Clinical

Laboratory

Improvement

Advisory

Committee

Summary Report

April 15-16, 2015

Atlanta, Georgia

U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES

Clinical Laboratory Improvement Advisory Committee
April 15-16, 2015, Summary Report

Table of Contents

RECORD OF ATTENDANCE

Committee Members Present

Dr. Burton Wilcke, Jr., Chair
Mr. Eugene Augustine, Jr.
Dr. Robert Baldor
Dr. Edward Chan
Dr. Monica de Baca
Dr. Gwendolyn Delaney
Dr. Ann Gronowski
Dr. Keith Kaplan
Dr. Roger Klein
Dr. Elizabeth Marlowe
Dr. Elizabeth Palavecino
Dr. Richard Press
Ms. Anita Roberson
Ms. Maureen Rushenberg
Dr. John Sinard
Dr. Hardeep Singh
Ms. Paula Vagnone
Dr. Linda Ward
Dr. David Wilkinson
Dr. Qian-Yun Zhang
Mr. Robert Di Tullio, AdvaMed (Liaison Representative)

Ex Officio Members

Dr. Barbara Zehnbauer, CDC (Acting)
Ms. Karen Dyer, CMS (Acting)
Dr. Sally Hojvat, FDA (Acting)

Designated Federal Official

Dr. William (Bill) Mac Kenzie, CDC

Executive Secretary

Ms. Nancy Anderson

Record of Attendance – cont'd

Centers for Disease Control and Prevention (CDC)

Dr. J. Rex Astles
Dr. Nancy Burton
Dr. Roberta Carey
Dr. Alexis Carter
Dr. Bin Chen
Dr. Nancy Cornish
Ms. Laura Conn
Dr. Marie Earley
Dr. James Ellison
Ms. Maribeth Gagnon
Dr. Amy Gargis
Dr. Shaw Gargis
Ms. Nedra Garrett
Mr. Jeffrey Hagaman
Dr. Cathleen Hanlon
Dr. Thomas Hearn (Retired)
Ms. Teresa Horan
Ms. Stacy Howard
Dr. Lisa Kalman
Mr. Sam Keith
Dr. Ira Lubin
Ms. Xiaoyue Ma
Ms. Alana McCoy
Ms. Leslie McDonald
Ms. Canditra McLemore
Ms. Graylin Mitchell
Mr. Michael Pentella
Ms. Anne Pollock
Ms. Nakeva Redmon
Dr. John Saindon
Dr. Paramjit Sandhu
Ms. Megan Sawchuk
Dr. Shahram Shahangian
Mr. Darshan Singh
Ms. Theresia Snelling
Mr. Jonathan Spencer
Ms. Heather Stang
Ms. Sonya Strider
Dr. Julie Taylor
Mr. H. Eric Thompson
Ms. Pamela Thompson
Ms. Monica Toles
Ms. Elizabeth Weirich
Ms. Karlyn Wilson
Dr. Laurina Williams
Dr. Lyna Zhang
Mr. Jonathan Zhong

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

Ms. Arlene Lopez, CMS
Ms. Karen Dyer, CMS
Ms. Cindy Wilkerson, DoD

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. The meeting was also available by webcast.

CLINICAL LABORATORY IMPROVEMENT ADVISORY COMMITTEE (CLIAC) -BACKGROUND

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 pertaining to improvement in clinical laboratory quality and laboratory medicine. In addition, the Committee provides advice and guidance on specific questions related to possible revision of the CLIA standards. Examples include providing guidance on studies designed to improve safety, effectiveness, efficiency, timeliness, equity, and patient-centeredness of laboratory services; revisions to the standards under which clinical laboratories are regulated; the impact of proposed revisions to the standards on medical and laboratory practice; and the modification of the standards and provision of non-regulatory guidelines to accommodate technological advances, such as new test methods and the electronic submission of laboratory information.

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 AND COMMITTEE INTRODUCTIONS

Dr. William Mac Kenzie, Designated Federal Official (DFO), Clinical Laboratory Improvement Advisory Committee (CLIAC), and Deputy Director for Science, Center for Surveillance, Epidemiology, and Laboratory Services (CSELS), Office of Public Health Scientific Services (OPHSS), CDC, welcomed the Committee and the members of the public, acknowledging the importance of public participation in the advisory process. Dr. Burton Wilcke, Chair, CLIAC, welcomed the Committee and called the meeting to order. All members then made self-introductions and financial disclosure statements relevant to the meeting topics.

Dr. Wilcke and Dr. Mac Kenzie recognized the five outgoing CLIAC members who also received letters of appreciation signed by the CDC Director for their service on the Committee. The members were Mr. Eugene Augustine, Jr., Dr. Robert Baldor, Dr. Edward Chan, Dr. Linda Ward, and Dr. David Wilkinson. Dr. Wilcke also welcomed the new members, Dr. Monica de Baca, Dr. Gwendolyn Delaney, Dr. Ann Gronowski, Dr. Elizabeth Palavecino, Ms. Anita Roberson, and Ms. Maureen Rushenberg, to the Committee.

Dr. Wilcke conveyed that the agenda topics included updates from the CDC, the Centers for Medicare & Medicaid Services (CMS), and the Food and Drug Administration (FDA) as well as an update from the CLIAC liaison to the CDC Office of Infectious Diseases Board of Scientific Counselors (BSC). In addition, there would be presentations and discussions on laboratory information exchange in health information technology (IT), and laboratory safety and quality from the perspective of lessons learned through the Ebola response. There would also be discussion on future CLIAC topics.

