Clinical

Laboratory

Improvement

Advisory

Committee

Summary Report

September 2-3, 2009
Atlanta, Georgia

U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES

Clinical Laboratory Improvement Advisory Committee
September 2-3, 2009 Summary Report
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VIII. Addenda

Record of Attendance

Committee Members Present
Ms. Elissa Passiment, Chair
Dr. Christine Bean
Ms. Susan Cohen
Dr. Nancy Elder
Ms. Julie Gayken
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. David Smalley
Dr. Emily Winn-Deen
Dr. Rosemary Zuna
Ms. Luann Ochs, AdvaMed (Liaison Representative)

Committee Members Absent
Dr. Ellen Jo Baron
Ms. Merilyn Francis
Dr. Carol Greene
Dr. Jared Schwartz

Executive Secretary
Dr. Thomas Hearn

Ex Officio Members
Dr. Alberto Gutierrez, FDA
Dr. Roberta Carey, 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
Dr. Shannon Barker
Ms. Diane Bosse
Ms. Suzette Brown
Dr. Bin Chen
Ms. MariBeth Gagnon
Dr. Devery Howerton
Dr. Lisa Kalman
Dr. John Krolak
Ms. Debra Kuehl
Dr. Nattawan Lanier
Dr. Ira Lubin
Ms. Leslie McDonald
Ms. Andrea Murphy
Ms. Sandra Neal
Ms. Abrienne Patta
Ms. Anne Pollock
Dr. John Ridderholf
Dr. AngelaRagin-Wilson
Dr. Shahram Shahangian
Ms. Colleen Shaw
Mr. Darshan Singh
Ms. Theresia Snelling
Dr. Susan Snyder
Dr. Julie Taylor
Mr. Howard Thompson
Ms. Pam Thompson
Ms. Frances Tyrrell
Ms. Irene Willaims
Dr. Laurina Williams
Ms. Malaika Washington

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

Ms. Carol Benson (FDA)
Dr. Elliot Cowan (FDA)
Dr. Uros Djekic (FDA)
Ms. Karen Dyer (CMS)
Ms. Daralyn Hassan (CMS)
Ms. Kathy Todd (CMS)
Ms. Gwen Williams (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. 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 the meeting would focus on three main topics: laboratory testing quality during public health emergencies using the novel 2009 H1N1 influenza A virus event as an example, ways to assess the performance and impact of waived testing, and the current state of HIV testing.

AGENCY UPDATES AND COMMITTEE DISCUSSION

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

Alberto Gutierrez, Ph.D.
Director, Office of In-Vitro Diagnostic Device Evaluation and Safety (OIVD)
Center for Devices and Radiological Health
Food and Drug Administration

Dr. Gutierrez, Director of OIVD as of July 2009, listed recent FDA staffing changes, notably the appointment of Dr. Margaret Hamburg as FDA Commissioner. He reported the agency received funding during the last fiscal year for a personalized medicine staff who will be heavily involved with issues concerning diagnostic devices and drugs. He discussed new guidances, notable new approvals, clearances, and emergency use authorizations, most of which concerned the novel H1N1 influenza A virus. The in vitro diagnostic multivariate index assays (IVDMIA) guidance document did not get published before the change of administration; however, publication is anticipated in the near future. He concluded with a review of the FDA Advisory Panel's decision not to recommend waiver of the HemoCue White Blood Cell Analyzer at this time and a discussion of the postmarket actions taken against Nichols Institute Diagnostics for misbranding.

FDA's LabNet Program: Improving Patient Safety by Increasing Reporting from Hospital Laboratories *Addendum B*

Jill Marion, BSE
LabNet Program Manager
Center for Devices and Radiological Health
Food and Drug Administration

Ms. Marion opened her presentation with an explanation of post-market surveillance and how it is used to monitor a medical device's performance. She provided information on FDA's adverse event reporting system, MedWatch, and their enhanced post-market surveillance program, MedSun, which allows "real-time" reporting of adverse events or patient safety issues. Ms. Marion described the FDA's LabNet Program which provides active surveillance of in vitro diagnostic devices to ensure their safety and effectiveness. She outlined the program's goals and current status and provided examples of reported events with adverse outcomes or the potential for harm. In closing, she related the future goals of LabNet were to increase the number of hospitals participating in the program and encouraged those interested to join the network.

Centers for Medicare and Medicaid Services (CMS) Update 2009, Part II *Addendum C*

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

Ms. Yost began her presentation with an overview of current CLIA statistics. She discussed the proposed rule for cytology proficiency testing (PT), published in January 2009, noting the public comments generated are available at www.regulations.gov. Ms. Yost stated CMS is currently considering their response to the many comments expressing the view that cytology PT of individuals should not be required, since there is a statutory requirement under CLIA that individuals who review and screen cytological preparations should be tested periodically for their proficiency. She also reviewed the cytology PT statistics and emphasized they demonstrate the value of cytology PT testing. Next, Ms. Yost identified CMS' top ten condition level and overall deficiencies. She reported CMS is continuing to work with the Clinical and Laboratory Standards Institute (CLSI) to develop two evaluation protocol documents that address alternative quality control and said the CMS interpretive guidelines will be revised accordingly. CMS has not determined if equivalent quality control, as described in the CMS guidelines, will remain once the CLSI documents have been approved. Commenting on the PT regulation she said a CLIAC workgroup will convene in the spring of 2010 to provide suggestions to the full Committee for making recommendations on changes needed to the CLIA PT requirements.

Ms. Yost elaborated on CMS's concerns regarding waived testing, noting the substantial increases in certificate of waiver (CW) laboratories and waived test systems. She referred to data from the CMS CW project that has been ongoing since it was initiated as a pilot project in 1999. Ms. Yost concluded her presentation with a brief review of the requirements and issues related to electronic health records (EHRs) and a synopsis of planned CMS Surveyor Basic Training.

Committee Discussion

- One member inquired about the privacy and intrusion issues associated with EHRs. Ms. Yost responded CLIA has baseline confidentiality requirements, while the Health Insurance Portability and Accountability Act requirements are more comprehensive. She agreed there are numerous concerns associated with this issue and said the individuals responsible for this project are aware of the sensitivities surrounding it and are working with the appropriate agency to address those concerns. Another member voiced a concern about EHR accessibility, stating patients, after obtaining their laboratory results, might start self-treating without contacting their physician.
- A member noted that cytology PT pass rates seem to increase each year and asked whether it was cost effective to continue to require cytology PT if this trend continues. Ms. Yost agreed CMS will have to consider if there are any alternatives that could address this issue. The Chair commented that with every turnover of personnel comes an opportunity for education and a need to increase awareness of quality, so she was unclear how one would ever reach a point where there is no longer

a need for cytology PT. Ms. Yost stated one alternative may be to reduce the frequency of cytology PT testing.

