

**Clinical
Laboratory
Improvement
Advisory
Committee**

Summary Report

November 2 - 3, 2016

Atlanta, Georgia

U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES

Clinical Laboratory Improvement Advisory Committee November 2 - 3, 2016, Summary Report

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RECORD OF ATTENDANCE

Committee Members Present

Dr. Ramy Arnaout, Chair
Dr. Sheldon Campbell
Dr. Monica de Baca
Dr. Gwendolyn Delaney
Dr. Roger Klein
Dr. Elizabeth Marlowe
Ms. Helen Mills
Dr. Elizabeth Palavecino
Dr. Richard Press
Ms. Anita Roberson
Ms. Maureen Rushenberg
Ms. Susan Sheridan
Dr. John Sinard
Dr. Hardeep Singh
Mr. Andy Quintenz, AdvaMed (Liaison Representative)

Committee Members Absent

None

Ex Officio Members

Ms. Karen Dyer, CMS
Dr. Alberto Gutierrez, FDA
Dr. Reynolds Salerno, CDC

Designated Federal Official

Dr. William (Bill) Mac Kenzie, CDC

Executive Secretary

Ms. Nancy Anderson, CDC

Record of Attendance – cont'd

Centers for Disease Control and Prevention (CDC)

Mr. Noah Aleshire	Mr. Derrick Lake
Dr. J. Rex Astles	Dr. Ira Lubin
Ms. Diane Bosse	Dr. Bereneice Madison
Ms. Paula Braun	Ms. Laura Martin
Dr. Tiffany Brunson	Dr. Alison Mawle
Ms. Jasmine Chaitram	Ms. Graylin Mitchell
Dr. Bin Chen	Dr. Atis Muehlenbachs
Dr. Nancy Cornish	Ms. Victoria Pullman
Dr. Melanie Duckworth	Ms. Victoria Phifer
Ms. Evelyn Dunn	Ms. Marcia Revelez
Dr. Marie Earley	Dr. John Ridderhof
Dr. Lin Fan	Dr. Martha Rider
Ms. Carol Fridlund	Dr. Paramjit Sandhu
Ms. Susan Fuller	Dr. Shahram Shahangian
Ms. Sonnet Gaertner	Ms. Theresia Snelling
Ms. Maribeth Gagnon	Ms. Heather Stang
Mr. Manjula Gama-Ralalage	Dr. Sonya Strider
Ms. Nicole Gregoricus	Mr. Thomas Taylor
Ms. Jacqueline Goolsby	Ms. Monica Toles
Dr. Thomas Hearn	Ms. Elizabeth Weirich
Dr. Alden Henderson	Dr. Laurina Williams
Dr. Harvey Holmes	Dr. Danielle Daniely Wilson
Ms. Stacy Howard	Dr. Yang Xia
Dr. Micheal Iademarco	Mr. Jonathan Zhong
Dr. Lisa Kalman	

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

Ms. Mikal Stoner, DOD
Dr. Peter Tobin, FDA
Ms. Regina Van Brakle, CMS
Mr. David Wright, 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. 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, the electronic submission of laboratory information, and mechanisms to improve the integration of public health and clinical laboratory practices.

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 considerations. 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 and took a roll call of the members present. Dr. Ramy Arnaout, 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.

CLIAC Recommendations Status Update

Addendum 01

Ms. Nancy Anderson, MMSc, MT(ASCP)

Branch Chief

Laboratory Practice Standards Branch (LPSB)

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. Anderson provided the Committee with an update of the recent recommendations made by the Committee. She noted that, per CLIAC's suggestion, the recommendations, including actions taken and current status, are now posted on the CDC CLIAC website (<https://www.cdc.gov/cliac/Meetings/Default.aspx>). Ms. Anderson informed the Committee that information about CLIAC recommendations could also be obtained from the Federal Advisory Committee Act database (<http://www.facadatabase.gov/committee/committee.aspx?t=c&cid=721&aid=76>).