AGENDA UPDATES AND COMMITTEE DISCUSSION

Centers for Disease Control and Prevention (CDC) Update ***Addendum 01***

Barbara Zehnbauer, PhD, FACMG, FACB
Acting Director
Division of Laboratory Systems (DLS)
Center for Surveillance, Epidemiology, and Laboratory Services (CSELS)
Office of Public Health Scientific Services (OPHSS)
Centers for Disease Control and Prevention

Dr. Zehnbauer's presentation highlighted the major activities currently underway within DLS. She discussed DLS' role in the Ebola response noting the Division is providing advice on clinical laboratory issues, especially involving safety, as well as providing staff to support CDC's emergency operations center. She related the Division supported CDC's Laboratory Safety Workgroup recommendations by creating improved laboratory training, contributing to the development of the Laboratory Leadership Service

fellowship, providing consultation with respect to CDC's exploration of external accreditation for all CDC laboratories, and making improvements to the CDC and ATSDR Specimen Packaging, Inventory, and Repository (CASPIR) specimen collection systems. Dr. Zehnbauer updated the Committee on the 2014 CLIAC recommendation for the development of a voluntary assessment or checklist to be used by waived testing sites and on the distribution of waived testing educational products, explaining that plans for this are underway through the expansion of a checklist that is already part of the *Ready? Set? Test!* booklet. She provided an update on the two-year contract awarded to the American Society for Cytotechnology Services, Inc., reviewing the assessment of the 2014 survey results and the laboratory time measure studies completed, and discussing the project's next steps. She briefly discussed Clinical Laboratory Integration into Healthcare Collaborative (CLIHC™) activities including the vetting of new coagulation test selection algorithms for development of a mobile application and evaluation of the Partial Thromboplastin Time **(**PTT**)** Advisor (one of the first Smart Phone apps to be released by CDC). Next, Dr. Zehnbauer provided updates on the three ongoing cooperative agreements to measure and improve the impact of laboratory practice guidelines (LPGs) in clinical medicine and public health. She also provided updates on the newborn screening project, Laboratory Medicine Best Practices activities (LMBP™) including systematic review collaborations with the American Society for Microbiology, the Genetic Testing Reference Materials Coordination Program, and CDC activities to develop standards for next-generation sequencing in clinical laboratories. Dr. Zehnbauer concluded with an overview of the CDC Laboratory Training Branch website.

Committee Discussion

- Regarding the LPG metrics project, a member asked if there is an effort to standardize metrics across institutions. Dr. Zehnbauer replied that it is difficult to harmonize recommendations across the different organizations, adding that DLS is creating a clearing house to promote the use of metrics for LPGs.
- The same member inquired whether the evidence-based literature review was part of the LMBP™ process. Dr. Zehnbauer explained that the first step in the process is the systematic review of published literature to develop the evidence-based recommendations. Evaluating the impact of the recommendations is a subsequent step.
- A member asked if applications, like the CLIHC PTT Advisor, will be incorporated or available as a companion tool to electronic health records (EHRs). Dr. Zehnbauer explained one path would be to provide a clinical decision support tool integrated into the EHR and another would be to provide a separate support tool for queries that would extract the relevant information from within the EHR system. CDC developed the PTT Advisor to support physicians trying to make decisions about most appropriate laboratory test ordering. The application is not integrated into the EHR, but may have the capability to adapt to EHRs with the appropriate middleware. Additional free applications are being investigated by CDC.
- The member added the integration of decision support tools is important from a microbiology perspective as more molecular testing panels that include a wide range of analytes for infectious disease testing are developed. Dr. Zehnbauer commented groups at the CDC are converting many of the guidelines and recommendations in

Morbidity and Mortality Weekly Report **(**MMWR) publications into interactive smart phone types of applications.

Centers for Medicare & Medicaid Services (CMS) Update ***Addendum 02***

Karen Dyer, MT(ASCP), DLM
Acting Director
Division of Laboratory Services
Survey and Certification Group
Centers for Medicare & Medicaid Services

Ms. Dyer provided the Committee with the current CLIA statistics and survey deficiencies and Certificate of Waiver Government Performance Review Act (GPRA) project data. She reviewed the issue of "off-label" use of waived glucose meters in specific patient populations when the manufacturer's instructions contain limitations indicating the systems have not been evaluated or cleared for use in patient populations such as those who are critically ill. She indicated the CMS Survey and Certification (S&C) Memorandum 15-11 entitled "Off-Label/Modified Use of Waived Blood Glucose Monitoring Systems (BGMS)" has been reissued in draft form to obtain feedback and promote education. Ms. Dyer provided an overview of the major changes to the CLIA Interpretive Guidelines including the incorporation of specific language regarding the need to follow manufacturer's quality control (QC) and test performance instructions for waived tests. She also explained the removal of references to Clinical and Laboratory Standards Institute (CLSI) microbiology guidelines that include exceptions to the CLIA QC rules for microbiology. She discussed the education and transition period for implementation of the CMS individualized quality control plan (IQCP) option for QC and the educational outreach including the development of an IQCP workbook in collaboration with the CDC. The workbook is primarily intended to provide assistance to physician office laboratories, but it can serve as a resource to all laboratories that choose to implement the IQCP approach. Next, Ms. Dyer provided updates on the status of the patient access rule, fecal occult blood testing proposed rule, progress towards updating the proposed proficiency testing (PT) regulations, the regulations implementing the Taking Essential Steps for Testing (TEST) Act (effective July 1, 2014), detailing the adverse actions for PT referrals, and the PT burden rule. Last, she provided the Committee information on the declined 2011 CLIA legislative proposal (A-19) which included a recommendation to change the CLIA law to allow routine oversight of Certificate of Waiver laboratories to ensure quality testing and facilitate patient safety.

Committee Discussion

- A member asked for clarification on distributive testing as it relates to the PT burden rule. Ms. Dyer explained distributive testing, as now defined in CLIA section 493.2, means "laboratory testing performed on the same specimen, or an aliquot of it, that requires sharing it between two or more laboratories to obtain all data required to complete an interpretation or calculation necessary to provide a final reportable result for the originally ordered test. When such testing occurs at multiple locations with different CLIA certificates, it is considered distributive testing." She added that the

key is the different CLIA certificates, so if one is doing testing within a laboratory under a single CLIA certificate, it is not considered PT referral.