- On the topic of laboratory information systems (LISs), the Chair raised the concern that as results are released from the laboratory and transmitted through multiple interfaces, information may be separated or distorted. This might not be detected without laboratory monitoring. Dr. Gutierrez noted LISs are considered medical devices; therefore, any errors with LIS transmission can be reported to the FDA.
- In summary, the Chair noted as key points from the discussion: concerns were expressed regarding information technology as related to privacy, confidentiality, and protection of information; and the Committee is interested in hearing about progress with the cytology PT regulation as well as considering what is needed in cytology as proficiency levels, based on PT results, approach 100%.

Centers for Disease Control and Prevention (CDC) Update

Addendum D

Roberta B. 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 announcing significant CDC leadership changes, including the appointment of Dr. Thomas Frieden as the new CDC Director and Agency for Toxic Substances and Disease Registry (ATSDR) Administrator. She described his priorities for organizational improvement and CDC's key strategic directions. Dr. Carey updated the Committee on the status of the CLIAC PT Workgroup and identified topics the workgroup will address. A workgroup report will be presented to the Committee at the September 2010 meeting. Similarly, she summarized the timeline and progress of the CLIAC Biochemical Genetic Testing Workgroup, whose recommendations will be developed to provide guidance both for clinical and public health biochemical genetic testing. Dr. Carey also updated the Committee on the goal and status of the Laboratory Medicine Best Practices Workgroup, emphasizing the solicitation of new topics for further evaluation. She concluded her presentation by outlining the progress of other work involving evidence-based laboratory medicine quality/performance measures, the Laboratory Medicine Roadmap Workgroup, and the Laboratory Medicine Integration Workgroup.

Committee Discussion

- One member commented about the lack of laboratory training in medical schools stating the importance of laboratory medicine is not emphasized. The issue becomes even more critical with the increase in waived testing and the transference of responsibility for laboratory testing to physicians. Dr. Carey agreed, saying there is a huge opportunity to integrate information on laboratory ordering, reporting, and

decision making into medical school curricula that are now becoming more case-based rather than strictly didactic lectures.

- Several members complimented the Integration Workgroup for addressing testing algorithms and providing guidance, but noted the challenge is incorporating that information into clinical decision support systems and day-to-day medical practice.
- In response to a Committee member's inquiry, Dr. Carey stated the Laboratory Medicine Best Practices workgroup is seeking additional topics for the coming year. The member suggested best practices in testing for influenza would be a timely topic and ample data should be available.
- One member stated pathologists need to communicate with laboratory personnel regarding patient clinical history. Increasingly, more junior staff fill out requisitions but are not in a position to provide the clinical information that is critical to laboratory test reporting. Dr. Carey suggested information technology (IT) barriers could be put in place that would not allow a test to be ordered without entering all required information.

Publication and Promotion of MMWR R&R – Good Laboratory Practices for Molecular Genetic Testing for Heritable Diseases and Conditions

Addenda E & F

Bin Chen, Ph.D., FACMG
Laboratory Practice Evaluation and Genomics Branch
Division of Laboratory Systems
National Center for Preparedness, Prevention, and Control of Infectious Diseases
Coordinating Center for Infectious Diseases
Centers for Disease Control and Prevention

Dr. Chen informed CLIAC of the June 12, 2009, publication of "Good Laboratory Practices for Molecular Genetic Testing for Heritable Diseases and Conditions" in CDC's *Morbidity and Mortality Weekly Report (MMWR) Recommendations and Reports(R&R).* She explained the purpose of the document is to highlight areas needing specific guidance to ensure quality testing, to clarify applicable CLIA requirements, and to address the need for specific quality assurance measures not included in existing CLIA regulations. She described the pre- and post-publication information dissemination to intended users and noted questions and comments received from the community. Dr. Chen concluded by elaborating on the planned next steps, including posting questions and answers on the Division of Laboratory Systems' (DLS) website. She directed the Committee's attention to several questions including steps to encourage implementation of the recommendations and ways to evaluate the impact of the publication.

Committee Discussion

- A member suggested engaging consumer advocates to assist in impactful dissemination of this information to the public. Dr. Chen said initial plans were being made to utilize patient advocacy groups and genetic alliances to help develop educational materials tailored for patient groups and consumers. Members concurred

it was important to develop informational materials that help consumers understand the recommendations.

- Several members commented payers, such as United Healthcare and Blue Cross/Blue Shield, are important partners to include in dissemination of this information.
- One member asked if there are plans to incorporate the *MMWR* recommendations in regulations. Ms. Yost replied there are no plans but the information is valuable and CMS will put a link to the document on their website. She also said information pertinent to CLIA could be incorporated into the CMS guidelines for laboratories and surveyors.
- Dr. Gutierrez suggested bringing the report to Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS). Dr. Chen responded the document was cited at the last SACGHS meeting and hard copies were requested for the members of the Committee. She said the National Institute of Health, Office of Biotechnology's next steps should be investigated.
- The Chair asked if there has been enough awareness in the healthcare community and if the Committee had suggestions for improving awareness. One member commented on receiving the *MMWR R&R* document from at least five sources. Dr. Chen stated the document was posted on the Genetic Alliance list serve, who also suggested development of specific educational materials addressing the patients, consumers, and patient advocates.
- One member stated the *MMWR R&R* has not yet reached the basic laboratory, bench level, or medical directors of laboratories. The member opined when it is distributed as a link or reference from an accrediting agency or from the government, people will take notice and ask what it means to them.
- Ms. Ochs commented it cannot be left up to the organizations to determine what it means to their members. A member commented, while the *MMWR R&R* is an excellent document for laboratorians, separate materials will have to be developed depending on which group is targeted. The material should be distilled to a couple of pages and individualized.

