Clinical

Laboratory

Improvement

Advisory

Committee

Summary Report

February 4-5, 2009
Atlanta, Georgia

U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES

Clinical Laboratory Improvement Advisory Committee
February 4-5, 2009 Summary Report
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Record of Attendance

Committee Members Present

Ms. Elissa Passiment, Chair
Dr. Ellen Jo Baron
Dr. Christine Bean
Ms. Susan Cohen
Dr. Nancy Elder
Ms. Merilyn Francis
Ms. Julie Gayken
Dr. Carol Greene
Dr. Geraldine Hall
Dr. Norman Harbaugh, Jr
Dr. Lee Hilborne
Dr. Paul Kimsey
Dr. James Nichols
Dr. Gary Overturf
Dr. Stephen Raab
Dr. Linda Sandhaus
Dr. Jared Schwartz
Dr. Emily Winn-Deen
Dr. Rosemary Zuna
Ms. Luann Ochs, AdvaMed (Liaison Representative)

Committee Members Absent

Dr. David Smalley

Executive Secretary

Dr. Thomas Hearn

Ex Officio Members

Dr. Alberto Gutierrez, FDA
Dr. Devery Howerton, CDC
Ms. Judith Yost, CMS

Record of Attendance - cont'd.

Centers for Disease Control and Prevention (CDC)

Mr. Todd Alspach
Ms. Nancy Anderson
Dr. Rex Astles
Ms. Shannon Barker
Ms. Diane Bosse
Dr. Roberta Carey
Ms. Yolanda Castillo
Dr. Bin Chen
Ms. Debbie Coker
Ms. MariBeth Gagnon
Dr. Lisa Kalman
Dr. John Krolak
Ms. Debra Kuehl
Dr. Nattawan Lanier
Dr. Xin Liu
Dr. Ira Lubin
Ms. Leslie McDonald
Ms. Andrea Murphy
Dr. Jan Nicholson
Ms. Abrienne Patta
Ms. Anne Pollock
Ms. Angela Ragin-Wilson
Dr. Shahram Shahangian
Dr. Colleen Shaw
Mr. Darshan Singh
Ms. Theresia Snelling
Dr. Susan Snyder
Dr. Julie Taylor
Mr. Howard Thompson
Ms. Pam Thompson
Ms. Malaika Washington
Ms. Glennis Westbrook
Ms. Irene Williams
Dr. Laurina Williams
Dr. Hui Zhou

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

Ms. Carol Benson (FDA)
Mr. James Cometa (CMS)
Ms. Daralyn Hassan (CMS)
Ms. Penny Kellar (CMS)
Ms. Penny Meyers (CMS)
Ms. Cindy Munger (CMS)
Ms. Harriet Walsh (CMS)
Ms. Alexandra Wong (FDA)

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. Thomas Hearn, Designated Federal Official, Clinical Laboratory Improvement Advisory Committee (CLIAC), and Deputy Director, National Center for Preparedness, Detection, and Control of Infectious Diseases (NCPDCID), CDC, welcomed the Committee and the members of the public, acknowledging the importance of public participation in the advisory process. He explained that the primary focus of the meeting would be the past, present, and future Clinical Laboratory Improvement Amendments of 1988 (CLIA) research activities conducted by the Division of Laboratory Systems (DLS). The meeting objectives were to solicit input on current and future research priorities, to identify ways to translate research findings into practice, and to solicit suggestions for evaluating the outcomes of those practices.

Ms. Elissa Passiment, Chair, CLIAC, welcomed the Committee and called the meeting to order. She introduced the new Committee member, Dr. Paul Kimsey. All members then made self-introductions and financial disclosure statements relevant to the meeting topics.

AGENDA UPDATES AND COMMITTEE DISCUSSION

Federal Advisory Committees Meeting Reports ***Addendum A***

Elissa Passiment, Ed.M., CLS (NCA)
Executive Vice President
American Society for Clinical Laboratory Science

Ms. Passiment reported on the first meeting of the Chairs of the 24 CDC Advisory Committees and on the meeting of the Coordinating Center for Infectious Diseases (CCID) Board of Scientific Counselors. The October 2008 CDC Advisory Committee Chairs meeting, convened by Dr. Julie Gerberding, CDC Director, was held to discuss CDC's budget and the Healthiest Nation Initiative as well as to provide networking and communication opportunities to the Committee Chairs. The Advisory Committee to the Director and some Committee Chairs formulated recommendations related to the agency budgeting process and to optimizing CDC organizational structure and programs. They also considered the value of creating a network of the Committee Chairs.

In December 2008, Ms. Passiment attended a meeting of the CCID Board of Scientific Counselors. During a portion of this meeting, four workgroups representing each of the National Centers within CCID met individually and focused on topics pertinent to their individual Centers. Ms. Passiment described her participation on the NCPDCID workgroup. The workgroup agenda included vaccine acceptance issues, healthcare personnel vaccinations, strategic planning, Center updates, and antimicrobial resistance. Ms. Passiment said the workgroup focused on vaccine acceptance issues and discussed how to educate the public about vaccines and provided specific, constructive feedback on NCPDCID's strategic planning report.