AGENCY UPDATES AND COMMITTEE DISCUSSION

Centers for Disease Control and Prevention (CDC) Update

Addendum 02

Reynolds M. Salerno, PhD

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. Salerno provided an update on the progress of the proficiency testing proposed rule covering the work that has been done, what is currently being done, and the process once the proposed regulation is completed. He reviewed the 5-year cooperative agreement to improve waived testing performance and outcomes through partnerships which was awarded to COLA Resources Inc. (CRI). Dr. Salerno discussed the cooperative

agreement for using medical data warehouses to inform laboratory quality improvement initiatives to improve health outcomes. He said the three awards are primarily focused on addressing two questions: what is the correlation between internal quality assurance and quality control programs and the accuracy and reliability of test results; and what is the extent and nature of the problems in the diagnosis and treatment of patients caused by inaccurate laboratory test results. This funding opportunity also includes provisions for the development and implementation of interventions for laboratory quality improvement initiatives.

Committee Discussion

- A member asked what kind of national benchmarks can be studied through the medical data warehouse cooperative agreements. Dr. Salerno replied the awards were just recently funded therefore CDC has not yet had a chance to delve into that, but will report on the status of these cooperative agreements at the next CLIAC meeting.
- One member asked if there are mechanisms within the medical data warehouses that capture patient-reported outcomes. Dr. Salerno replied he believes those measures are in place.
- Another member asked why the proficiency testing (PT) regulation was being updated. Dr. Salerno responded the current regulated analytes needed to be reassessed for relevancy and other analytes needed to be considered for addition to the regulated analyte list. Ms. Anderson added there will be changes in the microbiology section of the PT regulations, as well.
- One member commented that the current PT regulations are outdated. Many of the analytes are no longer significant in health care while others that are significant are not on the list of regulated analytes. The member asked if consideration had been given to changing the framework of the PT regulations such as placing all analytes on the regulated analyte list. Dr. Salerno replied the focus has primarily been on new analytes, but there may be an opportunity to consider broader regulatory changes. Ms. Dyer responded that the agencies have considered all aspects of PT when developing the proposed rule.

Centers for Medicare & Medicaid Services (CMS) Update

Addendum 03

Karen Dyer MT (ASCP), DLM

Director

Division of Laboratory Services

Survey and Certification Group

Centers for Medicare & Medicaid Services (CMS)

Ms. Dyer began with the CMS personnel changes then provided the Committee with a brief overview of the current CLIA statistics. Touching on CLIA modernization she said CMS continues to have meetings with the Energy and Commerce Committee and is providing technical assistance on the draft legislation before the committee. Regarding the President's Precision Medicine Initiative[®] (PMI), she related CMS is providing technical assistance and has prepared briefing documents regarding a cost model of what it would take for a research laboratory to obtain a CLIA certificate. She said the

Certificate of Waiver project has ended and the new Government Performance Review Act (GPRA) goal will concentrate on surveying provider performed microscopy (PPM) laboratories beginning October 2017. Ms. Dyer discussed the goal of ensuring surveyor consistency and the steps being taken to achieve that goal including virtual basic training, developing a structured surveyor training, and revising the federal monitoring surveys. She commented that CLIA will now allow primary source verification (PSV) as a process to confirm laboratory personnel credentials and educational experience. However, CMS is not issuing standards to be applied to PSV organizations. She said one outcome of this was the reissue of a survey and certification letter pertaining to verification of personnel qualifications, including nursing qualifications. The issuance of this letter generated confusion in the medical technology community, even though the policy was not a new one. Ms. Dyer commented CMS will be revisiting the CLIA personnel qualification requirements with the intent of clarifying the degree requirements for laboratory personnel. She noted that CMS continues to have multi-faceted problems with the drug testing laboratories and is considering solutions. In regards to CLIA and biosafety, she showed CLIAC the list of CLIA regulations that address risk management and biosafety. Finally, Ms. Dyer described the outreach activities being undertaken to educate medical technology students about CLIA.