PRESENTATIONS AND COMMITTEE DISCUSSION

Assuring Laboratory Testing Quality during Public Health Emergencies

Thomas Hearn, PhD
Acting Director
National Center for Preparedness, Detection, and Control of Infectious Diseases
Coordinating Center for Infectious Diseases
Centers for Disease Control and Prevention

Dr. Hearn introduced the topic "Assuring Testing Quality During Public Health Emergencies." He recounted lessons learned from the 2001 anthrax response regarding laboratory test selection and reporting and acknowledged that more work was needed in the area of communication. He stressed preparedness must address not only what we need

to do to react to crises but also what we need to do to prepare for crises before they occur. Dr. Hearn charged CLIAC to consider how the 2009 H1N1 influenza A outbreak and pandemic had impacted their work – what happened, what worked, and what could be done better. Prior to introducing the first presenter, Dr. Hearn reviewed the discussion questions for the Committee to address after hearing all the presentations. (***Addendum G***)

Novel Influenza A H1N1 Update ***Addendum H***

Dan Jernigan, MD, MPH
Deputy Director, Influenza Division
National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention

Dr. Jernigan presented an overview of the current 2009 H1N1 influenza A pandemic from the CDC perspective. He described how the first disease case was identified in the United States and reviewed the surveillance data gathered prior to the declaration of Pandemic Phase 5 by the World Health Organization (WHO). CDC's response to the pandemic has included distributing 25% of the strategic national stockpile of the antiviral drug Tamiflu (oseltamivir), enhancing surveillance through daily reporting of new cases from public health laboratories, developing and distributing a test kit for diagnosis, and submitting the available genetic sequences to GenBank. He indicated that unlike other influenza variants that affect the elderly with greater severity, the 2009 H1N1 influenza A virus appears to have a greater effect on individuals from 6 to 24 years of age. Dr. Jernigan concluded by enumerating the diagnostic test options available including CDC's PCR test and nine FDA-approved rapid influenza tests. In comparing seven of the rapid tests to PCR, the sensitivity of the rapid tests has been shown to be 18 to 69%.

FDA's Role in Ensuring Laboratory Testing Quality During Public Health Emergencies ***Addendum I***

Sally Hojvat, MSc, PhD
Office of In Vitro Diagnostic Device Evaluation and Safety
Center for Devices and Radiological Health
Food and Drug Administration

Dr. Hojvat described the use of the FDA's Emergency Use Authorization (EUA) to support the FDA's mission to get safe and effective medical devices to market as quickly as possible. The EUA allows either temporary approval of the use of an unapproved medical device or approval of the off-label use of an approved medical device during a declared public health emergency. Using 2009 H1N1 influenza A as an example, she reviewed the processes required to determine a "Public Health Emergency," the regulatory definition of an EUA, and how the EUA statutory criteria ensure devices released by the FDA, under a determined public health emergency, are both safe and effective. She provided a status report on the 2009 H1N1 influenza A EUAs issued

commercially, to the CDC, and to the Department of Defense (DoD). Dr. Hojvat emphasized FDA continues to work closely with CDC, the National Institutes of Health (NIH), and Health and Human Services (HHS) on both a short-term and long-term preparation/testing-needs strategy for the upcoming 2009-2010 influenza season.

CMS Perspective 2009 A/H1N1 Outbreak ***Addendum J***

Judy Yost, MA, MT (ASCP)
Director, Division of Laboratory Services
Centers for Medicare & Medicaid Services

Ms. Yost began her presentation with an overview of CMS' and CDC's coordinated efforts to develop a protocol for EUA test validation. She reviewed the CMS responses to the initial 2009 H1N1 influenza A outbreak including developing a policy memo to delay public health laboratory (PHL) surveys unless there was indication of immediate jeopardy or a complaint filed against the laboratory and making proficiency testing (PT) discretionary for one event or until further notice at the PHLs to facilitate adequate kit supply for patient testing. Additionally, CMS provided recommendations for testing laboratories to standardize procedures, training, and equipment in advance; to communicate with CMS regarding these efforts to assure CLIA compliance; and to network and coordinate with other laboratories in order to balance the workload. Ms. Yost said CMS's future outbreak response plans include suspending surveys as appropriate, facilitating communication between agencies, soliciting assistance from professional organizations, and prioritizing problems and workload.

Quality Challenges During the Spring 2009 Swine-Origin Influenza A Outbreak. A Clinical Laboratory Perspective ***Addendum K***

Danny L. Wiedbrauk, PhD
Scientific Director, Virology and Molecular Biology
Warde Medical Laboratory

Dr. Wiebrauk's presentation highlighted the successes and challenges of the 2009 H1N1 influenza A event from the clinical laboratory's perspective by recounting the experiences of his laboratory as they initiated testing for the new viral agent. He commended CDC's early posting of the 2009 H1N1 genetic sequences to GenBank, which allowed laboratories to verify laboratory developed tests. He requested CDC reconsider the restriction of their PCR protocol to non-profit use, thus preventing its use by commercial laboratories during this emergency. He also observed the impact of unexpected supply shortages which resulted in the need for clinical laboratories to modify methods and ultimately to undertake additional personnel education and training and validation studies. Dr. Wiebrauk also relayed how PHLs were burdened with performing diagnostic as well as surveillance testing and stressed PHL's role should be surveillance. By attempting to perform diagnostic testing, the PHL delayed patient reporting. He

suggested most of these delays could have been avoided by including clinical partners who have access to couriers, 24-hour testing capabilities, and interfaced computer systems, and thus the ability to handle a surge capacity workload.

Assuring Laboratory Quality in an Emergency, Experiences and Lessons from Novel H1N1 ***Addendum L***

Susan U. Neill, PhD, MBA
Director, Laboratory Services Section
Texas Department of State Health Services

Dr. Neill shared with the Committee how the Texas PHLs had been preparing and working with CDC prior to the 2009 H1N1 influenza A outbreak and, as a result, had the necessary equipment and knowledge to perform the PCR assay used for diagnosis of the virus. She explained that the outbreak created a surge to their entire system resulting in many challenges including rapidly diminishing freezer storage space, a need to organize and prioritize the overwhelming number of specimens received, staffing shortages, and performance of numerous additional validation studies. Dr. Neill said that, in some cases, PHLs performing diagnostic testing may have caused a delay in reporting results although she did not believe this affected patient outcome. She indicated that Texas PHLs plan to return to surveillance testing where they will watch for novel influenza viruses, identify resistance, and monitor changes in virus type. She concluded her presentation with a brief explanation of their preparation efforts and plans for future outbreaks.

Committee Discussion
Prior to opening the Committee discussion the CLIAC chair read the six questions to be addressed and then cautioned the Committee to clearly distinguish between the public health laboratory and the clinical laboratory in their comments. The questions are provided below, followed by points made during the discussion.

Did your laboratory or medical practice experience any challenges or learn any lessons from the recent event with novel H1N1 influenza that would better equip you for future experiences with public health emergencies?

- One member, while agreeing with the presenters that public health laboratories are not set up for diagnostic testing, disagreed that clinical laboratories should have been given access to the EUA tests earlier in the investigation of the outbreak. Based on experience, he felt more details about the epidemiology of the virus were needed before clinical laboratories should have been part of the testing process. The member cited several instances where the development of a testing protocol and initiation of diagnostic testing by clinical laboratory partners may have resulted in delayed or no public health reporting of their results, thereby circumventing the needed epidemiology. He suggested clinical laboratory partners should be engaged only after

the public health system has clearly established the epidemiology of the infectious agent.