Committee Discussion

- Several members stated scientific research on re-verification of vaccine safety and government promotion of vaccines has not countered fears of vaccination. They suggested providing vaccine information to schools, engaging the media, and providing support for programs to non-governmental and non-medical organizations to promote vaccine acceptance would be of more value.
- Ms. Passiment noted the toolkit developed by the National Public Health Information Coalition is an effort to utilize the media to help provide information about the importance of vaccination.
- Several members remarked research should focus more on vaccine acceptance issues and less on re-proving the effectiveness and safety of vaccines. Continuing to conduct research to show vaccines are safe might indicate to the public that the scientific community questions the safety of vaccines.
- One member commented increases in vaccination numbers could be stimulated by a new health ethic addressed by government on a national level.
- Dr. Hearn thanked Ms. Passiment for attending the meetings and commented that it is helpful to have a representative of the clinical laboratory on the CCID Board of Scientific Counselors.

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

Alberto Gutierrez, Ph.D.
Deputy Director, Office of In-Vitro Diagnostic Devices
Center for Devices and Radiological Health
Food and Drug Administration

Dr. Gutierrez began his presentation with an update on the organizational changes at the Food and Drug Administration (FDA), most notably the appointment of Mr. Don St. Pierre as Acting Director of the Office of In-Vitro Diagnostic Devices, replacing recently retired Steve Gutman, M.D., then continued his presentation with an overview of activities occurring at the FDA in the past six months. He reviewed several FDA guidance publications and activities: the publication of the Analyte Specific Reagents (ASR) Questions and Answers document, clearance of the rRT-PCR Flu Panel test, and the occurrence of two advisory panel meetings. Dr.Gutierrez continued with a synopsis of the warning letter sent to LabCorp informing them that OvaSure did not fit the definition of a laboratory-developed test and the resulting action of LabCorp removing the test from the market. He said FDA continues to work on several critical path programs, continues to struggle with user fee mandates, and continues to work extensively in the area of biomarkers. Dr. Gutierrez touched briefly on FDA's consideration of waiver of complete blood cell (CBC)/differential cell count devices and in closing mentioned Genentech's petition to consider regulation of laboratory-developed tests.

Committee Discussion

- The Chair commented that at the September 2008 CLIAC meeting members had determined that considering waiver of a CBC/differential cell count device was not advisable at the time. Dr. Gutierrez agreed and added the message he received from the FDA panel was that it was unlikely current devices could meet the criteria for waiver. The Chair noted that CLIAC had expressed concerns not about the device but about how the results might be used. She emphasized CLIAC had not come to a consensus about which of the tests that are part of a CBC/differential cell count could potentially be waived. Another member, who attended the FDA panel meeting, said the concern at that meeting centered on the pre- and post-analytical issues of testing rather than the analysis with a waived CBC device. The FDA panel had stressed the importance of defining exactly what tests would be included in any CBC/differential cell count device considered for approval as waived.
- One member sought clarification on FDA's position on translational research and laboratory-developed tests. Dr. Gutierrez said that FDA believes it has jurisdiction over laboratory-developed tests and considers them subject to regulatory review, although it is a gray area. With its limited staff and resources, FDA has chosen enforcement discretion in this area. He noted the number of laboratory-developed tests is enormous.
- A member asked if there were any plans to develop a guidance document that would assist in translation of research into testing for patient care. Dr. Gutierrez replied that FDA would encourage comment and advice in this area. Several members also commented FDA, CDC, academic centers, consortia, and CLIAC should work together on issues of transitioning research testing or laboratory-developed tests into clinical use in CLIA-certified laboratories.
- The Committee discussed the issues surrounding the transition of research into the clinical laboratory and the mechanisms involved. The Committee voted and passed the following recommendation: Convene a workgroup to identify issues, routes currently available, and gaps and information needed to properly translate research testing into use for patient care in CLIA-certified laboratories. Based on the findings and conclusions of the workgroup, development of appropriate guidance could be recommended.

Centers for Medicare and Medicaid Services (CMS) Update ***Addendum C***

Judith Yost, M.A., M.T.(ASCP)
Director, Division of Laboratory Services
Center for Medicaid and State Operations
Centers for Medicare & Medicaid Services

Ms. Yost began her presentation with a review of current laboratory demographic statistics. She reported on the recently published proposed rule for cytology proficiency testing (PT) and continued with an overview of changes found in the proposed rule. Ms. Yost reviewed the 2005 through 2007 pass-fail rates for cytology PT, noting the pass rates have increased in all three personnel categories, although pathologists who do not use a cytotechnologist initially to screen the slides continue to have the lowest pass rates. She discussed genetic testing oversight, listing

thirteen oversight actions CMS is taking in lieu of creating a separate genetic test specialty within CLIA, and emphasized points of cooperation with CDC and FDA in this effort.

Ms. Yost next described plans to begin updating the CLIA PT regulations and progress towards convening a PT workgroup in 2009. She noted CMS inspectors are continuing to conduct educational surveys in the laboratories for the quality control requirements in CLIA section 493.1256; however, sanctions are taken if the requirements in all other areas of CLIA are not met. Ms. Yost said the Clinical Laboratory and Standards Institute (CLSI) is developing two guidance "Evaluation Protocol" documents for alternate quality control and CMS is participating on the CLSI subcommittees that are developing the guidelines. Ms. Yost again reviewed the PT referral warning that CMS issued to laboratories. She described CMS' collaborative efforts with accrediting organizations and exempt states to standardize inconsistent policies through the CMS Partners in Laboratory Oversight group. This group is attempting to develop data-driven performance measures in order to focus resources in a way that will improve quality and consistency across the CLIA program. Addressing the issues that continue to arise with the exponential growth of waived testing, Ms. Yost concluded her presentation with a brief review of the CMS Certificate of Waiver Project and attributed the reduction in number of waived laboratories having quality problems to educational efforts provided for personnel who conduct testing at these sites. CMS plans to work with their partners to reach sites that conduct only waived testing because the number of these laboratories is growing faster than CMS has the resources to visit each year.

