsequently include presentations by CDC staff and perspectives of other representatives for consideration at the next Committee meeting.

CLIA Update, Cytology Proposed NPRM

With respect to cytology PT, Ms. Yost provided a brief chronology of events leading up to the present collaboration between CMS and CDC to develop the NPRM. She pointed out that pathologists screening Pap smears without a cytotechnologist (primary screening pathologists) continue to fail PT at a much higher rate than either cytotechnologists or pathologists working with a cytotechnologist. In addition, she stated that representatives in the cytopathology community have proposed legislation to revise the statutory cytology PT provisions in CLIA for testing individuals rather than laboratories.

Committee Discussion: CLIA Update, Cytology Proposed NPRM

- With respect to primary screening pathologists, a member inquired about this year's preliminary test scores compared with last year's scores and stressed the importance of evaluating final test results for these individuals to assess the effectiveness of efforts to discourage the practice of primary screening by pathologists. Ms. Yost stated the preliminary results show fewer primary screening pathologists failing the first round of testing in 2006 compared to 2005.
- Asserting that primary screening pathologists typically practice in very small or rural settings unlikely to be inspected by accreditation organizations, the same member asked what CMS is doing to locate these practitioners. Ms. Yost identified several approaches available to CMS. Surveyors are trained to determine the status of cytology PT and to ensure that appropriate

remediation has taken place. She stated that when surveyors note serious issues in a laboratory, they can request a retrospective review of previously reported Pap smears by an outside professional entity. In addition, Ms. Yost said the possibility of creating a list of all primary screening pathologists with the intent to conduct focused inspections to verify that the regulatory process has been followed and to ensure there are no other problems in the laboratory is under consideration. She also indicated that problems have been uncovered through complaints made to CMS following implementation of cytology PT.

- Another member inquired specifically about plans to implement changes to the cytology PT scoring grid as recommended by CLIAC and about the expected impact on test scores if the recommended scoring grid is adopted. In response, Ms. Yost stated CLIAC's scoring recommendation will be included along with other scoring options in the NPRM. She informed the members there would be no retrospective adjustments to test scores, as regulations are implemented prospectively.
- In concluding her remarks, Ms. Yost reminded the Committee of the process for publishing the NPRM and subsequent final CLIA rule:
    - publish a proposed rule and establish a comment period to allow for input from the public and the cytology community,
    - formulate a response to each comment,
    - determine content of final rule based on the comments,
    - publish a final rule, and
    - establish an appropriate "rollout" plan prior to implementation of the final rule.

The Future of Laboratory Medicine – Simple Testing, Diverse Sites ***Addendum E***

Thomas L, Hearn, Ph.D.

Acting Director, Division of Laboratory Systems

National Center for Preparedness, Detection, and Control of Infectious Disease

Centers for Disease Control and Prevention

Dr. Hearn introduced the theme for this meeting, "Future of Health Laboratory Practice: Challenges to Laboratories Performing 'Simple' Testing in Diverse Sites." This was the final installment in the trilogy of topics, begun with the Spring 2006 CLIAC meeting, focusing on future challenges for laboratory medicine in public health, "complex" or nonwaived, and waived testing. He described the changes in laboratory demographics from 1993-2006, particularly noting the significant increase in numbers of laboratories performing waived testing, and remarked that a growing number of sites other than traditional laboratories, for example, skilled nursing facilities and Women, Infants, and Children Programs, are performing waived tests. Dr. Hearn presented questions for the Committee deliberations concerning the adequacy of current laboratory practices in assuring quality and assessing if the needs of public health and clinical care are being met in diverse and nontraditional settings. He then introduced the speakers and topics for the meeting.

No Committee Discussion

Current & Future Applications of Point of Care Testing ***Addendum F***

Paula Santrach, M.D.