- Dr. Jernigan explained that CDC began their approach to the 2009 H1N1 influenza A event using a case-based investigation, similar to foodborne outbreaks. When thousands of specimens began arriving at the PHLs, this approach was no longer practical and eventually CDC switched to an ecological approach. However, the clinical expectations for individual patient-based data remained, in order to better understand the risk factors for disease.
- Several members related how they went from a manageable test load to an overwhelming test load almost immediately, with the vast majority of specimens negative for influenza A.
- Difficulties with replenishing inventories of testing supplies and reagents as the demand for testing took off were noted by several members. One member concurred that the unavailability of reagents required laboratories to alter their methodologies resulting in time consuming method validation and testing delays.
- Most members agreed testing had no influence on improving patient outcomes. Some described how reallocating human resources and testing supplies from other critical laboratory testing to 2009 H1N1 influenza A testing (especially for epidemiological purposes) negatively impacted patient care in their institutions. One member added if therapy were critical to patient outcome, then tests should be developed that both identified the virus as well as the needed therapy.
- Several members commented that those individuals who interpret guidelines, prioritize testing, and set testing policy in their facility were key to ensuring the appropriate use of laboratory testing. Many members indicated that a stratified algorithm for testing would have clarified issues and alleviated much of the confusion they experienced.
- One member reminded the Committee that PHL capability and capacity varies widely across the United States. While PHLs focus on surveillance, some also have diagnostic responsibilities.

How could communication among laboratories or between laboratories and clinicians regarding testing conducted during public health events or emergencies be improved?

- CLIAC unanimously agreed that emergency preparedness and response plans must clearly communicate algorithms that define when to test, what test(s) to perform, why the testing is being performed, and how to use the test results.
- Because early knowledge of the 2009 H1N1 influenza A disease was limited and changed rapidly, members expressed frustration and noted that it had been confusing to keep pace with changing messages and information about testing.
- There was a general consensus that CDC's H1N1 algorithm guidance was confusing and that limiting its dissemination to publication in the *MMWR* was an added barrier to reaching and providing understandable information tailored specifically to physicians, nurses, other healthcare providers, commercial and public health laboratories, and the public.
- Several members voiced concern about the terminology used by public health officials during national press conferences and other media events that fed into, rather

than calmed, public panic. To a question about using the press more effectively in communicating with the public regarding who should be tested and why, Dr. Jernigan replied that CDC works very closely with the press, and added that an article about guidance on who should be tested may not generate a large amount of media interest.

- One member requested clarification on the published test sensitivities and asked where published reports on the sensitivities of rapid tests could be obtained. Dr. Jernigan stated a number of reports on rapid influenza test sensitivity are in the published literature and cited the August 7, 2009, *MMWR* article **"**Evaluation of Rapid Influenza Diagnostic Tests for Detection of Novel Influenza A (H1N1) Virus." (http://www.cdc.gov/mmwr/PDF/wk/mm5830.pdf)
- A member said the medical community should be given the clear message that the PCR test for influenza should be used for hospitalized patients as it is the most sensitive test method. Several members added that when asked about rapid antigen testing, the clear message should be not to perform this method unless results are confirmed by another method. All agreed that a stratified algorithm is needed to provide guidance on medical decisions, selection of the appropriate test for a patient, and matching the testing to the patient population. Dr. Jernigan agreed with CLIAC, indicating CDC is developing a clinical guidance document. He also alluded to a self-triage widget, a web-based tool that walks the user through scenarios and indicates when a doctor should be consulted.
- When asked by several members to clarify how physicians will know when to treat, Dr Jernigan replied the current guidance does not recommend that everyone be given treatment. Treatment is recommended for severely ill, hospitalized, high-risk patients. Clinicians should use the guidance provided by CDC and their judgment to make a medical decision.
- Several members sought clarification from the panel on the link between 2009 H1N1 testing and therapy. Dr. Jernigan informed CLIAC that CDC was about to release antiviral guidance addressing some of the issues that had been raised. http://www.cdc.gov/h1n1flu/recommendations.htm
- Most members agreed that recognizing the difference in surveillance testing and diagnostic testing was an important lesson learned and an important message to communicate to others.
- Ensuring the mission of the PHLs to perform surveillance is not compromised was seen as a critical message by CLIAC members. The public and healthcare communities need to understand the role of PHLs. Likewise; PHLs need to communicate with their partners in academic and private laboratories.
- The Chair emphasized the need to establish and test an improved communication plan at all levels, including state and federal.

Are considerations related to scheduled proficiency testing or other aspects of testing warranted to assure quality and flexibility during a public health emergency?

- Ms. Yost elaborated on the implementation of CLIA exceptions for public health emergencies during the initial 2009 H1N1 influenza A outbreak. In this instance, PT was discretionary for one event if laboratories did not have sufficient supplies available for testing patients and performing PT. Patient testing was the priority and

laboratories were given a code to submit to their PT program in lieu of submitting PT results for that event. If laboratories had sufficient supplies available, they were expected to perform PT. Ms. Yost explained that every exception to CLIA has been based on the circumstances of the situation. These exceptions are always considered temporary and all laboratories are expected to comply with the CLIA regulations as soon as possible.

Are laboratories aware that CLIA provides exceptions for verifying/establishing performance of new methods, quality control, and calibration during public health emergencies? How could information concerning these exceptions be clearly communicated?

- Several members expressed concern about lowering quality standards and compromising standards of testing during a healthcare emergency. A member commented exceptions made during an emergency may set a precedent that could be misinterpreted; e.g., those performing point-of-care testing in the emergency room may believe they never need to perform quality control.
- Ms. Yost clarified what exceptions to test verification might entail. For example, the use of fewer samples in verification studies is permitted when few positive samples are available. This is permitted with the caveat that as more samples and data become available, the laboratories will complete their test verifications. She emphasized exceptions are only provided under exceptional circumstances and customized based on the emergency.
- A Committee member suggested CDC create a standard verification panel of specimens and/or perform the validation of laboratory developed tests at CDC. This would allow for uniform and rapid verification of laboratory developed tests during emergency situations.

Are laboratory personnel considerations needed to assure quality and flexibility during a public health emergency?

- Several members indicated that patient care was negatively impacted when staff was moved from patient care and important clinical testing to assist in public health surveillance testing. The Chair said that shifting personnel may be appropriate during an emergency situation. A Committee member commented that personnel issues are different for each facility and the laboratory director must evaluate the situation and decide how to best utilize the personnel.
- Several members indicated the importance of waiving state licensure requirements and staffing contracts during emergencies to allow laboratories to fill in personnel gaps quickly. Another member commented that if this virus had been more virulent, staffing issues would have been much worse.

Are there considerations with respect to laboratory space and design that should be anticipated in case of a public health emergency?