- Another member requested clarification of the one-time narrow exception carve-out for intentional PT referral involving reflex testing. Ms. Dyer replied that all cases of PT referral or suspected PT referral are sent to the CMS Central Office for evaluation. She added that confirmatory testing can be performed if the laboratories are under a single CLIA certificate, but when the samples are sent to a site with a different CLIA certificate, that is considered PT referral and is not allowed.
- A member commented on the dichotomy between blood glucose testing for a critically ill patient in an intensive care unit and the routine monitoring of outpatients' glucose levels and noted that often a gray area exists with respect to what actually constitutes "off-label" use. The member asked if the issue of "off-label" is specific for glucose meters or if there will be a larger effort by CMS to distinguish and monitor "off-label" use for other waived tests. Ms. Dyer responded that CMS' actions with glucose will affect all other waived tests, and emphasized that for all tests, the manufacturer's instructions must be followed or it is considered "off-label" use.
- Another member added that even if a laboratory establishes performance of BGMS for use with critically ill patients, the test defaults to high complexity and the issue becomes the personnel qualifications. Most registered or licensed practical nurses performing these tests do not qualify to perform high complexity testing under CLIA. The member suggested that manufacturers obtain clearance on BGMS for critically ill patients.
- One member inquired if manufacturers exclude critically ill patient testing when obtaining FDA clearance because the tests do not function properly with that testing population or because they did not include that population in the application to FDA. Ms. Dyer replied that it could possibly be due to either situation.
- A member commented that Theranos promotes testing quickly and accurately on samples as small as a single drop. The member inquired how CDC, CMS, and FDA will ensure that the results are valid and safe. Ms. Dyer replied that the company has a Certificate of Compliance to perform nonwaived testing and may be working with the FDA to obtain approval on their testing system. However, that type of information would be proprietary.
- The AdvaMed representative asked if the Certificate of Waiver (CoW) sites receiving the letter of congratulations received a perfect inspection or if they could still receive one if minor issues were discovered. Ms. Dyer replied that it usually means there were no problems identified and reminded the Committee that the CoW visits are educational surveys and citations will not be given unless surveyors find serious problems.

Food and Drug Administration (FDA) Update ***Addendum 03***

Sally Hojvat, PhD
Director
Division of Microbiology Devices
Office of In-Vitro Diagnostic Evaluation and Safety (OIVD)
Center for Devices and Radiological Health (CDRH)

Food and Drug Administration

Dr. Hojvat began her presentation by providing an update on the Medical Countermeasures (MCM) Initiative to identify and resolve regulatory challenges to MCM development and recapping the MCM diagnostic 510(k) submissions and Emergency Use Authorizations (EUAs). She provided a brief update on the April 2014 FDA public workshop on high throughput next generation sequencing (NGS) and the national action plan for combating antibiotic-resistant bacteria. Dr. Hojvat reviewed the pre-market approvals, de novo down-classifications, CLIA waivers by application, and the past year's meetings. She concluded her presentation with an overview of recent FDA final and draft guidance documents.

Committee Discussion

- A member requested clarification on the publicly curated NGS databases for human genetic testing versus the information Dr. Hojvat presented pertaining to microbial genetics. Dr. Hojvat replied the databases for microbial genetics are more complete, but those available to the public are suboptimal so there is a need to have a set of criteria for metadata for inclusion in the library. The member commented that microbial databases can be used as a demonstration of clinical validity in instances where an assay screens for multiple variants to prevent the task of validation for every variant. Dr. Hojvat agreed, but emphasized the need for accurate sequences in the curated databases for commercial assay evaluation.
- One member requested elaboration on the EUA assessment process including the general timeline for approval and the safety of testing personnel for tests involving pathogenic organisms. Dr. Hojvat explained that the FDA has draft templates to guide the EUA approval process starting with study design. In the case of Ebola, it was difficult to compare molecular assays because there were no commercial assays available for comparison. FDA reviewed limits of detection along with cross-reactivity and interfering substances. She added that it is up to the testing laboratory to follow the CDC safety recommendations.

CDC OID Board of Scientific Counselors (BSC) Update ***Addendum 04***

Elizabeth M. Marlowe, PhD, D(ABMM)
Committee Liaison to CDC Board of Scientific Counselors
Office of Infectious Diseases (OID)
Assistant Director
Microbiology-Molecular Testing
Southern California Permanente Medical Group
Regional Reference Laboratories

Dr. Marlowe provided a summary on the December 2014 CDC OID BSC meeting. She summarized the key updates from OID, followed by an update and discussion about CDC efforts to enhance laboratory safety. She provided brief updates on the BSC Antimicrobial Resistance Working Group, the Infectious Disease Laboratory Working Group, and the Food Safety Modernization Act Surveillance Working Group (FSMA

SWG), which presented its fiscal year 2014 annual report for BSC approval. Dr. Marlow reported on the ongoing outbreaks caused by Middle East Respiratory Syndrome Coronavirus (MERS-CoV), enterovirus D68 (EV-D68), and Ebola virus. She indicated that the update given on CDC's response to the Ebola outbreak was followed by a discussion on the long-term outbreak response efforts.

Committee Discussion

- A member asked if other regulatory agencies use the CDC data from the FSMA SWG for the surveillance of food-borne illnesses. Dr. Marlowe clarified that the Interagency Food Safety Analytics Collaboration (IFSAC), is a joint effort by FDA's Center for Food Safety and Applied Nutrition, USDA's Food Safety and Inspection Service, and CDC's Division of Foodborne, Waterborne, and Environmental Diseases to improve coordination of federal food-safety analytic efforts and address cross-cutting priorities for food safety data collection, analysis, and use. The IFSAC Strategic Plan for 2012-17 focuses on four foodborne pathogens: *Campylobacter, Listeria, Salmonella,* and STEC O157. As part of these efforts, IFSAC has developed a new food categorization scheme to increase the accuracy and utility of the food categories used to describe foods implicated in outbreaks and to generate foodborne illness source attribution estimates.