Mayo Clinic

Rochester, Minnesota

Dr. Santrach presented an overview of the scope, drivers, current and future tests, and major issues surrounding point-of-care testing (POCT). She noted traditional laboratory instruments, for example, benchtop blood gas analyzers, are being used at the point of care while tests for B-type natriuretic peptide and pregnancy, originally designed for point-of-care use, are being performed in the laboratory, thus blurring the lines of demarcation. General trends of testing include moving from traditional settings to less traditional, non-professional ones and from complex to simpler testing procedures. Factors driving POCT include interaction with patients at the time of testing allowing more rapid clinical decisions, quicker reactions to outbreaks and emergencies, less stringent regulatory requirements, and the national laboratory technologist workforce shortage. Dr. Santrach listed the most common tests performed at the point of care, tests emerging for the future, and several tests that are no longer in use. She concluded her presentation with a discussion of issues surrounding POCT including a mixed evidence base for effectiveness, standardization and comparability of tests, complexity of data management and oversight, and the actuality that more rapid results do not always lead to better outcomes.

Committee Discussion

- One member observed most of the presentation centered on the hospital setting and stated that since much POCT is conducted in physician office laboratories (POLs), they should also be considered when addressing this topic. Dr. Santrach pointed out that many of the issues in hospital settings also apply to POLs and other non-medical sites, such as malls or accident

scenes, where testing is performed without any oversight. Little data are available to evaluate testing in these types of settings.

- Another member questioned the overall cost-benefit ratio of POCT given its inherent loss of economies of scale coupled with a paucity of evidence for improved patient outcomes. Dr. Santrach responded that although there are a number of POCT technologies that are cost effective, there may be overuse of some tests. She noted there is little evidence supporting the benefits of routine use of certain POCT, for example, conducting urine dipstick testing on all hospital admissions, and stated this is an area that needs to be reviewed.
- A member noted that putting tests in easy reach at the point of care tends to drive up test ordering volume and the potential for unnecessary testing. Several members commented that, in some cases, every patient complaining of a sore throat in a physician's office receives a rapid group A streptococcus (strep) test, whether or not they have symptoms of a viral infection. Another member pointed out the convenience of rapid tests encourages clinicians to order panels, which may include tests unrelated to a patient's care.
- A member asked for clarification on the regulation for waived testing and inquired if the FDA product clearance includes evaluation of pre-analytic or patient criteria. This member cited the example of laboratories performing waived group A strep tests on specimens other than those for which the test is approved, for example, testing perirectal swabs or stool samples rather than throat swabs as specified by the manufacturer. Ms. Yost noted that when test performance is modified with respect to either intended use or specimen type, the test is not considered waived, and the categorization automatically defaults to high-complexity. When CMS discovers such practices, the laboratory is then cited for operating outside the scope of its CLIA certificate.

- Several members commented on POCT reimbursement. One member pointed out since these tests are more expensive, there have been an increased number of requests for alternative CPT codes for waived tests under the aegis that they represent better patient care and therefore should receive higher reimbursement. However, the evidence for this is minimal in some settings; further, higher reagent costs for waived or POCT may be offset by reduced costs associated with decreased time in follow-up. Dr. Santrach noted reimbursement is a barrier for performing POCT in the home, citing reimbursement of prothrombin time, international normalized ratio as an example. A member responded that as the science of measuring episodes of care and patient outcomes is refined, reimbursement issues may be addressed.
- The question, "How fast is fast enough?", was raised by a Committee member, who also asked about the required level of precision for rapid tests and suggested consideration be given to which POCT applications offer the most value. This member noted the value of rapid testing for potential biological agents at incident sites but warned of consequences (for example, significant resources expended in mounting a response) when such tests are performed in the field by first responders who may lack sufficient training to perform tests properly.
- Throughout the discussion , Committee members pointed out advantages to properly performed POCT including:
  - alleviating problems associated with specimen transportation,
  - facilitating immediate treatment and improved antibiotic effectiveness, since it provides an answer before the patient leaves the office, and

- providing an excellent opportunity for laboratorians to become part of an integrated healthcare team.