Committee Discussion

- One Committee member was concerned about consumers being directed away from certain laboratories by their healthcare practitioners and asked if CMS kept records of problem laboratories. Ms. Yost replied that such records are maintained as public information by CMS regional offices and are accessible by phone or on the website as long as the laboratory is not accredited. She added CMS surveyors verify whether cited laboratories have taken proper actions in response to repeated deficiencies.
- Another member underscored the importance of an educated consumer, saying consumers also have the power to drive and promote quality.
- A member expressed a concern that inspectors might not always be familiar with all the specialty areas that they inspect and subsequently may not readily detect all problems. The member also questioned whether issues such as mishandling of specimens in the pre-analytic testing phase were being identified by inspectors. Ms. Yost clarified that, although CMS and other surveyors cannot always be experts in the technologies they are surveying, the process of laboratory surveys emphasizes quality assurance activities. She emphasized an inspection is more than reading manuals and reviewing records; it is also a tour of the laboratory, a gathering of data, and an interactive interview with management and people who actually do the work.
- A member expressed appreciation that the proposed cytology PT regulations require all testing challenges be field validated and questioned if unvalidated slides might have been a factor in the poorer performance seen the first year of cytology PT. Ms. Yost replied that

although the slides in the first year may not have all been field validated, they did have 100% consensus agreement by three pathologists before being placed in a test set. Currently, this requirement remains in effect. Ms. Yost also noted improvements shown by examinees in the first years of cytology PT paralleled that of persons taking the Maryland state test in its first years. Scores in other laboratory PT have also improved over time.

- Dr. Howerton noted an error on slide nine of the CMS Update slides. The slide listed the proposed scoring grids as the same for pathologists and cytotechnologists. Dr. Howerton stated that the proposed scoring grids are still different for pathologists and cytotechnologists, but that the point values have been changed for both.
- Another member applauded the streamlining of quality control for the microbial identification tests, but noted the streamlined approach cannot be used in California because the State's regulations are more stringent than CLIA. Ms. Yost replied CMS is working with State officials to find a solution.
- For reasons related to the costs of testing, a member noted an increase in the number of patients bringing in test results from another laboratory or home testing and not wanting to be retested. The member stated their policy is to put an alert concerning these results into the medical record and emphasized the importance of handling this type of information appropriately.

Centers for Disease Control and Prevention (CDC) Update ***Addendum D***

Roberta Carey, Ph.D.
Acting Director, Division of Laboratory Systems
National Center for Preparedness, Detection, and Control of Infectious Diseases
Coordinating Center for Infectious Diseases
Centers for Disease Control and Prevention

Dr. Carey began her presentation by describing significant CDC staffing changes, including the appointment of Richard Besser, M.D. as new Acting CDC Director and ATSDR Administrator. She updated the Committee on the publication status of the molecular genetic testing *Morbidity and Mortality Weekly Report Recommendations and Reports* (*MMWR R&R)*, noting it is being reviewed by the *MMWR* editorial office and expected to be published in Spring 2009. Work on a similar document for biochemical genetic testing is proceeding with formation of a CLIAC workgroup and a report to CLIAC from the workgroup planned for February 2010. Dr. Carey also updated the Committee on the activities surrounding revisions to the CLIA PT regulations, including the CLIAC PT Workgroup, and other new CDC guidelines. She reviewed CDC's Health Protection Goals for the 21st Century and CDC's research agenda. Dr. Carey concluded with a brief discussion of the U.S. healthcare crisis and an overview of CDC's Alliance for the Healthiest Nation Initiative.

Committee Discussion

- One member asked if the Molecular Genetic Testing *MMWR* could be reviewed by the

workgroup before publication, expressing a concern that *MMWR* staff edits and writing style changes may have altered the content intended by CLIAC.

- Dr. Carey replied CDC staff have held firm in maintaining correct content and every effort has been made to maintain the CLIAC recommendations. She said the CDC staff reviews each edit carefully and will ask the *MMWR* editorial staff about a final CLIAC review.

PRESENTATIONS AND COMMITTEE DISCUSSIONS

DLS Laboratory Systems Research – Past, Present, Future ***Addendum E***

Devery Howerton, Ph.D.
Chief, Laboratory Practice Evaluation and Genomics Branch
Division of Laboratory Systems
National Center for Preparedness, Detection, and Control of Infectious Disease
Centers for Disease Control and Prevention

Dr. Howerton began her presentation by listing the objectives for this CLIAC meeting, focusing on the need for feedback from the Committee on the current DLS research strategy. She provided an outline for the meeting with a summation of past, present, and future activities and posed some general questions to consider for future research efforts. After a synopsis of background information on CLIA studies, she provided a summary of past activities from 1988 through the present. Dr. Howerton concluded her presentation with a review of recent activities including quality improvement in genetic testing, DLS publications on waived testing, and external partner projects on overall laboratory medicine quality improvement.