PRESENTATIONS AND COMMITTEE DISCUSSION

Laboratory Information Exchange in Health Information Technology (IT)

Introduction ***Addendum 05***

Ms. MariBeth Gagnon, MS CT(ASCP)HTL
Health Scientist
Division of Laboratory Systems (DLS)
Center for Surveillance, Epidemiology, and Laboratory Services (CSELS)
Office of Public Health Scientific Services (OPHSS)
Centers for Disease Control and Prevention

Ms. Gagnon provided an introduction to the topic. She defined interoperability and discussed why the exchange of electronic health information is needed and the current barriers to making it a reality. She discussed the five goals of the Federal Health IT Strategic Plan and the nationwide interoperability Roadmap which describes the actions and roles needed to achieve the vision described in Office of the National Coordinator for Health Information Technology's (ONC's) *Connecting Health and Care for the Nation: A 10-Year Vision to Achieve an Interoperable Health IT Infrastructure*. She said the cornerstone of the Roadmap calls for a learning health system which will lead to better care, smarter spending, and healthier people. Ms. Gagnon concluded by introducing the presentation topics.

Laboratory Interoperability Plan *Addendum 06*

Karen Dyer, MT(ASCP), DLM
Acting Director
Division of Laboratory Services
Survey and Certification Group
Centers for Medicare & Medicaid Services

Ms. Dyer provided an overview of the ONC's draft action plan for achieving laboratory interoperability. She noted that CMS and CDC were brought into the workgroup after the basic plan had already been developed. Ms. Dyer reviewed the advantages of laboratory interoperability and provided an overview of the five building blocks that make up the laboratory interoperability plan. She related CMS' concerns about the plan, especially as related to the laboratory and CLIA and discussed the current suggested strategies for implementing the plan. She noted there is no regulatory requirement for laboratories to implement the actions recommended and no rationale provided in the plan regarding the potential advantages of laboratory interoperability. Ms. Dyer concluded by conveying that CMS, CDC, and FDA have begun conversations with ONC aimed towards revising the Laboratory Interoperability Action Plan.

Committee Discussion

- A member commented there must be an endeavor to educate patients as access to health records means patients need to be able to interpret the health records. Another member noted the results of a survey conducted in their facility showed that about 75% of clinicians were not comfortable with abnormal results being sent directly to the patients without interpretation. Most of the concerns were with the potential for misinterpretation of the test results. Ms. Dyer replied that patients' misinterpretation of abnormal results is one of CMS' concerns. She added many of the comments received in response to the patient access rule centered on interpretation of abnormal results. However, the HHS Secretary determined that the benefits of directly providing patients with their results outweighed the disadvantages.
- One member asked if advanced directives with respect to laboratory information are included in the laboratory interoperability plan. Ms. Dyer replied she did not know whether advanced directives are included. The member noted it seems that two issues are being tackled – commutability between institutions and a consumer friendly way to get data. It would seem the first is more important from a medical perspective. Ms. Dyer replied commutability between institutions is the overall goal of the larger interoperability plan. The first goal is specific for moving the information from the laboratory to the provider in a standardized format and to the patient if the patient has requested it.
- A member observed interoperability within institutions as well as integration of testing platforms with reporting systems has yet to be achieved. Further, there is no mention in the ONC plan about who is expected to implement it or how it is going to be funded, fostered, or tested and implemented. Until that happens, the plan lacks force. Ms. Dyer replied CMS is also concerned about who is going to pay for and implement the plan.

- Another member remarked a recent informal survey indicated a large number of academic health systems are already sharing laboratory data with patients and very few problems have been identified. The only variable seems to be the amount of time between the verification of a laboratory result and its release to the patient. It seems to be a tendency for most facilities to delay release. A second member noted their institution has a patient portal, but the patient portal suppresses a certain percentage of results; the argument being that information can be suppressed as long as the patient can get access either through the medical records or the laboratory. The problem is the patient does not know that information is suppressed. The member questioned whether institutions have the responsibility to follow CMS regulations and report all results, and also made the point that there are a variety of structures for laboratory test results in patient portals. Because laboratory professionals were not included in the design and information display in the portals, the outcome can be the misinterpretation of results.

aLOINC Order Code Initiative Update ***Addendum 07***

Ms. MariBeth Gagnon, MS, CT (ASCP) HTL
Health Scientist
Division of Laboratory Systems (DLS)
Center for Surveillance, Epidemiology, and Laboratory Services (CSELS)
Office of Public Health Scientific Services (OPHSS)
Centers for Disease Control and Prevention

Ms. Gagnon provided an update of the Standards and Interoperability (S&I) Framework initiative, aLOINC Order Codes, launched in January 2014. The groups' charge was to provide a common order code value set for the Laboratory Orders Interface and Electronic Directory of Services Implementation guides. She demonstrated how LOINC® is used and emphasized the difficulty laboratories may encounter in determining which code to use. Ms.Gagnon discussed the four key deliverables of the aLOINC project: 1) development of the aLOINC Common Order Codes Value Set, 2) provision of input to the Regenstrief Institute for Health Care (Regenstrief) on guidance for comparing user panels to LOINC® panels, 3) provision of recommendations to the ONC on how to use LOINC® for laboratory orders, and 4) provision of recommendations to Regenstrief on content updates based on the review of laboratory order LOINC® codes. She discussed the data reviewed and the analysis of the data that resulted in the common order code value set. Ms. Gagnon reviewed the lessons learned from the process and ended her presentation with a summary of the group's preliminary recommendations and related next steps.

Committee Discussion ***Addendum 08***

- The Chair introduced the five questions to be addressed by the Committee and instructed the Committee to discuss them in the order presented.

What challenges will laboratories face in achieving interoperability as described in the current ONC Laboratory Interoperability Action Plan?