Committee Discussion

- A member asked whether research testing in the context of clinical trials, for example where a patient is treated based on a test result provided by a non-CLIA certified laboratory, was still an issue. Ms. Dyer responded it has been discussed and the current issue being addressed is the need for a CLIA certificate when reporting any patient specific results.
- One member commented there is a considerable amount of interest in the patient community to help improve the health system and asked if there are mechanisms for patients to report bad outcomes due to poor quality laboratories and poor quality tests. Ms. Dyer responded the FDA has a website for adverse event reporting and for test issues.
- Another member asked if CMS had considered including cytotechnology and histotechnology in the outreach efforts. Ms. Dyer replied CMS hopes to expand educational outreach in the future.
- A member asked whether there are limitations on the testing that can be performed by nurses. Ms. Dyer replied there are not limitations and it comes back to the acceptance of a nursing degree as equivalent to a bachelor's degree in biology. That is why CMS is currently looking at clarifying the CLIA personnel requirements. She added those with a nursing degree must still meet the CLIA requirements for laboratory experience and training prior to performing testing.
- Another member asked why the Certificate of Waiver project was being discontinued since waived test systems are increasing and becoming more complicated. Ms. Dyer replied each GPRA goal has a set time frame at the end of which a new goal must be elected. She noted PPM laboratories have never been studied. Ms. Anderson added PPM laboratories may also perform waived testing and there has never been an opportunity to collect data on this aspect of waived testing. Ms. Dyer added that Certificate of Waiver sites will continue to be inspected if complaints are received.

- One member asked if waived tests have training modules. Ms. Dyer replied there are the CDC booklets and online course available at the CDC CLIA website. CMS will continue to distribute *Ready? Set? Test!* booklets as part of the new GPRAs project.

Food and Drug Administration (FDA) Update

Addendum 04

Alberto Gutierrez, PhD

Director

Office of In-Vitro Diagnostics and Radiological Health (OIR)

Center for Devices and Radiological Health (CDRH)

Food and Drug Administration

Dr. Gutierrez began his presentation with an update of the Payer Communication Task Force noting that Foundation Medicine's Foundation One comprehensive genetic profiling assay has been accepted for the pilot program. He discussed the draft guidance document *Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices* and the FDA's effort to limit the use of pre-market data and supplement it with post-market data to support regulatory decision-making. He related the FDA has finished the Medical Device User Fee Act 4 (MDUFA IV) negotiations noting laboratories took part in the negotiations. He provided a brief update on the PMI mentioning that two draft guidance documents had been issued, pointed out the two safety communications issued in 2016, and mentioned the interoperability workshop to take place on November 8, 2016. To end his talk, Dr. Gutierrez touched on CLIA waivers, Zika emergency use authorizations, the CLIA waiver guidance, and provided some examples of how to obtain a CLIA waiver for a test system.

Committee Discussion

- A member asked for an update regarding laboratory developed tests (LDTs). Dr. Gutierrez replied there have been some legislative initiatives and a hearing in the Senate with the expectation there will be more hearings in the Senate. The FDA is continuing to work on a guidance document for LDTs.
- One member asked if post-market data was being gathered on waived molecular test systems. Dr. Gutierrez explained that the FDA has the ability to require post-market data when a test system has been approved without adequate pre-market data or if there is a particular concern. It could also be required if it was a dual submission. Otherwise, the FDA does not have the authority to require post-market data for waived test systems.
- Another member commented that molecular testing for the diagnosis of infectious diseases has the potential to improve patient care. The member expressed concern that the personnel using the tests may not have the expertise to interpret results and that false positives could be generated in the office setting where vaccines are administered. Dr. Gutierrez agreed and commented that the waiver process requires fairly extensive flex testing. However, environmental contamination is an issue the FDA will be examining more carefully.
- Two members commented that a barrier to utilizing the waived tests, especially molecular tests for microbiology, is the ability to be paid for testing specimens. Other

members noted that it also takes longer to perform these tests which can be a barrier to using them in a physician office laboratory.

CDC OID Board of Scientific Counselors (BSC) Update

Addendum 08

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 began by providing a summary of the September 2016 Advanced Molecular Detection Day. She related the biggest challenge for next-generation sequencing is infrastructure and the need for more interoperable data. She then provided a summary of the September 2016 CDC OID BSC meeting. She summarized the key updates from the National Center for Immunization and Respiratory Diseases and gave an overview of the Zika panel discussion. She presented highlights from the National Center for Emerging and Zoonotic Infectious Diseases, the National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, and related the discussion around Hepatitis C. She delivered a summary of the updates provided by Dr. Frieden on emergency preparedness and emerging infectious diseases and summarized the key updates from the Center for Global Health and the Food Safety Modernization Act Surveillance Working Group. Dr. Marlowe ended her presentation with a summary of Dr. Rima Khabbaz's presentation *OID Planning for the Future*.