Introduction/Overview Current Research Activities ***Addendum F***

Devery Howerton, Ph.D.
Chief, Laboratory Practice Evaluation and Genomics Branch
Division of Laboratory Systems
National Center for Preparedness, Detection, and Control of Infectious Disease
Centers for Disease Control and Prevention

Dr. Howerton began with an overview of the current research focus to fill gaps and strengthen existing systems. She summarized the DLS projects conducted in the past year, giving graphical representations of U.S. laboratory demographics and distribution of those participating in PT. She mentioned ongoing projects related to promoting quality in genetic testing and discussed several DLS projects to identify evidence-based quality and performance measures associated with pre-and post-analytical testing processes. In conclusion, Dr. Howerton presented the

Committee with four questions to consider during the following presentations on the Laboratory Medicine Best Practices (LMBP) projects currently being conducted by DLS. (See ***Addendum F***)

Evidence-Based Laboratory Performance Measures: Chronic Kidney Disease
Addendum G

David Smith, R.Ph., Ph.D.
Center for Health Research
Kaiser Permanente

Dr. Smith stated the goal of the cooperative agreement between CDC and Kaiser Permanente was the creation of evidence-based performance measures in laboratory medicine with a focus on pre-dialysis chronic kidney disease (CKD). After discussing CKD in terms of prevalence, clinical outcomes, and comparative cost of care, he defined Phases I and II of the project. For Phase I, he described how the Kidney Disease Outcomes Quality Initiative guidelines were used as a starting point to identify potential performance measures, with testing for proteinuria ultimately being selected. Next, the U.S. Preventive Services Task Force framework for screening was applied to determine the answers to key questions pertaining to proteinuria testing and its effectiveness as a performance measure to predict patient outcomes. The goal of Phase II is the development and implementation of the proteinuria testing performance measure framework to determine the net benefit of treatment strategies for CKD. Dr. Smith concluded his presentation by discussing future directions and strategies to identify high-risk CKD patients.

Evidence-Based Best Practices in Laboratory Medicine: Evidence Evaluation Methods ***Addendum H***

Edward Liebow, Ph.D.
Health Research Leader
Battelle Centers for Public Health Research and Evaluation

Dr. Liebow began by describing the objectives for Phase 2 of the LMBP project, which built on earlier proof-of-concept work from Phase 1 conducted in 2006-2007. He provided an overview of the pilot methods used in Phase 2, which consisted of systematic review methods on data from published and unpublished sources, evaluation methods by expert panelists, and evidence-based recommendations by the LMBP workgroup. Two topics were identified for pilot evidence review: critical values reporting and communication and patient specimen identification. Subsequent evaluation criteria were then used to determine an overall strength of evidence rating. Dr. Liebow described how this evidence rating applied to selection of the respective practices, noting additional considerations included associated harms and/or benefits. In conclusion, Dr. Liebow discussed the aspects of organizational sustainability for future efforts,

presented potential topics for Phase 3, and requested Committee feedback.

Committee Discussion

- A member noted one of Dr. Howerton's slides showed a decrease in the number of physician office laboratories (POLs) participating in PT from 1996 to 2006 and asked for an explanation. Dr. Howerton replied she did not have an explanation for the decrease but could re-examine that subset of data to determine whether the laboratories had changed their certification or were no longer performing testing. She added POLs performing non-waived testing are mandated to perform PT. The same member asked if there are fewer numbers of POLs. Dr. Howerton replied the number of POLs is increasing but many are only performing waived testing.
- A member asked whether the evidence review process and the LMBP study take into account the potential harms and benefits of practices under consideration. Dr. Liebow explained the reason for performing evidence reviews is to focus on quality problems and that harms and benefits are taken into account in preparing the evidence summaries.
- The same member commented it seems evidence-based studies are a growing industry and recognized the importance of the LMBP study having subject matter experts perform the reviews. However, the member expressed concern that in many cases there are not good or sufficient data to conduct the appropriate evidence-based reviews.
- The Committee discussed the use of meta-analyses, such as the process being used in the LMBP study, and expressed a number of advantages and disadvantages for this type of data analysis. Alternate methods for collecting and assessing data were also proposed.
- A member who had served on the LMBP workgroup stated meta-analyses are good if there are data on which to do meta-analyses, however, the member concurred there are very little data on which to do evidence-based reviews. From experience, the data that do exist for evidence-based reviews are not very good, resulting in the downgrading of studies. Since so much is indeterminate, many conclusions are drawn on experiential data rather than actual objective data.
- Another member added meta-analysis may not be the right way to do this work, but suggested instead one could pose a specific question with submeasures to determine prospectively if a particular practice is effective and then conduct a trial study to collect pre- and post-implementation data.
- A third member commented the LMPB study identified the limitations of the data and where improvements are needed, but suggested studying pre- and post-implementation data is insufficient due to limitations imposed by including only a single institution in a study.
- One member remarked the criteria used for judging laboratory medicine reviews needs to be realistic. There are few randomized control trials in laboratory medicine. Perhaps those performing meta-analyses should be less critical. In dealing with patient outcomes, other types of evidence data also need to be used.
- Several members acknowledged that performance improvement data exist within organizations but there is not a good venue for sharing this information in usable form.
- Another member added when designing a retrospective or prospective study, representatives of outliers should be included. Otherwise, the best practices criteria resulting from the study

may be so rigid or narrow that outliers are never recognized.

- A member was pleased that CDC is evaluating the integration of laboratory testing into the total care of the patient and is an active partner in the chronic care model towards improved patient care and outcomes.
- The Chair concluded the discussion by summarizing the expressed need for laboratory best practice data and encouraged the collection and sharing of unpublished data by CLIAC members and others in laboratories or professional organizations.