- The Chair observed that Committee discussion thus far had brought forward the following challenges: some facilities do not even have in-house operability, let alone inter-facility operability; laboratories sometimes do not have the final say in terms of what information or data are being released; and funding of the Action Plan has not been addressed.
- A member noted achieving interoperability is going to require effective coordination of efforts among a wide variety of entities.
- A member commented the measurement and evaluation framework must be built into the Plan, patient reports must be accurately routed, and it must be determined who will have clear responsibility for each of the components of the Plan.
- One member inquired about the outcome of the 2012 CLIAC recommendation sent to the HHS Secretary and follow up to the publication of the CDC White Paper. Ms. Gagnon replied that the ONC's S&I Framework director, Dr. Doug Fridsma, had presented his response to the HHS letter at the August 2013 CLIAC meeting. She added CDC is in the process of submitting the White Paper to the *Journal of Healthcare Information Management* for publication. Ms. Dyer added it may be time to be more coordinated and proactive and advocate for an organizational response to the recommendations made in the CDC White Paper.
- A member remarked another challenge to interoperability is that even if laboratories use the same LOINC® code and method, it still remains for them to use the same units and reference intervals for a particular test, and to agree on what should be flagged as abnormal.
- A member noted the interoperability roadmap is essentially a call for software development. The member expressed concern about what seems to be a fundamental misunderstanding about how software is developed and added there is an appropriate process for developing software successfully. The development must start with use cases that address what is trying to be achieved. Interoperability needs better defined use cases. Very specific definitions must be assigned to what is meant by interoperability, it cannot simply be defined as the exchange of data and everyone is going to be healthier. There must be clarity about what kind of functionality needs to be achieved.
- A member asked what extent competition among software vendors will be an obstacle to achieving harmonization if the vendors do not see it in their business interests to harmonize.
- One member questioned how laboratories can become engaged in the process of achieving interoperability to be sure that their issues are defined and to offer suggestions for how to create a timeline to keep moving forward.

What are achievable goals for interoperability that can be readily evaluated going forward?

- The Chair observed that one goal is to determine what kind of functionality needs to be achieved before the architecture of the software system is developed. A second goal would be to separate the issue of patient access to information from the larger picture of laboratory information exchange and interoperability.
- One member commented that commonality of the patient identifier is needed. For a record to be interoperable from one system to the next, one has to start out with an

identifier that is absolute. Somebody needs to dictate what that identifier is, and then everybody has to use it. Another member added perhaps there should be a national patient identifier and noted this topic has been widely debated.

- A member suggested a goal for achieving interoperability could be addressed by initially including only the 100 laboratory tests most commonly performed.
- Another member suggested using incentives or goals to encourage participation in the efforts to achieve interoperability.
- A member commented that, when setting goals, the end product must be clearly defined.
- Another member suggested that an expert panel be convened to discuss what the goals should be.

Which stakeholders need to be engaged in vetting a draft laboratory interoperability plan?

- The Chair noted there are a number of stakeholders in this kind of endeavor. Among them are laboratories, healthcare providers, patients, governmental agencies, payers, IT specialists, bio-informaticians, and software developers.
- A member commented the whole public health infrastructure is another stakeholder.
- One member remarked that more input from either ONC or a committee such as CLIAC would be powerful.

What mechanisms should we use to effectively communicate a final laboratory interoperability plan to clinical and public health laboratories?

- No mechanisms were suggested.

How can federal agencies encourage laboratory code standardization and the uptake of changes to enhance laboratory interoperability?

- The Chair opined this question assumes the answer to the implementation of the plan will be via a mechanism based on incentives or encouragement. The implementation would not be anything that would be required or standardized. The question implies the mechanism for achieving interoperability is still somewhat ill-defined. A member observed that defining the end product therefore, would seem to be a good goal.
- Another member replied the end product has to be based upon the current state of knowledge. It could be a recommendation to convene, for example, a stakeholder group or somebody to gather information, but with some pre-defined goals.
- A third member observed that care should be taken with the use of the word product because it suggests there is an actual piece of software that is going to evolve, as technology changes, and become different ways of doing the same thing. One key to getting started in the right direction is a more specific definition of interoperability; that and a list of the use cases that the ultimate solution needs to be able to achieve. The types of functionality that the solution enables must be determined not how to do it or what code to use.
- A member wondered if the interoperability framework could be tackled in phases. Dr. Hojvat responded that implementation of health IT can be thought of in three levels or phases: the first is assuring that health IT or technology is safe, the second is assuring that technology is used safely in clinical practice, and the third is assuring

that technology is used to improve patient care. The first level, safe technology, would include data security, availability, integrity, and, to some extent, standardization.

- The Chair stated the goals are patient-specific and health care oriented but the data can be used for more than one purpose. In addition to the patient, data can also be used for public or community health purposes. Dr. Hojvat concurred.
- A member contended that before the health IT phases are considered, we have to define what data are going to be collected, and how they will be collected and codified before proceeding to the next step, which is how to share the data.
- Ms. Dyer responded because there are so many aspects to achieving interoperability, it needs to be prioritized. Several members shared similar opinions.
- Dr. Zehnbauer added as the laboratories' advocates it might be useful for CLIAC to again make the HHS Secretary aware of laboratories' priorities and concerns.
- Dr. Mac Kenzie added ONC is very interested in having CDC or CMS take over the laboratory action plan project. They want to include laboratories in the overall roadmap and to that end they have asked the CLIA agencies to delineate in the roadmap the next steps for the laboratories. The Committee has said we need to prioritize, create standards, and work forward on a reasonable timeline knowing where we are going. A workgroup is a good idea to begin to work on standards and set some priorities.
- The Chair responded the Committee could recommend a workgroup be brought together and asked the Committee if it was also important to communicate to the HHS Secretary that a lot of work needs to be done before the laboratory interoperability action plan can be carried forward.
- Mr. DiTullio recommended the stakeholders be identified first to ensure all perspectives are included and nothing is missed.
- A member suggested the Committee read over the CDC White Paper and CLIAC letter sent to ONC in 2012 since it contains elements, put in a thoughtful format, that have been discussed and then consider making a recommendation the following day.
- On day two of the meeting a member presented three slides (***Addendum 8a***) consisting of background and a possible CLIAC recommendation. After a brief discussion that resulted in some additional wording the Committee passed the following recommendation to be sent to the HHS Secretary.