Committee Discussion

- A member asked how long surveillance was continued after a disease outbreak. Dr. Marlowe replied she did not know but would imagine surveillance continues as long as there are cases.
- Regarding the spread of the Zika virus, the Chair noted that *Aedes aegypti* and *Aedes albopictus* overlap ranges and asked if there was discussion about the relevancy of this in regard to the spread of the Zika virus endemically in the US. Dr. Marlowe replied that wasn't discussed.
- The Chair inquired about the cost-benefit for PulseNet. Dr. Marlowe responded there was a publication covering that topic. A member commented much of cost-benefit analysis is modeling consisting of what would have happened or could have happened after not intervening. Another member agreed and added that is a pervasive problem in pathology.
- The Chair asked if interacting or communicating directly with the public on the issues presented to the OID BSC had been discussed. Dr. Marlowe replied there was considerable discussion about this, particularly about educating the public and raising awareness of antibiotic resistance and prescriptions.

PRESENTATIONS AND COMMITTEE DISCUSSION

Cytology Workload

Cytology Workload Assessment and Measure

Addendum 05

Ms. MariBeth Gagnon, MS CT(ASCP)HTL

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 introduced the cytology workload study conducted by CDC based on a CLIAC recommendation in February 2012. The study had two parts, a workload assessment to survey workload practices when using three image-assisted screening devices and a time measure study to determine screening time when using these instruments. Ms. Gagnon briefly mentioned the results of the survey and shifted the topic to the time measure study. She explained the purpose and the design of the time measure study that included prescreening, screening, and post screening activities. Ms. Gagnon discussed a list of the activities for each category and definitions of some activities and presented the characteristics of the study participants including the instrument they used and the results of the study. She finished her presentation by introducing the next two presenters.

Cytology Time Measure Study

Addendum 06

Mr. Tom Taylor, Jr., PE, MSDS

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

Mr. Taylor presented the analysis of the time measure study. He defined the screening terminology used in the study and illustrated the percentage of slides that were examined for each category of analysis (field of view only, full manual review only, and field of view and full manual review). He then discussed the distribution of the workload per slide for each of the three instruments for each of the analysis categories. Mr. Taylor presented a bar graph showing the breakdown of different activities used in the examining process by analysis category and instrument. He showed the distribution of data according to percentile of their median time across all slides by the median time spent on each slide for field of view only and field of view plus full manual review. Mr. Taylor reported median screening time was a better measure than mean time, since the data were skewed and had a non-normal distribution. He concluded his presentation by giving the key findings of the study based on the data he presented.

Committee Discussion

- A Committee member asked if the outliers for the field of view plus full manual review data compared to the percent agreement were checked for the actual diagnosis for those slides. The committee member suggested that this would be fairly easy to do because there are strict guidelines for diagnosis categories and may give insight to the amount of skewing seen in the data. Mr. Taylor answered that this analysis was not done and agreed that trying to determine the reason for the skewing of the data would be useful since many confounding variables can contribute to the skew.

Cytology Workload Issues

Addendum 07

Dr. Alberto Gutierrez, PhD

Director

Office of In-Vitro Diagnostics and Radiological Health (OIR)

Center for Devices and Radiological Health (CDRH)

Food and Drug Administration

Dr. Gutierrez began the presentation by explaining why the FDA was interested in cytology workload and a brief history of how workload assessments were done by the manufacturers and used by FDA to approve image-assisted devices. He also discussed the development of a CLIA/FDA formula to calculate workload when using these devices for Pap smear screening. Referring to the CDC workload study, Dr. Gutierrez presented the analysis of the 25th, 50th, and 75th percentile times (in minutes) it took for field of view, full manual review, and field of view and full manual review inspections for each of three instruments. He explained how, in most cases, the data corresponded well with the data used to develop the CLIA/FDA formula. However, using the CLIA/FDA formula with the TIS+ instrument, based on the study data the cytotechnologist would have to review more slides than FDA thinks should be screened. Dr. Gutierrez suggested one solution would be to create a new equation to decrease the workload limit for the TIS+ instrument. However, that would make it more complex and would not likely be feasible for cytotechnologists. A simpler mechanism would be to use the same formula but decrease the 100 slide limit to 80 slides for the TIS+. Dr. Gutierrez did not present the last three slides in his presentation, but briefly summarized the information they covered.