Clinical Decision Making: Promoting Appropriate Reporting and Understanding of Molecular Genetic Test Results ***Addendum I***

Lee Hilborne, M.D., MPH, FASCP, DLM(ASCP)
Professor of Pathology and Laboratory Medicine, UCLA
Southern California Medical Director, Quest Diagnostics
Global Health, RAND Corporation

Ira Lubin, Ph.D. FACMG
Laboratory Practice Evaluation and Genomics Branch
Division of Laboratory Systems
National Center for Preparedness, Detection, and Control of Infectious Disease
Centers for Disease Control and Prevention

Dr. Lubin and Dr. Hilborne provided informational background on genetic test reporting and interpretation leading to the development of an improved generic molecular genetic test report template. Dr. Lubin discussed the need to properly order genetic tests and interpret the results in light of essential patient and family information. He emphasized that failure to consider such relevant information when ordering tests or interpreting results can compromise patient care. He then discussed findings and conclusions from published studies that described the general principles and components of a test report and a proposed framework for reporting molecular genetic test results designed to promote understanding and appropriate use of results for patient management.

Dr. Hilborne continued with a discussion on next steps in the development and implementation of the test report template and proposed framework. In closing, Dr. Hilborne offered questions for discussion: How should the findings be leveraged to improve the use and provision of molecular genetic testing and laboratory medicine? How can this work help CLIAC develop recommendations to the Department of Health and Human Services (HHS) for promoting effective reporting and use of test results?

Committee Discussion

- One member inquired about provisions that protect patient-specific genetic data from disclosure to insurance companies, employers, and others. Dr. Hilborne responded disclosure

of patient data is a valid concern as evidenced by the heightened interest in developing and enforcing regulations that address privacy of patient data. He added the sharing of and access to patient data is covered under the Health Insurance Portability and Accountability Act (HIPAA). Another member noted the Genetic Information Nondiscrimination Act (GINA) protects individuals with DNA or family history-based genetic data indicating a predisposition to increased medical risks from discrimination. The member added while GINA protects individuals from job and health insurance discrimination, it does not protect them from life insurance and long term disability discrimination nor does it protect them if they already have a genetic condition. Another member also emphasized healthcare providers are required to ensure their clients have an understanding of HIPAA and their protected rights prior to testing or treatment.

- A member asked how the impact and value of the reporting system discussed by Drs. Lubin and Hilborne would be assessed. Dr. Hilborne responded the intent is to solicit feedback from a broad spectrum of caregivers on interpretation of the report and its impact on patient care versus the interpretation and impact of a traditional report.
- Another member suggested it would be important to solicit input on the report from attorneys, since the information that would be included could put some providers at risk for litigation.
- A member remarked she liked the idea of the e-Course educational tool aimed at teaching physicians about the reports, but advised including clinicians and their specialty societies in its development and distribution. Dr. Hilborne stated individuals with affiliations to scientific professional societies had been included in the development of the model. He assured the member when roll out occurs, the scientific community (including clinicians) will be fully engaged in the training and implementation.
- Another member asked for clarification on how the term “molecular genetic testing” was defined in the context of this report. Dr. Hilborne acknowledged there is confusion about terms pertaining to genetic testing and clarified their generic report was focused on heritable genetic conditions.
- One member noted the importance of including the testing method used on the report.
- Several members discussed concerns about standardized formatting and keeping the report intact during transmission. One member pointed out a properly formatted report can be generated only to have the formatting and often-relevant information lost in translation when referred to or through another laboratory. Dr. Hilborne commented the goal is to get the entire community to accept one format. He stated getting the major players engaged early and in agreement on report formats should provide the best opportunity for including consistent information that is not dropped when testing is referred from one laboratory to another. He also noted the proposed educational efforts would focus on relevant information to be included on the report. Several other Committee members indicated the need for standardized report formats that could be used in other testing areas such as microbiology.
- Several members commented the Laboratory Information System (LIS) industry needs to have a better understanding of the importance in retaining the integrity of the reporting format, relevant interpretation, and comments. Dr. Hilborne responded improving LIS systems was far beyond the scope of the workgroup, but several LIS representatives were

involved in the workgroup activities. This led to multiple Committee comments on the limitations of LIS, especially their capacity to interface with other information systems. A member suggested the LIS interface issue become a topic of a future CLIAC meeting. Dr. Gutierrez reminded the Committee LIS systems are regulated by the FDA as class I medical devices and must meet all FDA quality system regulations.

Institute for Laboratory Medicine ***Addendum J***

Julie Taylor, Ph.D.
Acting Deputy Director
Division of Laboratory Systems
National Center for Preparedness, Detection, and Control of Infectious Diseases
Centers for Medicare & Medicaid Services

Dr. Julie Taylor briefly described the Division of Laboratory Systems' six previous Institutes on Critical Issues in Health Laboratory Practice. She discussed the key opportunities for addressing laboratory practice issues identified during the 2003, 2005, and 2007 Institutes. Dr. Taylor reviewed post-2007 Institute activities including the Laboratory Medicine: National Status Report, which may be accessed at **http://www.futurelabmedicine.org.** She closed with a brief overview of the Roadmap and Integration Workgroups and recognized the efforts of volunteers and leaders of the Institute for Laboratory Medicine (ILM) and the workgroups.