HHS should convene a multidisciplinary stakeholder group that

- Includes, but is not limited to, representatives from ONC, CMS, FDA, CDC, industry representatives, health IT developers/vendors, all CLIA approved accrediting organizations, informaticians, laboratory directors/professionals, provider end-users, patient/consumer representatives, and other relevant professional organizations
- Proposes a framework for achieving safe and effective laboratory interoperability (both system and patient facing) that encourages innovation and defines how to operationalize interoperability (and related deliverables) with detailed use cases
- Provides both short term next steps and long term goals with definable measurable actions and outlines who is responsible for these actions

- Puts into place robust measurement and evaluation strategies for goal achievement

The Committee would like HHS to also consider these points:
Illustrative components that should be addressed by the framework include those described in:

- the CDC White paper: *The Essential Role of Laboratory Professionals* http://www.cdc.gov/labhit/paper/Laboratory_Data_in_EHRs_2014.pdf
- a 2012 letter from CLIAC to HHS (https://wwwn.cdc.gov/CLIAC/pdf/2012_Oct_CLIAC_%20to_Secretary_re_EHR.pdf)
- Aim to create conditions that promote safe/effective laboratory data interoperability
- Consider incentives and other levers for actions such as new regulation, existing regulation (e.g. CMS Conditions of Participation), evidence-based recommended practices (e.g., ONC SAFER Guides), accreditation (e.g. College of American Pathologists - CAP, The Joint Commission - TJC) and certification
- Framework would also need to consider creation of new incentives, funding and/or revenue streams to support lab data interoperability

Note: A letter expressing the Committee's recommendation pertaining to advancing a more connected, interoperable health information technology infrastructure was sent to the HHS Secretary on May 6, 2015. ***Addendum 8b***

Laboratory Safety and Quality: Lessons Learned Through the Ebola Response

Laboratory Safety and Lessons Learned from the Ebola Response ***Addendum 09***

Nancy Cornish, MD
Medical Officer
Elizabeth G. Weirich, MS
Public Health Analyst
Division of Laboratory Systems (DLS)
Center for Surveillance, Epidemiology, and Laboratory Services (CSELS)
Office of Public Health Scientific Services (OPHSS)
Centers for Disease Control and Prevention

Dr. Nancy Cornish introduced the speakers for the next session, Ms. Weirich, Dr. Campbell, Dr. Burton, and Dr. Pentella, who spoke on laboratory safety and quality gaps discovered through the Ebola response. She described a vision to address these gaps using a systems-based, multidisciplinary approach including clinical and public health laboratories working together with professional organizations, federal agencies, and manufacturers. Ms. Weirich provided an update on laboratory safety gaps identified during CDC's rapid emergency preparedness (REP) team visits to 44 U.S. hospitals to evaluate their capacity and preparedness to receive, identify, and treat patients with suspected or confirmed Ebola virus disease (EVD). The REP team identified laboratory testing issues including the lack of risk assessments and failure to follow the

Occupational Safety and Health Administration's (OSHA's) bloodborne pathogen standards; laboratory instrumentation issues such as lack of data on decontamination of automated laboratory instruments and supplies; and insufficient training in work practices and personal protective equipment. Dr. Cornish provided the Committee with a brief overview of potential aerosol and droplet generating procedures along with primary routes of infectious disease transmission as described by the CDC-convened Biosafety Blue Ribbon Panel MMWR (http://www.cdc.gov/mmwr/pdf/other/su6101.pdf) and the 2007 Healthcare Infection Control Practices Advisory Committee guideline (http://www.cdc.gov/hicpac/pdf/isolation/Isolation2007.pdf). Next, she addressed suggestions to assure the safety of laboratory instruments, expand training and education, develop partner collaborations, and provide workforce competencies. Dr. Cornish concluded with an update on the development of a voluntary, non-punitive system to report laboratory-acquired infections which is currently in HHS clearance.

Emerging Infections: The Plain Ol' Clinical Laboratory Perspective

Sheldon Campbell, MD, PhD ***Addendum 10***
Associate Professor of Laboratory Medicine
Director, Medical Microbiology Course
Director, Laboratories at VA CT Healthcare System
Director, Microbiology Fellowship

Dr. Campbell began with an overview on how to perform a clinical laboratory risk assessment including a determination of the need for each testing site to develop a reliable and up-to-date assessment. He discussed the risks associated with instrumentation and processes during the pre-analytic, analytic, and post-analytic testing phases. Dr. Campbell provided an overview of the Emory University Hospital and Nebraska Medical Center Ebola response procedures emphasizing that these facilities have a high probability of seeing patients with EVD as opposed to other sites where EVD is on a long list of possibilities. He concluded with a list of issues and gaps that need to be addressed to monitor and improve safety when routinely testing for emerging pathogens in the clinical laboratory environment.

The Potential Role of Industrial Hygienists and the Health Hazard Evaluation (HHE) Program at NIOSH in Bioaerosol Exposure Assessments ***Addendum 11***

Nancy Burton, PhD, MPH, MS, CIH
Senior Industrial Hygienist
Hazard Evaluations and Technical Assistance Branch (HETAB)
Division of Surveillance, Hazard Evaluations & Field Studies (DSHEFS)
National Institute for Occupational Safety and Health (NIOSH)
Centers for Disease Control and Prevention (CDC)

Dr. Burton began with a description of industrial hygiene including typical roles of an industrial hygienist, the American Board of Industrial Hygiene (ABIH) professional organization, credentials required to become a certified industrial hygienist, and the Code

of Ethics established by ABIH. Next she provided an overview of OSHA and the National Institute for Occupational Safety and Health (NIOSH) illustrating the differences between the two regulatory agencies. Dr. Burton provided a brief description of NIOSH activities and expanded on the health hazard evaluation program listing the benefits of a health hazard evaluation, the request process, site visit activities, and the rights of NIOSH, employees, unions, and employers during the health hazard evaluation process. She discussed reasons for NIOSH exposure assessment, the types of recommendations that are provided, and examples of prior evaluations involving biological hazards. Dr. Burton concluded her presentation by providing NIOSH's role in bioaerosol sampling and identifying potential bioaerosol exposures.

What Can Public Health Labs Do To Improve Biosafety in Our Nations Labs?