Committee Discussion

- A Committee member asked if the study was representative of all sizes and types of laboratories in the country. Ms. Gagnon replied that the study relied on voluntary participation, which may have encouraged better-performing laboratories to participate. The cytotechnologists that volunteered to participate screened an average of 76 slides per day and spent about half of their day on activities other than screening. Very few study participants screened >100 slides per day and only one cytotechnologist screened over 125 slides per day.
- Committee members asked for clarification about the specific objectives of the study and how the data would be used (e.g. development of new policies or guidelines). One member noted the study had focused on time and efficiency and asked whether assessing patient safety and diagnostic accuracy had been included. Ms. Gagnon

clarified that the time measure study was meant to determine how long it takes to perform field of view and full manual review screening using the image-assisted devices and to compare those times with that calculated using the FDA algorithm for workload on the instruments. During the study, an observer reviewed the slides to confirm that all slides needing a full manual review were triaged correctly. The study was about proper triaging and the number of slides screened rather than an assessment of diagnostic accuracy. Determining diagnostic accuracy requires additional steps that were not part of this study. Other quality determinations that a laboratory uses to determine the individual workload limit, such as competency evaluations and comparison of the cytotechnologist abnormal rate to the laboratory abnormal rate, were also looked at. The number of slides screened each hour was also reviewed to determine if the cytotechnologist became rushed and pushed through more slides at the end of the day to make a quota. Workload records were examined for the three prior months to determine if the participating cytotechnologists screened at their usual rate during the study.

- One Committee member asked if the proposal to change the formula for the TIS+ instrument would make workload assessments more complicated for those that use more than one instrument. Dr. Gutierrez agreed that it would be more complicated in that situation.
- Another Committee member asked if there would be a way to build in a weighting factor for the CLIA/FDA formula to take into account extra time for slides that are more difficult to screen. Dr. Gutierrez responded that a weakness of the current study was that assessing the difficulty of the slide was not part of the evaluation. Therefore, that type of difference between the instruments could not be analyzed since the slides screened with each device were different.
- A member expressed concern that the study evaluated workload without considering accuracy and noted that the two may be related. The member also said it would be good, if possible, to set workloads based on the diagnoses being made, but acknowledged that would be challenging.
- A Committee member suggested that a study be conducted to determine if the time differences are due to differences in set-up time for the instrument or actual review time. Dr. Gutierrez responded that the FDA would consider that.
- A member suggested that competency was likely embedded in the data and a second member said it would be interesting to consider the years of experience for the participants. The member reminded the Committee that cytotechnologists' individual workloads are to be evaluated every six months and set by the laboratory director.
- A Committee member asked if the PT records of participants were reviewed. Ms. Gagnon replied PT scores were not considered in the design of the protocol. She stated one might assume if the cytotechnologist had failed PT, the laboratory would not have given them permission to volunteer.

Update on Clinical Laboratory Biosafety

Update on CLIAC's Biosafety Recommendations

Addendum 09

Reynolds M. Salerno, PhD

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. Salerno began his presentation with a review of the April 2016 CLIAC recommendations on biosafety. He related that a number of questions derived from the April 2016 CLIAC discussion are being explored by DLS with the goal of developing guidance documents and training materials to address the questions. To that end, DLS has assembled a taskforce made up of individuals from a broad array of disciplines and occupations. He related DLS has engaged in a few specific biosafety activities since the April 2016 meeting:

- Delivered a lecture at the 2016 ASM Microbe Conference which focused on the lessons learned from the Ebola crisis. The lecture emphasized that the clinical laboratory community needs much better biosafety information and tools, especially on risk assessment.
- Developed an outline for a paper designed to create a proposal for a substantive clinical laboratory biosafety work plan that would include steps to address:
 - risk assessment;
 - development of safety management systems, methodologies, and templates;
 - biosafety competencies and training in the clinical laboratory environment;
 - safety accreditation in the clinical laboratory;
 - details about assessing the hazards of instrumentation in clinical laboratories; and
 - laboratory-acquired infections.
- Created a public health ethics case study around biosafety and clinical laboratory medicine which was presented to the CDC Public Health Ethics Committee meeting in September 2016 and will be used to develop an educational tool.
- Helped the broader biosafety community consider the realities of the modern clinical laboratory by promoting the inclusion of the clinical laboratory perspective in the sixth edition of *Biosafety in Microbiological and Biomedical Laboratories*.
- Furthered development of a web-based laboratory-associated incident reporting system.
- Generated 12 new biosafety courses for CDC employees which are in the process of being cleared for public use. In addition, DLS is in the process of developing seven more biosafety courses.

Committee Discussion

- Two members asked if the infrastructure for reporting laboratory incidents assured anonymity for the person reporting. Dr. Salerno replied the original intent was for anonymity, however information technology security experts are not certain

anonymity can be guaranteed especially since this would be a national reporting system on a government website. The other issue is the difference between tracking and investigating an individual event versus identifying trends. The intent of this reporting system, he said, would be to identify trends.

- Another member suggested CDC use the Aviation Safety Reporting System as a model. The member asked if consideration was being given to including other types of laboratory safety incidents that occur. Dr. Salerno replied that is being considered.
- One member asked whether the biosafety group considered CDC's original recommendation made during the Ebola crisis that institutions should have a separate laboratory to perform testing for agents such as Ebola. Dr. Salerno responded the publication being developed includes a section on the history of biosafety in the clinical laboratory setting which discusses the role that the federal government has played in helping to confuse the situation. The emphasis of the publication is that it is time to create clear standards and guidance documents.
- A member noted that the National Association of Regional Councils funded a study on the ideal elements of a consumer reporting system. The study included recommendations by patients and experts and may be a helpful resource in developing the current system.
- One member commented that the College of American Pathologists (CAP) has guidelines that address the steps to be taken if a test is misread and concurred that a national database for reporting laboratory errors and other issues would be useful. Another member added that a national database would allow laboratories to learn from each other.
- One member suggested the best way to implement the biosafety changes would be to include them on accreditation checklists. Another member concurred and suggested that checklists be created to assist laboratories in creating their reports and include an option to send the information to the national database.
- A member commented that two separate tools, one focused on biosafety reporting and one focused on patient safety issues related to the laboratory, would be more effective than a broad-based safety reporting tool.
- Another member commented it is also important to address how data is collected in order to obtain relevant information.
- A member asked whether the safety courses being developed by CDC are also geared to be useful to the clinical laboratory community as training tools. The member suggested that if this is not the case a subset of the courses be developed that could be used by the clinical laboratory community. Dr. Salerno replied some of the basic courses could be valuable to any laboratory but some are geared towards the CDC or academic research laboratories. They are also specific to the biosafety issues being faced by CDC, therefore not representative of the broad clinical laboratory community. However, the development of these courses will allow CDC to identify the gaps and develop courses that are specific to the clinical laboratory setting.
- The Chair asked if there was discussion about the perception of whistleblowers and the fear of retribution with the use of reporting systems and how that concern could be allayed. Dr. Salerno responded there has been a lot of discussion on that point that is why the team is adamant on the point of anonymity. It is a point that is preventing rapid progress on this project.

After considering the comments made during the biosafety discussion, the Committee made the following recommendation:

- ❖ CLIAC proposes that the voluntary Laboratory Associated Incident Reporting System (proposed by the CDC Blue Ribbon Panel recommendation in 2012) protect the privacy and confidentiality of reporting individual(s) and larger entities, e.g. via anonymity. The system should borrow from the principles of existing event-reporting systems and focus on incidents, near-misses, and mitigation measures that affect the safety of laboratory professionals. Finally, it should foster a non-punitive culture for reporting.