Roadmap Workgroup Report ***Addendum K***

Lee Hilborne, M.D., MPH, FASCP, DLM(ASCP)
Professor of Pathology and Laboratory Medicine, UCLA
Southern California Medical Director, Quest Diagnostics
Global Health, RAND Corporation

Dr. Hilborne, co-lead of the ILM Roadmap Workgroup, opened by providing graphs showing why laboratory services are critical to medical decision-making and noted opportunities exist to improve laboratory testing services in all phases of the total testing process, especially in the pre- and post-testing processes. He stressed the importance of laboratory stakeholders collaborating in achieving goals and discussed the Workgroup's vision of maximizing laboratory medicine's contribution to optimizing healthcare quality. He went on to explain the Workgroup's development of a strategic plan to use existing HHS framework and the Institute of Medicine's (IOM) six quality domains (safe, effective, patient centered, timely, efficient and equitable) in a laboratory context to develop a roadmap that could provide a framework for the proposed ILM. He then used a specific example to demonstrate how the roadmap would work. Dr. Hilborne concluded by describing the next steps in refining the roadmap and establishing the proposed ILM as the umbrella organization to establish partnerships, supplement education and research,

and improve patient outcomes.

Report from the Integration Working Group: Optimizing the Ordering and Interpretation of Laboratory Tests *Addendum L*

Michael Laposata, M.D., Ph.D.
Pathologist-in-Chief
Vanderbilt University Hospital
Professor of Pathology and Medicine
Vanderbilt University School of Medicine

John Hickner, M.D., MSc.
Chairman, Family Medicine
Cleveland Clinic

Dr. Laposata and Dr. Hickner, co-leads of the ILM Integration Workgroup, provided an overview of the Workgroup's formation, their charge, and ambitious agenda. Dr. Laposata opened the presentation with a brief history on both his personal observations and reports in the literature pertaining to mistakes in physician test ordering and result interpretation. He discussed the evolution of solution prototypes to improve test ordering and result interpretation and acknowledged the role of DLS in the formation of the Workgroup.

Dr. Hickner continued by discussing the Workgroup's charge and goals, the eight problems identified by the Workgroup as most affecting laboratory test ordering and result interpretation, and proposed strategies to address the identified problems. He closed with a summary of the Workgroup's current and proposed projects.

Committee Discussion

- One member commented not only are clinicians confused about laboratory tests but, in addition, not all laboratory staff understand all aspects of the testing. The member explained that staff who work in the areas of specimen accessioning or client services, where critical communication of laboratory testing information with physicians and customers frequently transpires, may not have the appropriate educational background to discuss test ordering or results. Dr. Laposata agreed, noting that unfortunately, it is an accepted practice in the laboratory setting not to have the pathologists or trained laboratorians engage directly with physicians and laboratory clients.
- A member observed that for most family practice physicians, time and reimbursement issues were by far the greatest barriers to physician-laboratory consultation. The member suggested the test ordering protocols described by the Integration Workgroup co-leaders had great potential for positive impact on physician test ordering and encouraged the development of better payer incentives for laboratory consultation and test ordering.
- In response to several additional member comments on the consultative role of the

laboratory, Dr. Laposata conceptualized what he called the "diagnostic cockpit," a pilot program at Vanderbilt University Hospital that will connect the entire patient care team in an effort to create reports that are succinct, timely, and highly effective in patient care and treatment.

- Several members raised the point that not providing interpretive fees to doctoral level laboratorians who are not physicians continues to be a significant barrier to laboratory consultative services and noted the continuing but failed efforts of several professional organizations to gain approval through CMS and HHS for payment of these interpretive fees. They also cautioned that without a strong collaborative effort, non-physician interpretive fees were unlikely to become a reality.
- Another member stressed as long as the laboratory is viewed as an ancillary service and not an integral member of the healthcare team, effective clinical consultation will be negatively impacted, non-physician interpretive fee incentives will fail to be secured, and laboratory visibility will continue to be the major barrier. He went on to suggest point-of-care testing as a vital key to giving a face to the laboratory. He further stated direct interaction of laboratorians with healthcare teams could positively impact face-to-face communications and laboratory interpretation reimbursement issues. Several members concurred that laboratorians need to get out of the laboratory and become a visible healthcare team member. Other members corroborated where this had been accomplished, communication between the laboratory and healthcare providers was significantly improved.
- One member asked if advances in computer software could assist the physician in test selection and interpretation. Dr. Hilborne responded several models were under development, citing the English internet site "Map of Medicine" at www.mapofmedicine.com. He described its potential in test ordering and consultative assistance, adding more models and software for similar purposes could be expected in the future.
- Several members voiced concern about the limited to non-existent laboratory training included in the medical school curricula and on the dwindling occurrence of medical rounds within the laboratory. An additional concern noted was that as medical schools switch to an organ-based curriculum structure, basic principles of physiology and cross cutting issues such as laboratory medicine might be overlooked. The members said in their experience clinicians, medical residents, and interns need significant guidance in test ordering, test interpretation, and appropriate test utilization. They suggested that for laboratory medicine training to be meaningful, instruction should occur in the last year of medical school and continue into the postgraduate period. Dr. Laposata responded to these comments by quoting from a book he wrote for medical students, which noted the absence of laboratory medicine in their curriculum.
- While accepting the exclusion of genetic testing issues from the Integration Workgroup activities, a member advised the Workgroup co-leaders to be cognizant the genetics community may not be dealing with some of the issues the Integration Workgroup is addressing. The same member encouraged the Workgroup to address the appropriate use of the clinical consultant, e.g. the genetic consultant, to improve laboratory consultative services and to include test sample and collection issues when addressing test-ordering

issues. Another member added clinical consultants are a necessary component of the laboratory team and their presence has improved test utilization and interpretation, particularly in highly complex medical specialty areas. In response to the member's statement on the Integration Workgroup's exclusion of genetic testing issues, Dr. Hickner stated the Workgroup decided genetic testing was beyond the scope of the Workgroup, but he did not rule out the possibility of the Integration Workgroup addressing genetic testing issues in the future. Dr. Hilborne seized this opportunity to articulate how the Roadmap Workgroup's strategic plan would be poised to address such concerns.