Michael Pentella, PhD, D(ABMM) ***Addendum 12***
Director of the Bureau of Laboratory Sciences
Hinton State Laboratory Institute.
Massachusetts Public Health

Dr. Pentella provided an overview of the activities that the Massachusetts Department of Health State Laboratory performed to prepare for EVD testing, including providing a risk assessment template to clinical laboratories to assist in predicting, identifying, and mitigating risk associated with Ebola testing. Next, he highlighted Ebola preparation activities of the Indiana State Department of Health and the Wadsworth Center, Department of Health, New York State. Dr. Pentella discussed the post-Ebola public health laboratory perceptions. He presented an overview of public health laboratory activities that will be conducted as a result of funding from the CDC National Center for Emerging and Zoonotic Infectious Diseases FY 2015 Ebola Funding – Epidemiology and Laboratory Capacity (ELC) Supplemental. Dr. Pentella noted the formation of the Biosafety and Biosecurity Committee by the Association of Public Health Laboratories (APHL) and listed the proposed priorities of the committee. He concluded his presentation by providing CLIAC with a list of issues clinical laboratories should address to ensure safe, reliable testing for emerging pathogens.

Committee Discussion ***Addendum 13***

- A member asked how CMS surveyors or accreditation organization inspectors ensure that laboratory directors are meeting the CLIA requirement that they ensure the physical plant and environmental conditions of the laboratory are appropriate for the testing performed and that they provide a safe environment in which employees are protected from physical, chemical, and biological hazards. Dr. Campbell replied that from his experience as an inspector, the laboratory safety program is reviewed including the safety policy, and documented evidence of safety program that is actively working to identify hazards and perform mitigation.
- The same member inquired if the process for safety inspections was robust enough to ensure a safe working environment. Dr. Campbell replied that the inspections are process-oriented rather than outcome-oriented and thus have inherent limitations. He

stated that data on the numbers of laboratory associated infections would be needed to adequately address the question process for safety.

- Another member added that there are many safety related questions in the CAP laboratory general checklist and effectiveness of the safety program is dependent on the observation of the CAP laboratory inspector. Dr. Zehnbauer clarified that CAP provides a separate inspection checklist for laboratory directors and the findings from all the checklists should be used to assess the laboratory's safety program.
- A member asked about the safety inspection process for laboratories that are not CAP accredited. Ms. Dyer replied that CMS performs an outcome-oriented survey process to determine the laboratory's regulatory compliance and to assist laboratories in improving patient care by emphasizing those aspects that have a direct impact on the laboratory's overall test performance. The surveyor will inspect the laboratory's safety records and record any obvious safety violations.
- Another member inquired about the OSHA standards for laboratories. Dr. Burton commented that all laboratories that work with patient specimens are required to follow OSHA bloodborne pathogen standards, but due to the lack of OSHA inspectors not all sites are inspected on a routine schedule. If a complaint is made, then OSHA will inspect the laboratory to determine if it fails to meet safety regulations. Another member added that OSHA does not routinely inspect clinical laboratories, but everyone should be provided the opportunity to contact OSHA directly to file a complaint if they feel unsafe.
- One Committee member asked how laboratories are interpreting the concept of universal (now standard) precautions to prevent exposure to any patient's bodily fluids. Dr. Cornish commented that laboratories may need education and awareness on standard precautions. Dr. Pentella added that laboratories strive to follow standard precautions with all patient specimens. He noted that the issue is concern by laboratory professionals that standard precautions may not be enough when dealing with Ebola.
- A member commented that the Agency for Healthcare Research and Quality published a report on the role of simulation in preparedness training to help detect breaches in safety protocols as they evolve (http://www.ahrq.gov/research/findings/factsheets/errors-safety/simulproj15/index.html#note2) and asked if there was a way to leverage this type of strategy, currently being used in health care, to address preparedness training in the laboratory. Dr. Pentella replied that risk assessments are not used frequently in many laboratories, but he encouraged their use and noted their value.
- The Chair introduced the five discussion questions related to the topic of laboratory safety and quality for the Committee to consider.
    1. What types of tools, training, and educational resources are needed to assess and better assure the safety of personnel who perform diagnostic testing?
    2. How can HHS raise awareness about available, accurate, and effective tools, training, and educational resources for laboratory safety?
    3. What communication mechanisms should be considered (e.g. webinars, social networking, others) for promoting these resources?
    4. What role should laboratory inspectors and accrediting organizations play to assure that laboratories establish and observe safety procedures?

5. How can federal agencies, public health and clinical laboratories, and laboratory professional organizations work together to monitor continuous improvement of instrument safety?

The Committee did not respond to the questions individually but offered the following comments and recommendations.

- Two members noted that there seems to be conflicting views on whether universal precautions are sufficient in the context of EVD. One member added that the inconsistency in recommendations from different places gives the impression that there is uncertainty and people will become overly cautious and question the concept of universal precautions.
- Another member commented on the discordance between the community hospitals, state public health laboratories, and the CDC on EVD testing procedures and emphasized the need for harmonization of all current testing guidelines by the different organizations and governmental agencies. A member added that new guidelines should be developed using evidenced-based data.
- A member observed it is the manufacturer's responsibility to determine the proper decontamination protocol for testing equipment. Several members agreed that manufacturers should be responsible for providing recommendations for decontamination of their instruments. One member noted that when a manufacturer was contacted, the manufacturer could not provide protocols or recommendations. This further supports the need for guidelines for laboratories regarding proper decontamination protocols and possible aerosol production for laboratory equipment used for testing specimens that could contain infectious agents. The AdvaMed representative replied that manufacturers have validated cleaning procedures to protect the personnel performing equipment service and repair along with those individuals in the factories who remanufacture instruments for resale. He stated that manufacturers are responsible for providing these decontamination protocols to laboratories who use the equipment for testing. In addition, the AdvaMed liaison commented that users of laboratory instruments or reagents must adhere to the manufacturers' product labeling which for every test system cleared by the FDA says to use universal precautions for all specimens.
- One member suggested CDC develop user-friendly educational materials for EBV testing similar to the *Ready? Set? Test!* booklet including information addressing specimen handling, sample preparation, and resources for questions. The member noted that information provided in a simple, straight-forward manner may help allay some concerns.
- The Chair recalled that after the development of the first blood test for HIV, the Surgeon General's Report on AIDS was published describing what the nation should do to prevent the spread of AIDS. He suggested a report on EBV could provide people with the information needed to alleviate the fear factor associated with Ebola.
- Another member suggested CDC perform studies on testing procedures to determine the proper inactivation methods for Ebola.
- A member added that training and competency assessments for laboratories testing for infectious diseases should be required. A second member mentioned there are gaps in the availability of such training. Dr. Zehnbauer commented that the