- Dr. Jernigan related to the Committee that an evaluation was conducted by CDC in collaboration with the Association of Public Health Laboratories (APHL) in preparation for a public health emergency. The evaluation contained models for surge capacity and examined the laboratory resources and space processes. http://www.bt.cdc.gov/publications/feb08phprep/section1/phlab.asp A follow-up study by APHL will reveal how well the models predicted the surge outcomes and areas that need improvement. A Committee member said it would be beneficial to compare the RAND Corporation surge capacity model to the CDC model. http://www.rand.org/pubs/technical_reports/TR317/
- The Committee discussed the current financial crisis and how it has affected the PHLs. A Committee member expressed concern that more stringent biosafety laboratory regulations would be perceived as an unfunded mandate to PHLs. Resources could be a major burden in meeting the space and design requirements of these regulations.

Are there planning activities laboratories should be engaged in to more readily address future public health emergencies?

- A Committee member asked what the national agenda is for meeting the challenges of the 2009 H1N1 influenza A event. Dr. Jernigan reported that a President's Council of Advisors on Science and Technology gap assessment and report has been written and several Institute of Medicine reports have covered the issues discussed by the Committee. He said that there is a need to identify which body should address the diagnostic laboratory issues. Within CDC, areas that need improvement have been identified and have resulted in several state public health department grants.
- Dr. Neill provided an update on the Surge Task Force, a collaboration of large commercial laboratories, hospital laboratories, public health laboratories, CDC, CMS, and others. The Surge Task Force was created to identify and resolve significant issues in laboratory surge capacity during emergencies. She said many of the problems identified were due to communication and messaging issues. The task force expects to have a draft plan by September 15, 2009, which will include recommendations on who to message, when to message, what to message, and what type of communication is needed. The task force hopes to develop a plan that will include accurate points of contact for reference, hospital, and public health laboratories. She clarified that the task force is not developing the messages that will be communicated, just the communication plan.
- Several members mentioned that guidelines for laboratory testing in an emergency need to be written at the institutional level using CDC guidance. These guidelines should consider how testing will be performed if personnel are affected by the event.

Assessing the Performance and Impact of Waived Testing ***Addenda M & N***

Nancy Anderson, MMSc
Chief, Laboratory Practice Standards Branch
Division of Laboratory Systems

National Center for Preparedness, Prevention, and Control of Infectious Diseases
Coordinating Center for Infectious Diseases
Centers for Disease Control and Prevention

Ms. Anderson introduced the topic and speakers for the CLIAC discussion on assessing the performance and impact of waived testing. She began by reminding the Committee that over the last 15 years, there has been a significant increase in waived tests and laboratories with a CW. She mentioned the numerous times that CLIAC has addressed waived testing and reiterated the Committee's latest recommendation on the topic - that CDC gather data to study the impact of waived testing on patient outcomes and clinician behavior. In response to this recommendation, Ms. Anderson reviewed available data pertaining to waived testing performance including data from the CMS CW project and previous CDC Sentinel Monitoring Networks' studies. She also listed several CDC waived testing publications, including the 2005 *MMWR R&R* on "Good Laboratory Practices for Waived Testing Sites." She concluded her overview of available data by describing a current CDC project evaluating influenza rapid testing in outpatient settings and providing a list of 29 waived testing references. The aggregate literature provided no clear measure of impact on patient outcome and Ms. Anderson emphasized the limitations and challenges in assessing waived test impact and outcomes.

Ms. Anderson next explained that a possible untapped source of data on waived testing performance may be CMS-approved PT programs that offer voluntary PT for waived testing. She said five of these programs had offered to share waived testing PT data with CLIAC. After introducing the speakers, she provided CLIAC with several questions to consider in their deliberations, asking them to consider the gaps in waived testing data, and how to better address the gaps and measure the impact and outcomes of waived testing.

CLIA Certificate of Waiver (CW) Program

Addendum O

Daralyn Hassan, MT
Division of Laboratory Services
Centers for Medicare & Medicaid Services

Ms. Hassan provided background and an update on the status of the CMS CW Project. She related that an initial survey of CW and provider-performed microscopy procedures laboratories from 1999 to 2001 revealed quality problems. In 2002, CMS instituted an educational program that includes surveying two percent of all CW laboratories each year as one step towards more clearly identifying and correcting the problems. Using data from 2002-2007, she showed that the program has raised the laboratories' awareness of the need to follow the manufacturer's instructions for testing, identified laboratories that were testing beyond the scope of their waived testing certificate, and provided education on CLIA, laboratory testing, and good laboratory practices. In conclusion, Ms. Hassan reviewed the probable next steps: project continuation, collaboration with CMS partners, and potential changes to the CLIA law that would affect CW laboratories if enacted.

Committee Discussion

- A Committee member asked if nurses could act as CW laboratory directors. Ms. Hassan replied yes, the only CLIA requirement is that the CW laboratory has a director; there is no educational requirement for that person.

Waived Testing Performance Data from the American Academy of Family Physicians (AAFP) Proficiency Testing Program ***Addendum P***

Verlin K. Janzen, M.D.
American Academy of Family Physicians

Dr. Janzen began with a brief overview of AAFP and its external quality control (QC) program, AAFP-PT. This CMS and COLA-approved comprehensive program has an enrollment of over 2,600 laboratories, is geared towards physician office laboratories (POLs), and awards continuing education credits to physicians and laboratory personnel. In 2008 AAFP conducted a practice profile survey which revealed 92% of family physicians perform laboratory testing in their offices at an average rate of 37 tests per day, over 60% of which are waived tests. Dr. Janzen reviewed a sample of recent POL PT performance data for commonly ordered waived tests, noting laboratories enrolled in the AAFP-PT program had a high percentage of passing scores. In summary, he said a number of waived laboratories successfully perform PT. He expressed concern about waived testing conducted in nursing homes, where there may not be physician oversight. Overall, he noted test quality is variable, with some waived tests performing better than nonwaived tests. Education regarding selection of appropriate test methods may improve patient results.

Proficiency Testing–Waived Tests ***Addendum Q***

Daniel C. Edson
President
American Proficiency Institute (API)

After illustrating the enormous rise in CW testing laboratories in the U.S. since the implementation of CLIA ‘88 and the distribution of CW laboratories under the purview of CMS and the CMS-approved accrediting organizations, Mr. Edson presented API PT data for several analytes showing performance trends for waived tests for 1994, 2001, 2004, and 2008. He observed that the testing sites were office laboratories, clinics, and point-of-care locations within hospitals and testing personnel were predominately non-medical technologists. The study data showed that although PT failure rates tended to decline in the period between 1994 and 2008, erythrocyte sedimentation rate failures were higher than expected and increased during that time period. Another study, comprised of data from 1994 to 2004, showed failure rates for all of the quantitative

analytes studied had declined. However, although there had been a decline in microbiology PT failures in that timeframe, relatively high failure rates still existed for *Neisseria gonorrhoeae* and urine culture PT. He concluded that continuing education was needed for microbiology laboratories, that grading criteria for sodium should be re-evaluated, and he encouraged more peer-reviewed publications from other PT providers.