- In addressing the Roadmap Workgroup's vision and use of the IOM domains in defining their quality domains, one member suggested more emphasis on the economics of healthcare quality. Dr. Hilborne replied the economics of healthcare was effectively captured by the IOM quality domains. As the Institute sets its priorities and specific elements are defined, the economics of healthcare quality will be a key component.
- One member suggested the patient-centered IOM domain could be defined better by choosing the words "shared decision making" placing emphasis on the role, the accountability, and the need to enable patients to become more empowered in their own healthcare. Dr. Hilborne agreed, indicating the Roadmap Workgroup would take this under advisement.
- Dr. Hilborne also advised CLIAC that comparative effectiveness research is gaining attention with respect to improving healthcare quality and allowing physicians and the public to make evidence-based decisions about treatment or testing options. For example, Dr. Hilborne considered whether it is better to provide a better test to 10% of the population or a cheaper test to everyone. In response a member stated laboratorians should take a consultative approach and ultimately perform the test that allows the physician to make the correct medical decision and provide the best patient outcome and concluded the laboratory community should collaborate with colleagues and try to reduce testing costs in cases where the costs are higher than necessary.
- The CLIAC AdvaMed liaison representative stressed industry wants to ensure a test is used correctly and appropriately. She reflected on the Integration Workgroups' test ordering projects presented by Dr. Hickner, indicating the proposed development of testing protocols, interpretation guidance, and newsletter could ultimately lead to professionally recognized laboratory practice guidelines. She explained industry currently spends millions of dollars marketing a test, educating customers, and conducting post-market effectiveness studies. She suggested industry money could be better focused if laboratory practice guidelines existed to which industry could specifically develop their tests, determine levels of evidence needed, and identify the type of economic analysis needed to provide appropriate information.

Developing an Agenda for Laboratory Practice Based Research: A Delphi Approach ***Addendum M***

Stephen S. Raab, M.D.
Department of Pathology

University of Colorado Denver

Dr. Raab described a project using the Delphi approach to rank quality gaps and critical deficiencies in healthcare information identified at the 2007 Institute on Critical Issues in Health Laboratory Practice: Managing for Better Health. As part of the project, 29 panel members used a web-based tool to rank the importance of 50 statements as indicators of areas for additional study or evaluation. The tool was designed to prevent group bias or conformity in their decision making by maintaining the anonymity of the participants. After two rounds, the top ranked statements were:

1) Evaluate the frequency of laboratory test misinterpretation by clinician and the negative impact on health outcomes.
2) Develop standardized measures of error in anatomic pathology.
3) Develop evidence-based laboratory performance measures.
4) Determine how barriers to national standardization may be removed.

Dr. Raab concluded that this was a process to develop a national consensus from a variety of stakeholders to identify the most important issues for research funding and not a process to determine the best treatment of disease.

Committee Discussion

- A Committee member wanted to know if more laboratorians than clinicians participated in the process. Dr. Raab responded that 29 of the initial 33 representatives participated in the first round and that the group contained more non-pathologists than pathologists. He then elaborated that the data could be re-evaluated to include only one stakeholder group to see if the results were similar.
- One of the Committee members wanted to know what CDC planned to do with the information collected from the Delphi project. Dr. Hearn applauded the methodology and rigor used by the Delphi approach but reiterated that, although this study provides important information, it is not the only piece of information used in making research decisions.

Future Research Activities ***Addendum N***

Devery Howerton, Ph.D.
Chief, Laboratory Practice Evaluation and Genomics Branch
Division of Laboratory Systems
National Center for Preparedness, Detection, and Control of Infectious Disease
Centers for Disease Control and Prevention

Dr. Howerton began her presentation by asking the CLIAC members to consider what DLS should focus on for future research. She described the ongoing studies that include evidence-based best practices, performance measurement, clinical decision support for genetic testing, rapid influenza testing in outpatient settings, workgroups related to the 2007 Institute, and the current PT regulatory initiatives. She provided a logic model to define the research strategy and

explained that the goal is to develop a comprehensive research agenda that will drive quality improvement in laboratory medicine through research and development of evidence-based practices and standards. She listed topics of interest for the research agenda that include the Delphi study results, the growth of waived testing and molecular testing, building the evidence base for practice standards, rapid disease testing, clinician-laboratory interface, and laboratory workforce issues. She concluded by posing six specific questions to guide the Committee discussion.

Committee Discussion

The Committee members were asked to list the priorities in the context of CLIA and laboratory improvement for a sustainable research agenda.