Laboratory Training Branch (http://www.cdc.gov/labtraining/) has developed many online trainings including "Packing and Shipping Division 6.2 Materials: What the Laboratorian Should Know - 2014." She agreed that assessment is needed to evaluate the impact of the training and whether changes in practice occur after the training has been completed.

- One member noted the lack of qualified bio-safety officers and need for bio-safety officer training to create knowledgeable personnel to fill the gap.
- Dr. Wilcke, the CLIAC chair, called for formal recommendations.

The Committee made the following recommendation:

With regard to emerging infections, HHS should:

1. Provide oversight that ensures assessment of the safety and decontamination of laboratory instrumentation by manufacturers.
2. Ensure that biosafety training and assessment is required of all CLIA-certified laboratories, including personnel responsible for the preanalytical, analytical, and postanalytical phases of testing.
3. Ensure oversight, input, and resources into studies evaluating the safety of all laboratory practices, instrument testing, etc., so that studies are sound, robust, evidence-based, and applicable.
4. Develop a process for investigating and reporting laboratory acquired infections.

Note: A letter expressing the Committee's recommendation pertaining to clinical laboratory biosafety, especially with regards to emerging infections in the United States, was sent to the HHS Secretary on May 6, 2015. ***Addendum 13a***

Future CLIAC Topics Discussion

The Chair opened the discussion, revisiting suggestions for future CLIAC topics.

- A member suggested an FDA update on laboratory developed tests.
- One member commented on the rapid expansion of molecular and genetic testing including panels that test for risk of certain diseases. The member referred to testing being offered by health care providers and direct-to-consumers, suggesting discussion on the regulatory aspects of this testing may be warranted.
- Two members suggested that CLIAC consider the topic of laboratory test selection and decision support to prevent over-ordering of tests in the preanalytic phase of laboratory testing.
- A member suggested including an update on the Institute of Medicine report on diagnostic errors in health care and the laboratory recommendations that are part of that report.
- Dr. Mac Kenzie indicated that suggestions for topics from CLIAC members are always welcome. Ms. Anderson added that a Federal Register notice will soon be published asking for ideas on future CLIAC topics as well as providing information on the process to suggest candidates for CLIAC nomination. The Committee will be informed when the Federal Register notice is published.

BACKGROUND INFORMATION ***Addendum* 14**

ACRONYMS ***Addendum* 15**

NOMINATION INFORMATION ***Addendum* 16**

PUBLIC COMMENTS

AdvaMed ***Addendum 17***
ASCLS ***Addendum 18***

ADJOURN

Dr. Wilcke and Dr. Mac Kenzie acknowledged the staff that assembled the meeting program and thanked the CLIAC members and partner agencies for their support and participation. The following are the Committee recommendations passed at this meeting:

Recommendation on Health IT:
HHS should convene a multidisciplinary stakeholder group that

- Includes, but is not limited to, representatives from ONC, CMS, FDA, CDC, industry representatives, health IT developers/vendors, all CLIA approved accrediting organizations, informaticians, laboratory directors/professionals, provider end-users, patient/consumer representatives, and other relevant professional organizations
- Proposes a framework for achieving safe and effective laboratory interoperability (both system and patient facing) that encourages innovation and defines how to operationalize interoperability (and related deliverables) with detailed use cases
- Provides both short term next steps and long term goals with definable measurable actions and outline who is responsible for these actions
- Puts into place robust measurement and evaluation strategies for goal achievement

The Committee would like HHS to also consider these points:
Illustrative components that should be addressed by the framework include those described in:

- the CDC White paper: *The Essential Role of Laboratory Professionals* http://www.cdc.gov/labhit/paper/Laboratory_Data_in_EHRs_2014.pdf
- a 2012 letter from CLIAC to HHS (https://wwwn.cdc.gov/CLIAC/pdf/2012_Oct_CLIAC_%20to_Secretary_re_EHR.pdf)
- Aim to create conditions that promote safe/effective laboratory data interoperability

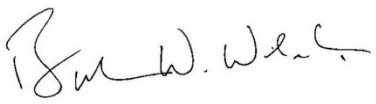
- Consider incentives and other levers for actions such as new regulation, existing regulation (e.g. CMS Conditions of Participation), evidence-based recommended practices (e.g., ONC SAFER Guides), accreditation (e.g. CAP, TJC) and certification
- Framework would also need to consider creation of new incentives, funding and/or revenue streams to support lab data interoperability

With regard to emerging infections, HHS should:

1. Provide oversight that ensures assessment of the safety and decontamination of laboratory instrumentation by manufacturers.
2. Ensure that biosafety training and assessment is required of all CLIA-certified laboratories, including personnel responsible for the preanalytical, analytical, and postanalytical phases of testing.
3. Ensure oversight, input, and resources into studies evaluating the safety of all laboratory practices, instrument testing, etc., so that studies are sound, robust, evidence-based, and applicable.
4. Develop a process for investigating and reporting laboratory acquired infections.

Dr. Wilcke and Dr. Mac Kenzie announced the Fall 2015 CLIAC meeting dates as November 18-19, 2015, and adjourned the Committee meeting.

I certify this summary report of the *April 15-16, 2015,* meeting of the Clinical Laboratory Improvement Advisory Committee is an accurate and correct representation of the meeting.



Dated: 06/18/2015

Burton Wilcke, Jr., Ph.D., CLIAC Chair