Good Laboratory Practices for Waived Testing – Update ***Addendum G***

Sharon Granade

Health Scientist, Laboratory Practice Standards Branch

Division of Laboratory Systems

National Center for Preparedness, Detection, and Control of Infectious Diseases

Centers for Disease Control and Prevention

Ms. Granade presented an update on the marketing of the *MMWR Recommendations and Reports:* Good Laboratory Practices for Waived Testing Sites (http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5413a1.htm). After reviewing the background of the MMWR that resulted from CLIAC's recommendations, she reviewed efforts to disseminate and to promote awareness of the report, listing a number of professional organizations to which the *MMWR* publication was provided via several venues. She detailed the Health Marketing and Communication Planning process used, described development and concept testing of new materials to promote good laboratory practices (GLPs), and outlined future marketing and evaluation efforts. In concluding her presentation, Ms. Granade queried CLIAC for additional suggestions to maximize GLP marketing efforts.

Committee Discussion

- It was suggested that CDC approach schools of public health and state public health outreach programs with information to promote the GLPs to POLs.
- A member suggested the *MMWR* could be mailed with CLIA certificates, and another stated sales representatives could be enlisted to provide posters and brochures as a courtesy when visiting POLs. A third member proposed working with state or large metropolitan medical societies.
- Ms. Granade concurred with a suggestion that professional risk managers be informed of the *MMWR* publication noting this was a previous CLIAC suggestion.
- A member remarked physicians consider their office a place where they provide patient care, not laboratory services, and suggested marketing the GLPs through professional groups representing family practitioners, medical assistants, and medical office managers, such as the American Academy of Family Physicians and the Medical Group Management Association. Another possible vehicle for reaching physicians and medical practitioners is internet-based communication such as websites and listservs.
- It was suggested that concepts addressing POL testing quality be marketed directly to consumers via popular magazines, as exampled by the pharmaceutical industry, thereby giving the message to physicians that patients are watching.
- In commenting on draft versions of GLP promotional posters, several members advised it would be better to avoid use of sports metaphors.

Good Laboratory Practice: Certificate of Waiver Urine Dipstick Job Aid ***Addendum H***

Karen Breckenridge, MBA, MT(ASCP)

Knowledge Manager

National Laboratory Training Network

Ms. Breckenridge described a project conducted as part of a cooperative agreement between the Association of Public Health Laboratories (APHL) and CDC. The project's goal is to strengthen the quality of office laboratory testing services by improving skills of the staff performing waived tests through development of a job aid/training resource product for POLs holding CLIA Certificates of Waiver (CW). CMS and CDC data indicate a need for POL job aids. After research involving questionnaires and laboratory surveyor input, the first job aid product from APHL, now in field testing, is for urine testing using a dipstick. The job aid includes a checklist, a list of interfering substances, and step-by-step instructions. A uniform template for future job aid development has also been created. When finalized, APHL plans to post the job aids on its website so they can be downloaded and will be widely accessible to the public.

Committee Discussion

The Committee was very receptive to the introduction of job aids for use in waived testing sites. Members overwhelmingly supported the adoption of job aid example "A" and provided the following comments and suggestions for refinement of this tool:

- The discussion included several suggestions for revisions to the language on the urine dipstick procedure provided on the job aid poster. One member saw a need to be more specific about the phrases "sample freshness" and "delay in testing." Another member

suggested that “Test personnel for color blindness” be changed to read, “Are you color blind?” A third member pointed out use of the “current” manufacturer’s insert should be specified to avoid inappropriate re-use of outdated inserts.

- It was suggested the job aid be written in the form of a checklist with consistent use of active verbs.
- A member recommended dating the job aid, adding a reference to the *MMWR,* and including a list of the most common procedural errors.
- Another member suggested that both sides of the job aid be used and that the graphics be made more exciting and appealing.
- Addressing the difficulties presented by variations in testing techniques was discussed, including an example of how scant samples are sometimes incorrectly poured over a dipstick rather than completely dipping the strip into a urine specimen.
- Another member commented on the importance of qualitative analysis of the urine specimen color. The member also noted the typical dimensions of urine collection containers do not match well with that of dipsticks, requiring the sticks be bent to completely immerse them, in violation of manufacturer directions and suggested the job aid illustrate the most common way to immerse test strips without bending them.