- A Committee member suggested the first step should be a white paper that identifies a common language and provides definitions for terms like "appropriate test," as well as describes how to measure patient outcomes. Another member stated that any proposed activity should consider four criteria: patient safety, total cost of care, resource management, and patient outcome. Another member asked that the broad population be evaluated, stating that issues that address 90-98% of the population often do not include pediatrics, the elderly, genetic rarities, or other smaller populations.
- A comment was made that few research papers are available that address the link between process and outcome. Members stated that the value of laboratory testing should be assessed and asked that programs be identified that have improved care and reduced errors so that best practices can be written based on these examples.
- A member suggested that the relationship between the laboratory and the clinician needs to be further explored. Another member added that developing a clinical support system similar to the one used by the United Kingdom could help physicians and their staff order the right test and follow the correct path of laboratory testing to achieve the desired patient outcome. This system should be linked to the electronic health record and include waived and point-of-care (POC) testing, as well as central laboratory testing, embedded within the possible pathways.
- Another member suggested there needed to be better communication among the healthcare team and that laboratorians become expert consultants. A model similar to that used in pharmacology, in which the laboratory can provide consultation to the healthcare team, was suggested as an intermediate step of where laboratories should be. The radiology model, in which the laboratory is an integral part of the team and is reimbursed for their services, should be the goal for the laboratory to achieve within the healthcare system.
- The Committee identified several concerns regarding waived testing. These include the rapid growth and availability of waived tests, the differences in utility and efficiency between waived testing and nonwaived testing performed in traditional laboratories, risk benefit ratios for patients, cost implications, and the need to look at the impact of waived testing on patient outcomes.
    - Some members recommended physician offices and acute care settings with waived and nonwaived POC testing be approached to identify whether patient outcomes are improved with waived testing and if the decision to use waived testing is impacting their

staff, especially the nursing staff.
    - A suggestion was made to look at the pre- and post-analytical waived testing processes and their impact on patient outcomes. The CLIAC member noted that FDA approval as a waived test only considers the analytic phase of testing. There are numerous issues in the pre- and post-analytical phases that need to be considered.
    - Some Committee members emphasized that consumers, purchasers, and payers may not understand that testing quality can differ depending on the method used and the site where testing is performed.
    - A member recommended using a business model approach with respect to waived testing and improving the quality of healthcare. It was suggested that purchasers of laboratory services could pressure payers not to reimburse for services that do not provide the best patient outcomes.
    - Ms. Yost thanked the members for their comments on waived testing and stated that support is needed to get to the next step, since CMS can only evaluate a small sample of waived laboratories each year.
- The Committee suggested continuing the evaluation of current laboratory services in the context of CLIA regarding pre- and post-analytical phases of testing. The areas mentioned for evaluation include interpretation of test results, information technology, and the misuse or overuse of laboratory testing.
- Several members suggested comparing the similarities and differences between CLIA, the International Organization for Standardization (ISO), and other accreditation standards in an effort to become better harmonized. They asked if data were available to show the benefits of meeting the CLIA quality standards. Dr. Hearn mentioned that CLIA includes minimal standards, but it would be advantageous if laboratories could achieve the higher goal of ISO accreditation when possible.
- Another member questioned the effect of CLIA on epidemiological testing and suggested public health disease reporting across the states be improved.
- A Committee member wanted to know if data were available that would support PT by method versus PT by analyte and if a move toward PT by method might be considered by CMS, particularly in the area of genetic testing. The member also requested that research continue to include the quality, understanding, and ordering of genetic testing.
- A member stated there is an opportunity to educate stakeholders on the importance of the laboratory with respect to diagnosis of hospital-acquired infections (HAI). It was suggested that an *MMWR* article might identify best testing practices and provide data from before and after implementation of these practices to demonstrate the value of testing and show that diagnosis of these infections is made based on laboratory testing results.

PUBLIC COMMENTS

- **NYC DOHMH's Primary Care Information Project Testimony Laboratory Interfaces** ***Addendum O***

- **Translation of Academic RUO to Clinical Laboratory** ***Addendum P***

- **Waived Test Categorization** ***Addendum Q***

ADJOURN

Ms. Passiment acknowledged the CDC staff that assembled the meeting agenda and provided meeting support, and thanked the CLIAC members and partner agencies for their support and participation. The Chair provided a summary of the Committee discussions as follows:

- CLIAC requested that the Chair communicate to the CDC Advisory Committee that research on the public's acceptance issues of vaccinations is more important than performing research on vaccine safety issues.
- The Committee identified a need for a white paper or guidance document defining the terms used in laboratory research in order to guarantee mutual understanding by all stakeholders.
- There should be greater involvement of scientific organizations and societies as the project on promoting effective use and understanding of test results moves forward.
- There is a need for an in-depth analysis of POC and waived testing and the potential impact on patient care.
- A review is needed of current CLIA regulations for the pre- and post-analytic phases of laboratory testing to determine if changes are necessary. This should include interpretation of test results, and information technology.
- Topics suggested for future CLIAC agendas:
  - The laboratory profession's ability to communicate effectively with others that are part of the health care team and with the public
  - Issues of specimen handling between laboratories in the pre-analytic phase of testing
  - Issues concerning LIS interfaces and the potential for loss of information during transfer across information system interfaces or within electronic health records

The following reflects the Committee's recommendation from this meeting:

- Convene a workgroup to identify issues, routes currently available, and gaps and information needed to properly translate research testing into use for patient care in CLIA-certified laboratories.

Ms. Passiment announced the next CLIAC meeting would be September 2-3, 2009 and adjourned the Committee meeting.

I certify this summary report of the February 4-5, 2009 meeting of the Clinical Laboratory Improvement Advisory Committee is an accurate and correct representation of the meeting.

_____ Dated: 4/29/2009

Elissa Passiment, EdM, CLS(NCA), CLIAC Chair