The Impact of Waived Tests ***Addendum R***

Paul Bachner, MD, FCAP
Professor and Chairman
Pathology and Laboratory Medicine
University of Kentucky
Lexington, KY

Dr. Bachner reviewed the criteria for waiver under CLIA. He related the College of American Pathologists (CAP) position on waived testing and its position on regulatory oversight of testing performed in emergency rooms, radiology departments, and operating rooms as compared to waived tests performed in POLs. He reviewed CAP's experience with its waived testing PT program, citing increases in enrollments for several analytes and noted for testing facilities that maintain CAP accreditation, PT is required for most analytes. Dr. Bachner said CAP has data to show continuous participation in PT improves proficiency and accuracy for all analytes, and that receiving "unsatisfactory" performance scores in PT provides laboratories an incentive to investigate issues and make procedural adjustments. He described CAP's PT performance specifics and performance levels comparing waived and CMS-regulated tests for several analytes. In conclusion, he stated although the original concept of waived testing was acceptable when a small number of tests were performed in laboratories and POLs, with the advance of technology, the idea that thousands of tests critical to patient care and safety do not need any oversight is disturbing.

PT Program Presentation (MLE) ***Addendum S***

Connie Laubenthal, MS, CLS (NCA)
American College of Physicians
Medical Laboratory Evaluation (MLE) PT Program

Ms. Laubenthal began her presentation with a brief overview of the MLE PT program. The MLE program was established in 1973 as a means for small laboratories, particularly POLs, to verify the accuracy of their testing. The participant base in the U.S. has now expanded to include hospitals and independent laboratories; however, in the past ten years, overall U.S. enrollment has decreased due to many laboratories performing only waived testing. Using data gleaned from the HemoCue (hemoglobin/glucose), Rapid Antigen Detection (streptococcus group A), and Whole Blood Glucose modules for 1999 and 2009, she showed that approximately 20% of the participants were CW laboratories

with percentages remaining stable over time. Of these, POLs are the largest subscribers; the majority are affiliated with primary care specialties. Further, the enrolled waived laboratories are predominantly located in states that have their own laboratory regulations. She noted that the number of accredited CW laboratories enrolled in PT had increased from 1999 to 2009 for all three modules; however, accredited CW laboratory participation has never approached 50% of the total CW PT enrollment. Finally, Ms. Laubenthal compared the performance of laboratories that perform nonwaived testing to the performance of CW laboratories using data gleaned from the HemoCue (hemoglobin/glucose), Rapid Antigen Detection (streptococcus group A), and Whole Blood Glucose modules for 1999 and 2009.

Proficiency Testing Trends and Method Performance ***Addendum T***

Barbara Hill, MT (ASCP)
PT Manager
Wisconsin State Laboratory of Health

Ms. Hill provided information from the Wisconsin State Laboratory of Health PT program. She listed several reasons for enrolling in PT for waived tests, remarking the majority of their participants enroll first because of an organizational commitment to a quality assurance plan and second because PT is a convenient process for documenting competency training. Ms. Hill described the WSLH PT program's "regulated" versus "waived" configurations. She provided data on enrollment in the Streptococcus Group A Antigen and Influenza modules for 2004-2009, noting the percentage of CW laboratories has increased significantly and surpassed the decreasing percentage of laboratories that perform nonwaived testing. She presented similar findings for the same years for Infectious Mononucleosis, Anti-HIV, and Coagulation (Protime/International Normalized Ratio) modules, although the percentages of CW laboratories did not surpass the percentage of nonwaived testing laboratories for these modules. In conclusion, Ms. Hill noted the passing rates of CW and regulated laboratories were similar, but the data did not reflect performance for all sites using waived methods.

Committee Discussion

The Chair guided the Committee's discussion, asking members for comments and personal perspectives in response to specific questions from the CDC. Each question is provided below, followed by relevant points made during the CLIAC discussion. Additional Committee discussion points are notated after the responses to the CDC questions.

Where are the gaps in what we now know about waived test performance and its impact?

- The Chair commented it is unclear whether the PT data for waived tests was collected from CW laboratories only or included laboratories that perform both waived and nonwaived testing.

- A member stated there is a large gap in the PT studies presented because of the low number of CW laboratories participating in PT. For this reason, the data presented may be skewed.
- Several members remarked the analytical phase of patient testing has been addressed and suggested the pre- and post-analytical testing phases and their impact on patient outcome now be the focus of waived testing studies.
- Determining the distribution of problems throughout the different types of CW testing facilities was another gap mentioned. One member commented the quality of testing varies between testing sites. Therefore, the actual performance of waived tests should be studied. The quality differences between the various testing environments should be addressed by practice-based research.
- Another member stated that, in practice, physicians conduct point-of-care testing because they want an immediate result, but they may also request follow-up laboratory testing, which leads to duplicate testing, and in some cases, discordant results. The member suggested addressing the cost effectiveness of point-of-care testing, the frequency of duplicate testing, and actions taken on discordant results.
- Citing Ms. Hassan's account of CW laboratories held accountable for immediate jeopardy, a member stated such action was inconsistent with the idea that a waived test should result in no harm and perhaps the criteria for waiving a test should be changed. The member emphasized the need for accountability to address the fact that the risk appears to be higher than anticipated. Several members agreed there are risks associated with issues of immediate jeopardy in waived testing. There is a gap in the oversight and accountability of CW testing sites. Investigation of this gap should be facilitated.
- The Committee discussed the formation of a workgroup to address pre- and post-analytic issues of waived testing. A member suggested delaying the workgroup formation until additional information is presented by CDC and CMS.

How should CDC address the gaps?

- A member commented on decisions made to perform a test using a waived versus nonwaived testing method, stating it is neither the Committee's nor CDC's role to determine whether a certain test improves patient care. The member further suggested the Committee's role is to ask if care is improved by performing a waived test on-site rather than delaying the result by sending the specimen out to a laboratory to be tested.

-How can waived testing performance be assessed in nontraditional testing sites?

- This question was not addressed during the Committee discussion.

-Should waived test performance be assessed for particular analytes or test systems? If so, which should we focus on?

- A member recalled that the Committee had addressed the issue of confirming pregnancy tests during the February 2007 CLIAC meeting. After patients tested positive by a home pregnancy test, physicians would order a laboratory test to confirm it, suggesting physicians did not trust the results of the home tests.

-Should a waived test study focus on specific types of testing personnel? If so, what groups should be assessed – nurses, medical assistants, others?