New Hampshire Trainings: Good Laboratory Practices for Waived Testing Sites

Addendum I

Christine Bean, Ph.D., MBA

Director, New Hampshire Public Health Laboratories

Dr. Bean summarized New Hampshire's Public Health Laboratory's training program. The training, based on the 2005 *MMWR* publication, "Good Laboratory Practices for Waived Testing Sites," focused on a target audience consisting of the office managers and laboratory personnel in POLs. She described the locations, personnel, topics, and materials used in the program and feedback and evaluation data demonstrating most participants felt the training met or exceeded their expectations. The participants expressed that the training had increased their knowledge about quality assurance, writing procedures, and laboratory personnel training and indicated changes they would make in their laboratories as result of the training. Dr. Bean said next steps consist of additional trainings, POL membership in the Laboratory Response Network (LRN), and inclusion of POLs and waived testing sites in the State Public Health Laboratories' quality assessment in March 2007.

Committee Discussion

- One member asked if POLs were members of the LRN. Dr. Bean replied that anyone who plays a role in the healthcare delivery system could be part of the state's network, emphasizing POLs play a significant role in first line screening in the context of events such as avian flu or influenza. Dr. Turner added that North Carolina has developed an LRN within the state that includes a state point of contact and its own criteria and educational program and suggested other states could develop a similar network of laboratories.

- In response to the question of whether retrospective assessment demonstrated attendee follow through with planned improvements in their laboratories, Dr. Bean replied this evaluation is in the planning stages.
- A member noted out of the 900 laboratories identified in New Hampshire, only 48 people attended the training and inquired about the plan to reach the rest of the laboratories. Dr. Bean replied that three additional trainings are being planned for 2007 and a plan is being devised to capture one of the next trainings on web cast. Compact discs (CDs) will then be produced and distributed for use in training to maximize resources and address the problem of high turnover in these laboratories. A member suggested offering training that covers more than one topic to attract a wider range of participants.
- Another member suggested focusing on physician organizations within the state, for example, the Academy of Family Physicians and other medical societies, which would be more effective for reaching POLs than focusing on laboratories. The member reminded the Committee that laboratory testing is only a small part of the job in a POL. Staff does not self-identify as laboratorians and tend to believe whatever the sales representatives tell them.
- A member inquired if POLs with a CW are required to be associated with any professional entity or are subject to any oversight. Dr. Turner replied that although random surveys of CW sites are conducted every year by CMS and that the focus of the surveys includes an educational component, the sheer number of CW sites prevents surveying everyone. Dr. Hearn agreed that since sites that conduct only waived testing are not subject to required onsite inspections, it is a challenge to reach POLs or CW sites that are not linked to professional organizations that could provide education and training. Dr. Turner noted North Carolina is one of the only public health laboratories that maintain a training program, a

difficult task since training and education programs are often the first to suffer when budgets are cut.

Workgroup Report: The Impact of Rapid and Molecular Tests for Infectious Disease Agents on Public Health ***Addendum J****

Barbara Robinson-Dunn, Ph.D., D(ABMM)

CLIAC Workgroup Chair

Dr. Robinson-Dunn presented the report of the Workgroup meeting held on November 2, 2006. The Workgroup was charged with considering key issues relating to the impact of rapid and molecular testing technology for infectious disease agents and ways to assure quality testing is performed, specimens are collected and maintained for confirmatory testing or epidemiologic activities, and any required reporting of public health disease is carried out. Dr. Robinson-Dunn reviewed the Workgroup's discussion, which was organized around three topic areas that included: Rapid and Molecular Testing - Now and in the Future; Identifying Public Health Gaps and Challenges; and Assuring Quality and Maximizing Public Health Impact.

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

Committee Discussion: The Impact of Rapid and Molecular Tests for Infectious Disease Agents on Public Health ***Addendum K****

Dr. Turner thanked Dr. Robinson-Dunn and the Workgroup members for their efforts in providing input for CLIAC consideration. Committee members discussed the report, provided clarification in some areas, and made additional suggestions concerning rapid and molecular testing issues. Much of the Committee discussion was centered around rapid test result interpretation, public health infectious disease reporting, and issues related to communication between public health and POLs or other laboratories. As each topic was addressed, the Committee noted the current status of testing, identified public health gaps and challenges, and suggested ways to fill the gaps and meet the challenges. A summary of the major points raised by CLIAC follows:

Rapid Test Use, Interpretation , and Reporting

- Users of rapid tests need assistance in understanding their intended use, performance characteristics, and limitations. Stakeholders with knowledge of the testing should make recommendations using performance-based information as to which rapid tests are appropriate for specific diagnostic indications.
- The test report should indicate the result was obtained using a rapid test to alert the user of this fact and possible limitations of the testing.
- A positive result from a rapid test for an infectious disease agent may influence a clinician's differential diagnosis and limit the consideration of other possible causative disease agents.
- It is important that users of rapid tests understand how test sensitivity, specificity, and disease prevalence can affect test results.
- In addition to specifying the proper use of the test, product inserts should be user-friendly

and include the following:

- what the test is not intended to do and when it should not be used;
- plain language discussions of lower limits of detection and confidence intervals; and
- public health disease reporting requirements.

- Tests for select agents should not be performed in POLs or waived laboratories.

Multiplex Testing

- The regulatory approval process should include consideration of the potential for a large number of diverse tests to be included in multiplex panels. Dilemmas arise when laboratories are obligated to report positive results for a test that was not ordered. In addition to infectious disease testing, this is an issue in other laboratory specialties, such as testing for drugs of abuse and cardiac markers.
- To aid in appropriate reimbursement for multiplex testing, the use of order sheets that direct the test requester to order a panel rather than a single test may be helpful.

Cost and Reimbursement of Testing/Lack of Specimen Availability

- Shipping specimens or isolates to the public health laboratory is a cost barrier for traditional laboratories and is even less likely to occur in POLs.
- Costs could be reduced if state epidemiology offices developed a formulary of preferred tests. States might then be able participate in a bulk purchasing pool and reduce testing costs. The cost savings could be applied to costs for shipping specimens or used to support improvements in communications. Additionally, to help offset some costs, state laboratories could supply shipping containers.

- Reimbursement experts are needed to assist in addressing cost issues.

Public Health Reporting

- The states should agree to national public health reporting requirements while taking into account endemic diseases for individual states.
- Reporting should be automated; however, electronic reporting remains a challenge because of the lack of interoperability among the numerous information systems in use.
- Participation by AdvaMed could be beneficial in promoting the development of electronic public health reporting mechanisms.
- Manufacturers and state health departments should work with physicians and their staff to arrive at workable mechanisms for public health reporting.
- Manufacturers should consider building rapid test result reporting mechanisms into point-of-care products. For example, it would be beneficial if there was a mechanism to alert the test operator that public health reporting is required when a positive result is obtained.
- Billing codes could serve as triggers to alert users of the need for public health reporting.

Communication

- Electronic public health communication should link state epidemiology programs and state public health laboratories.
- All clinical laboratory directors should be included in sentinel systems.
- Communication between public health and other laboratories could be improved by developing infectious disease reports that could be sent to all testing sites. The list of laboratories in each state could be generated using CLIA certificate information.

- Consider linking public health laboratories not only to small laboratories and POLs but also to environmental and veterinary laboratories.
- Acknowledge the challenges that arise from centralized versus decentralized public health systems.

Education

- Consider ways to educate physicians and others, i.e., office managers, about the positive ramifications of public health reporting, risks inherent in failing to report, and correct disposal of biological waste.
- Target office managers through professional organizations such as the Medical Group Management Association to communicate the value of public health disease reporting.
- Consider cultural diversities when embarking on educational efforts. People obtain healthcare information from trusted sources (community organizations, churches,) not necessarily from healthcare professionals or "the system."
- Educate rapid and molecular test users that, with respect to HIPAA concerns, communicable disease reporting is a legally authorized and required activity in all states and territories. HIPAA should not interfere with patient care.