- A member suggested the impact of waived testing performed by nursing personnel on patient care be considered. The member elaborated stating that nurses are often short-staffed and overburdened by the addition of waived testing to the workload.
- One member addressed concern about risk indicators such as changes in personnel and lack of training, and suggested laboratories are not following basic requirements. The indicators point to performance failure and need to be addressed. Another member commented the risk may be even higher than is realized and although education is always good, stronger intervention and oversight is needed.
- A member commented there is an issue in general with the personnel performing waived tests and oversight is needed.

How can the impact of waived testing on patient care be measured?

- A member proposed assessing whether the "risk of harm" in performing a waived test was more significant than the "risk of improvement" in patient care if test results are more readily available.

Additional Committee Discussion

- A member stated there will always be laboratories that perform better than others. Many laboratories believe waived testing is devoid of any regulation and is often performed by personnel with no laboratory training, similar to a consumer who might purchase and perform an over-the-counter test. However, one advantage of point-of-care testing in an intensive care unit or neonatal intensive care unit is that a minimal amount of blood may be required to complete a broad panel of tests. Therefore physicians, nurses, and other healthcare providers should be taught about the risks and complexities of testing, proper test performance, and the limitations of results.
- A member asked if criteria existed to specify when a waived test needed to be repeated. The member also stated there was a need to know if persons performing waived tests were qualified to conduct the testing. The member asked if there were any standards that apply to waived tests and what happened when complaints were received against a laboratory. In response, Ms. Yost clarified, by law waived tests are considered simple and the only requirement is to follow the manufacturer's instructions. She explained CMS has neither the authority nor revenue to visit CW laboratories regularly, however, CMS investigates every laboratory complaint.
- A member expressed concern about waived tests that do not include requirements for QC testing. Another member suggested the lack of QC may contribute to differing attitudes between personnel who perform waived testing and those qualified to perform nonwaived testing.
- Several members acknowledged the need for PT for waived tests, suggesting a different number of challenges and a different set of grading criteria be used. Another member added PT may help address problems shown to have arisen from personnel turnover in CW laboratories.
- A member commented on how waived test performance could vary due to the preserved or fixed state of PT samples as opposed to test performance where fresh, unaltered specimens are tested. It was noted that matrix effects are hard to

characterize and comparisons cannot be made between testing methods due to these issues.

- A member said that CW laboratories must, first of all, know what is expected of them and commended educational efforts such as the *MMWR R&R* "Good Laboratory Practices for Waived Testing Sites." Additional materials that more simply explain the *MMWR R&R* content need to be developed and distributed to CW facilities.
- In response to Ms. Hassan's suggested next steps by CMS, one member proposed making recommendations regarding the definition of a waived test, proficiency requirements for CW testing sites, personnel requirements for waived testing, and routine oversight of CW testing sites. The Committee was advised that changes in these areas regarding waived testing would require a change in the CLIA law.
- One member proposed that all CW sites complete a yearly survey that includes questions addressing personnel changes, personnel training, and documentation. The survey could be designed to raise awareness in the laboratories about issues such as the importance of following the manufacturer's instructions and retention of training records. Survey results could be flagged to indicate problems in the laboratories. The member noted that if only two percent of the 130,000 CW laboratories are inspected each year, 50 years will be needed to assess all laboratories. A survey would reach 100% of the CW laboratories in one year and raise awareness regarding good laboratory practices, although it would not address fraud. Several members agreed a survey would be a good tool for the yearly assessment of CW testing facilities. The Chair clarified the law regarding CW sites, saying the Secretary of Health and Human Services can require compliance because the laboratory has already agreed to make records available, so administratively CMS could implement a survey.
- The Committee voted and passed the following recommendation: CMS should survey each CW laboratory to: 1) determine which tests they perform, 2) identify who performs the testing, 3) verify that all testing personnel have been trained and shown to be competent for each test they perform, and 4) verify that the laboratory has a current copy of the manufacturer's instructions for the test, and that testing personnel follow these instructions when performing testing. A pilot study of a subset of CW laboratories should be conducted prior to extending the survey to all CW laboratories.
- Ms. Yost stated CMS has developed a plan and has been working with accrediting organizations to address waived testing issues without changing the law or regulations. One part of this would be to ask testing sites for a list of tests they are performing. This would allow CMS to determine whether the sites are testing beyond the scope of the CW. However, the CW program is user funded and any expenditure must be vetted through management. Ms. Yost added to increase the inspections to more than two percent per year would require additional funding for an increase in staff in each state. A member inquired about information received from CMS when a CW is issued. Ms. Yost said CMS currently does not provide additional information, but does make available brochures, a link to the *MMWR R&R*, and other pertinent information.
- Several members commented the intent of the law for waived testing is not being followed. One member suggested a review of FDA data on the number of applications for waived devices, rejection percentages, and reasons for rejection. Dr. Gutierrez responded the FDA is aware of the difficult nature of and issues that are

associated with test device waivers. He explained that some devices are waived by law. The FDA website provides information on the criteria used for determining waiver of a test.

- Ms. Yost noted the Committee discussions had been directed toward changing the law regarding waived tests. She clarified, the regulations state a laboratory issued a CW must pay the applicable fee and follow the manufacturer's test instructions. The law does not provide CMS the ability to perform surveys, require proficiency testing, or charge fees because it excludes CW sites from the two CLIA subsections on standards and inspections. CMS is not authorized to lobby Congress for changes in the law; citizens must lobby for changes through legislation. Changing statutes is also beyond the purview of CLIAC; the Committee is responsible for providing advice regarding CLIA oversight of testing within the regulations mandated by statute. Ms. Yost and the Chair urged caution when considering amending the laws. However, she suggested that by showing evidence that supports the need for oversight, CMS may be able to collect additional information or develop some standards for waived tests.
- A member stated anything can be included in the labeling of a product, but nothing will make a person read the label. Manufacturers often sell products through distributors and do not know their users.
- Dr. Hearn wondered whether manufacturers could encourage their salespeople to help educate the waived laboratories.
- One member asked what the difference was between the FDA's intervention with a major pharmaceutical company for recommending product usage different than stated in the package insert and the failure of waived testing personnel to follow the manufacturer's instructions. Dr. Gutierrez responded the issue is who the responsible party is. He stated if a manufacturer is selling or promoting the device for off-label usage, the manufacturer is liable; but when a laboratory or other user does not follow the manufacturer's instructions, the user assumes liability.

The Current State of HIV Testing ***Addendum U***

Elliot P. Cowan, Ph. D.
Center for Biologics Evaluation and Research
Food and Drug Administration

Dr. Cowan opened his presentation with a description of two types of HIV testing: traditional, laboratory-based tests and rapid testing performed at point-of-care. He focused on rapid HIV testing describing the benefits and drawbacks of waiving these types of tests, recounting past CLIAC discussions, and summarizing FDA's approach to the resolution of access issues. Dr. Cowan concluded by introducing the next speaker, Dr. Bernard Branson.