Next steps/Summary:

Dr. Hearn concluded the discussion by offering some suggestions for next steps in conveying the concerns of the Workgroup, which were subsequently supported by CLIAC. They are summarized as follows:

- Dr. Robinson-Dunn will attend the CDC CCID Board of Scientific Counselors meeting in the

near future to represent CLIAC and bring forward the highlights of the Committee discussion (see Note on page 41);

- CLIAC suggestions and concerns should be shared with APHL and the Council of State and Territorial Epidemiologists;
- Physicians and staff of POLs need to be engaged in the issues discussed by involving their professional organizations rather than focusing on laboratory organizations; and
- Additional data should be collected to address the extent of the problems identified by CLIAC.

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

Rapid HIV Antibody Testing Update ***Addendum L***

Devery Howerton, Ph.D.

Acting Chief, Laboratory Practice Standards Branch

Division of Laboratory Systems

National Center for Preparedness, Detection, and Control of Infectious Diseases

Centers for Disease Control and Prevention

Dr. Howerton presented a brief history of rapid HIV antibody testing and the controversy leading to the decision to grant waived status to some rapid HIV tests. The use of rapid HIV antibody

testing is being promoted to decrease the time for test results, increase access to testing and detect new cases, and to support CDC's 2006 recommendations to include HIV testing as a routine part of healthcare. Dr. Howerton's summary introduced the three presentations that followed on HIV test performance evaluation, testing in public health settings, and the use of rapid HIV testing in the private sectors.

No Committee Discussion

Findings from the Model Performance Evaluation Program for Rapid HIV Antibody Testing ***Addendum M****

Dr. Howerton described the CDC Model Performance Evaluation Program (MPEP) for rapid HIV antibody testing, which is a voluntary, non-regulatory external quality assessment program that provides challenge samples and questionnaires on testing practices to enrolled laboratories biannually. She explained the benefits to public health evolving from the program and described challenge samples, demographics of the participating laboratories, performance statistics, and laboratory testing practices including use of QC materials and confirmatory testing.

Committee Discussion:

- A Committee member asked about data for indeterminate results not mentioned in the presentation. Dr. Howerton clarified that only positive and negative challenges were included and the appropriate response for rapid test systems would be "invalid".

- Noting an increase in false positive and false negative results, a member suggested this may result from more people performing rapid testing, thus increasing the potential for incorrect results. Documenting the total number of testers involved might provide data to allow future correlation of the percentage of false positives and false negatives based on the number of testers.
- One member expressed concern about the data on confirmatory testing practices indicating that some sites do not confirm results or repeat the test with the same kit or up to three rapid test kits as a confirmatory mechanism. Dr. Howerton explained the next presentation would address this as some protocols are now being evaluated for running multiple rapid HIV tests as confirmation. Another Committee member added that even though some laboratories say they use other rapid tests for confirmation, they are also performing Western Blot; multiple methods are used.
- Concerning CLIA-waived rapid tests, a member inquired whether considering only CLIA-waived HIV tests rather than all rapid HIV tests would show a greater number of false negatives and false positives. Dr. Howerton said the data had not been analyzed from that perspective but this could be done.
- Another member asked about options for hepatitis B immunization for testers in point-of-care settings. Dr. Howerton explained that in accordance with Occupational Safety and Health Administration requirements, the use or handling of blood or blood products requires the site to offer vaccine and testing opportunities.
- One member explained their institution could possibly provide data related to rapid HIV test performance and errors in POCT. Dr. Hearn stated such data are needed and should be used

to identify interventions and best practices to help inform others. The challenge is determining how to better capture the information.

In concluding her presentation, Dr. Howerton referenced the latest MPEP Rapid HIV Test Report and directed those interested to the MPEP website for additional reports and links to other sites containing information about HIV testing (www.phppo.cdc.gov/mpep/default.aspx).