Evolving Diagnostic Technologies and Emerging Issues Related to HIV Testing
Addenda V & W

Bernard M. Branson, M.D.
Associate Director for Laboratory Diagnostics
Divisions of HIV/AIDS Prevention
National Center for HIVAIDS, Viral Hepatitis, STD, and TB Prevention
Centers for Disease Control and Prevention

Dr. Branson began his discussion of the current state of HIV testing by providing an historical perspective of the changing landscape for HIV diagnostics and diagnostic algorithms. He described the transformation of the state of the art since 1989. Current guidelines permit health-care providers to provide preliminary positive rapid HIV test results, in situations where tested persons benefit, before confirmatory results are available. He noted, when additional rapid tests become available, the Public Health Service will re-evaluate algorithms using specific combinations of two or more rapid tests for screening and confirming HIV infection. He presented several validation studies for HIV confirmatory testing and noted the difficulties laboratories face in conducting performance validations. In conclusion, Dr. Branson asked for the Committee's comments on algorithms for confirmatory testing and central validation of combination-test algorithms. He also requested suggestions for a menu of combination-test algorithms, insight on tools to assist laboratories in appropriate selection of algorithms for different settings, and ideas for ways to make laboratories, testing sites, and clinicians aware of revised algorithms and result reporting requirements. Finally, he requested Committee perspective on possible mechanisms to facilitate implementation of public health and clinical practice recommendations.

Committee Discussion

Prior to opening the Committee discussion, the CLIAC chair read the seven questions to be addressed. The questions are provided below, followed by points made during the CLIAC discussion.

Does the Committee agree that a menu of combination-test algorithms is appropriate for different testing settings and circumstances?
Can the Committee comment on the proposed plans for central validation of combination test algorithms?

- The Chair asked Dr. Branson for clarification on the meaning of central validation of combination-test algorithms. Dr. Branson stated he was referring to the protocols for large validation studies using all available tests. This would be the method for making a recommendation for combination-test algorithms.
- A member asked Dr. Cowan if data collected in multi-center studies using FDA cleared assays could be submitted by manufacturers to allow them to expand their claims rather than each manufacturer trying to repeat the study. He responded it was possible, but the manufacturer's desire to claim use of their test in a particular multi-test algorithm would probably depend upon how their test had been used in the algorithm. If theirs was not the primary test, it would be unlikely they would pursue this route.

- The same member asked if a manufacturer could submit the data generated from a multi-center, multi-test newborn trial to the FDA to validate a new performance claim. Dr. Cowan replied yes, as long as the manufacturer supplies data that validates the new claim they want to include in the package insert. However, the FDA would have to ensure the trials were run appropriately.
- A member asked if CDC could make a sample bank available so laboratories could perform necessary validation studies. Dr. Hearn replied that in the case of samples from newborns it may be impossible simply due to lack of available specimens.
- One member stated, in some cases, laboratories have a clinical need to test but there is no approved test for a specific population, nor do they have adequate numbers of that population to officially validate the test. A centralized, multi-centered study might be a solution to that situation.

What would CLIAC suggest for making laboratories, testing sites, and clinicians aware of the revised algorithms and result reporting requirements?

- A member suggested that revised algorithms and communications be incorporated into an *MMWR*. Dr. Hearn commented the information would need to be communicated in many different ways and suggested the Clinician Outreach Communication System and the Laboratory Outreach Communication System. Dr. Carey proposed having clinical and laboratory professional organizations co-support and disseminate the information so that it reaches the intended audiences.

What tools could be used to assist laboratories and testing sites make the appropriate selection of one or more algorithm(s) that would serve the needs of their population?

- Ms. Ochs suggested the agencies could recommend certain types of tests be used but the specific test could not be stipulated.

Does the Committee agree that clinical laboratories should be permitted to report reactive immunoassay results in situations where tested persons benefit?

- A member asked for clarification on why a result from a single rapid HIV test could be reported out, but a result from a single nonwaived test performed in a laboratory by laboratory personnel could not be reported. Dr. Cowan responded preliminary positive results from rapid HIV tests may be reported out when the tests are used at the point-of-care. This is seen to be of benefit to the patient because they can receive their results without having to return for follow-up.

How can clinical laboratories accommodate the provider's role in selection of follow-up tests after a reactive immunoassay result?

- One member expressed concern about clinicians requesting specific tests in an algorithm. This could result in the laboratory having to maintain quality control for a large number of tests or lengthen turn around due to ordering tests the laboratory does not perform in house. Dr. Branson responded the intent was to give providers the option of choosing the type of test they would like used as follow-up, but not for them to choose the specific test. The member responded if the laboratory is knowledgeable about the recommended test for follow-up or confirmation, the physician should not be given the option of making the decision. Another member commented most

physicians would not want to make that decision. A member suggested including in the test report the primary and secondary tests used for clinicians who may have use for that information.

Please comment on mechanisms to facilitate implementation of evolving public health and clinical practice recommendations in good laboratory practice.

- Dr. Branson clarified that this request was asking how to address situations where there is a gap between what is available and what is needed in terms of clinical practice recommendations and good laboratory practice. The Chair suggested professional and industry roundtables might be a source for recommendations.
- One member noted recommendations for validation or establishing performance can be made on the basis of a centralized source of accumulated data. However, if a laboratory follows the recommendation but has not been able to establish their own performance for a test, the laboratory subsequently will receive a CLIA citation. Ms. Yost commented there can be a dichotomy between professional organizations' recommendations and the availability of commercial test kits with specific claims that are consistent with those recommendations.

PUBLIC COMMENTS

Association of Molecular Pathology's H1N1 Outbreak Response ***Addendum X***

Georgia State Surveyor's Plea to Strengthen Waived Testing Requirements ***Addendum Y***

AAB-PT's Plea to Strengthen Waived Testing Requirements ***Addendum Z***

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 following reflects the Committee's recommendation from this meeting:

- CMS should survey each CW laboratory to: 1) determine which tests they perform, 2) identify who performs the testing, 3) verify that all testing personnel have been trained and shown to be competent for each test they perform, and 4) verify that the laboratory has a current copy of the manufacturer's instructions for the test, and that testing personnel follow these instructions when performing testing. A pilot study of a subset of CW laboratories should be conducted prior to extending the survey to all CW laboratories.

Ms. Passiment announced the next CLIAC meeting would be February 9-10, 2010 and adjourned the Committee meeting.

I certify this summary report of the September 2-3, 2009 meeting of the Clinical Laboratory Improvement Advisory Committee is an accurate and correct representation of the meeting.

_____ Dated 10/ / 2009