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

CLIA-waived Rapid HIV Testing in the Public Health Sector ***Addendum N***

Duncan MacKellar
Team Leader, Diagnostic Applications, Behavioral & Clinical Surveillance Branch
Division of HIV/AIDS Prevention, Surveillance and Epidemiology
Centers for Disease Control and Prevention

Mr. MacKellar explained that the expanded use of rapid HIV testing helps reduce undiagnosed infections, late diagnoses, and perinatal transmission of HIV. He presented data from four CDC-sponsored post-marketing surveillance studies of CLIA-waived rapid HIV testing and described the performance of the tests in use, characterized the quality assurance practices and outcomes, and described the magnitude of CLIA-waived rapid HIV testing in the public health sector.

Based on the data, Mr. MacKellar's conclusions regarding the use of rapid HIV testing in public health settings included the following: test availability is improved, testing practices are reliable, most people receive their results, and HIV diagnosis is increased. He stated that because many people with preliminary positive test results do not return to clinics to receive their confirmed results, there is still a need to evaluate the feasibility and performance of a point-of-care rapid test algorithm to improve accuracy of results and patient care.

Committee Discussion

- A Committee member remarked that the 75-79% rate of clients who return for their confirmatory test result was impressive and asked if there was a baseline rate for returning clients to show the extent of increased returns since the implementation of rapid testing. Mr. MacKellar responded the latest counseling and testing report from public health sites shows the rate of people returning for their confirmatory results has increased but a substantial portion still do not return.
- A Committee member commented that some people in high-risk populations are tested multiple times as they go in and out of various healthcare systems, such as emergency departments or jails. These people may be receiving incomplete information because of healthcare systems that do not link all healthcare providers.
- Addressing the impact on public health, another member described a state program providing additional RNA testing with negative screening tests, which has resulted in identifying a great number of early positive cases including two HIV outbreaks. The increased use of rapid tests has a major impact on new testing methodologies and public health interventions because other test methods are not considered if a screening test is negative. Mr. MacKellar

responded that a primary HIV infection study is being conducted and may be expanded to rapid testing sites so that clients will have the opportunity to submit a blood specimen for acute HIV infection screening. Members discussed home access or over-the-counter testing related to public health reporting, notification of partners/contacts, anonymity or false identity, lack of confirmatory testing, counseling, and failure to seek treatment.

- Committee members asked about the amount of training needed to achieve effective testing and about occupational exposure for testers. Mr. MacKellar responded that six hours has proven adequate and added the CDC-sponsored training includes safety issues.

Following a public comment related to increasing access to and availability of HIV testing, the following additional points were raised by the Committee:

- Members noted there is a need for data demonstrating whether HIV testing would increase if the rapid tests were over-the-counter. Dr. Cowan (FDA) confirmed the home-collection kit for anonymous HIV testing is still an option and added that some of the requirements for manufacturers' studies are to define the intended users and test performance in those populations.
- One member surfaced the issue of test performance and the accompanying decrease in positive predictive value when testing is conducted on low-risk populations, especially if a test was intended to be available to the general public as an over-the-counter test. Dr. Cowan explained one of FDA's requirements for consideration of approval is that manufacturers perform studies that include representation of the intended users and the population that would be tested. To adequately cover the spectrum of all intended users for an over-the-counter test, the study would need to include low-risk people to address test performance in

different populations.

CDC-RAND Study: Evaluation of the Use of Rapid HIV Testing in the United States

Addendum O

Laura Bogart, Ph.D.,

Behavioral Scientist, RAND Corporation

Dr. Bogart discussed the results of a study to determine the scope of rapid HIV testing across private hospitals and private community based health settings and the barriers to rapid HIV test use among private providers. A national sampling of hospitals from twelve metropolitan areas of the U.S., proportional to HIV AIDS prevalence, was surveyed. She stated the survey data demonstrated a steady increase in hospital-based testing, primarily for occupational exposures, and that a high percentage of rapid, non-waived tests were being performed in the laboratory versus at the point of service. A second survey of community clinics and community based organizations showed rapid HIV tests were used infrequently in these settings. The majority of testing was performed on site and almost half for occupational health. Community based organizations tended to refer clients elsewhere. Dr. Bogart stated testing capacity was a strong predictor of rapid test use.

Committee Discussion

- The speaker was asked if the cost of rapid tests influenced the volume of rapid testing.

Another member acknowledged that, based on test costs, in their setting the option of using a standard enzyme immunoassay method outweighs using a rapid test. Dr. Bogart agreed that the cost of rapid testing is a barrier and a cost component is part of their ongoing study.

- A member asked if the large volumes of HIV testing in correctional facilities were included in the study. Dr. Bogart explained they were excluded because a universal survey of community clinics and community-based organizations was the study objective and procedures would be different for other types of sites; however, an advisory board to the present study has suggested that correctional facilities be studied next.

Dr. Turner thanked the presenters and suggested the Committee may wish to revisit the subject again in a few years.

SPECIAL PRESENTATIONS

Dr. Rita Helfand, Acting Deputy Director, National Center for Preparedness, Detection, and Control of Infectious Diseases, CDC, Dr. Hearn, and Dr. Turner recognized the contributions of five retiring members whose terms will end on June 30, 2007:

Ms. Paula Garrott

Mr. Kevin Kandalaft

Dr. Valerie Ng

Dr. Barbara Robinson-Dunn

Dr. Jean Amos Wilson

PUBLIC COMMENTS

- **Angela Caliendo, Association of Molecular Pathology** ***Addendum P***
- **Matthew Schulze, American Society for Clinical Pathology** ***Addendum Q***
- **David Mongillo, American Clinical Laboratory Association** ***Addendum R***
- **James Sykes, The AIDS Institute** ***Addenda S1 & S2***
- **George Birdsong, American Society of Cytopathology** ***Addendum T***

IN MEMORIAM

Dr. Thomas Hearn paid tribute to the life and career of Joseph L. Hackett, Ph.D., former director of special programs at the Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD), FDA, who passed away on February 2, 2007.

ADJOURN

Dr. Turner acknowledged the staff that assembled the meeting program and thanked the CLIAC members and partner agencies for their support and participation. The following reflects outcomes from this meeting:

- Dr. Robinson-Dunn will represent CLIAC at the CDC CCID Board of Scientific Counselors meeting on March 15-16, 2007 to bring forward the concerns and suggestions regarding the impact of rapid and molecular tests for infectious disease agents on public health.*
- As CLIAC Chair, Dr. Turner will present the CMS planned approach and the Committee's suggestions for genetic testing oversight to the Secretary's Advisory Committee for Genetics,

Health, and Society (SACGHS) on March 26, 2007.**

- CLIAC agreed that CMS and CDC should work with experts to further clarify the critical issues in genetic testing oversight and subsequently include presentations by CDC staff and the perspectives of other representatives for consideration at the next Committee meeting.
- Dr. Hearn urged the members to notify either him or Dr. Turner of any issues or topics that may need to be brought to the Committee to ensure the wisest use of its time in session.
- The Chair reminded the Committee that the next meeting will be held on the CDC Roybal Campus and that while the members would be housed off-site, the hotel will provide shuttle service to and from CDC.

Dr. Turner announced the next CLIAC meeting is scheduled for September 5-6, 2007, and adjourned the Committee meeting.

I certify this summary report of the February 14-15, 2007, meeting of the Clinical Laboratory Improvement Advisory Committee is an accurate and correct representation of the meeting.

_____ Dated: 4/30/2007

Lou Flippin Turner, Dr.P.H., CLIAC Chair

NOTES:

* Subsequent to this meeting, it was determined that although Dr. Robinson-Dunn would not make a formal presentation to the CCID Board of Scientific Counselors in March, she would

participate in the meeting to represent CLIAC and provide input regarding CLIAC's discussion of the impact of rapid and molecular tests for infectious disease agents on public health.

** Subsequent to this meeting, it was determined that Dr. Turner would not address SACGHS in March. A one-page summary of CLIAC's suggestions for oversight of genetic testing was provided to that Committee. (See ***Addendum U***)