Clinical and Public Health Laboratory Preparedness and Response *Addendum 10*

Victor Waddell, PhD

Bureau Chief, Arizona State Public Health Laboratory
Executive Director, Arizona Biomedical Research Commission
Arizona Department of Health Services

Dr. Waddell presented an overview of the relationship between public health laboratories and clinical laboratories during novel and emerging threats. He outlined the role of the public health laboratory (PHL), described the laboratory response network (LRN), and showed how the laboratories in the LRN are distributed across the U.S. He enumerated the past responses coordinated via the LRN, reviewed the current Zika virus response, and discussed the PHLs' implementation challenges. Dr. Waddell provided an overview of the Arizona PHL's surge testing planning noting that while the LRN has an extensive surge capacity Arizona's PHL only has three levels of surge capacity. He emphasized that it is necessary for a PHL to be able to work with other laboratories within their state and with other states noting that during the Zika virus response the Arizona PHL was working with two of the state's larger commercial laboratories. Dr. Waddell ended his talk with ideas to be considered when discussing improving preparedness and response to public health threats.

Committee Discussion

- A member commented that dealing with surge capacity is problematic and asked how the Arizona PHL handled it. Dr. Waddell replied thus far there has been no local transmission of Zika virus but for past outbreaks the Arizona PHL has moved to a seven day a week operation while using existing staffing, cross-training staff, and shifting staff around.
- One member noted that Dr. Waddell had asked if the commercial laboratories should be involved sooner. The member commented that sometimes there is less paperwork and it is faster to send samples to a commercial laboratory. However, the cost is high and patients often end up paying for the tests. The member asked if tests that represent a national safety issue could be covered by insurance. Dr. Waddell responded he had observed the same issues. PHL testing is free since it is funded at

the federal level but money is needed to fund testing at a commercial level. The member noted patients may opt out of testing if it is not free which could result in unknown pockets of infection. There is also the potential of over testing due to public fear, therefore, ways to screen individuals need to be examined. Dr. Waddell replied that pre-screening could be challenging.

- Another member commented it might be useful to include the public in the conversation about reimbursement.
- One member asked about distribution of the funds provided by Congress for Zika. The Chair responded the money was broadly distributed with some going to CDC, much of which will be passed to the states.
- A member commented the issue is broader than the immediate Zika virus event. It involves planning ahead for public health security.
- Another member suggested that PHLs could form alliances with the PHLs in other regions of the country as a solution to dealing with surge. Dr. Waddell responded Arizona has that type of agreement with the neighboring states' PHLs.
- A member commented that one critical issue is the correct and consistent transmission of information. The member agreed that partnerships must be formed before a crisis occurs and added they should include the large university laboratories, commercial laboratories, and patients. Another member asked if Dr. Waddell had collaborated with national groups and he responded this had been done at the local level.
- One member asked if the biosafety issues around Zika virus testing had been addressed by Arizona. Dr. Waddell answered no, other than the normal biosafety work.
- The Chair asked whether Dr. Waddell had a figure for the return on investment of preparedness. Dr. Waddell responded there have been studies and work is being done on this with the Association of Public Health Laboratories to build models that can be used to demonstrate the fiscal value of preparedness.
- The Chair noted that when the initial cases of Zika were reported in Florida, the governor had promised everyone would be able to be tested for the virus, which caused delays in testing. He asked how communication between the public health laboratory and government representatives is handled in Arizona. Dr. Waddell again noted they have not seen local transmission of Zika in Arizona. However, a Zika conference was held that included the governor's office. The governor's office is aware of what the issues would be if testing was offered for everyone and there is interest in a second, follow-up conference.
- A member asked whether people who are Zika positive are being tracked and studied. Dr. Waddell replied the Arizona public health laboratory would willingly forward samples to CDC for additional study. However, the Arizona public health laboratory does not have the capacity to conduct a study.
- Committee members broached the topic of the cost of developing a test. It was agreed that the cost could vary widely depending on many factors such as availability of samples, the level of validation needed, and the type of test being developed. The Committee also noted that taking preparedness to the level of developing a test for every known agent is neither cost effective nor practical.

Institute of Medicine (IOM) Workgroup

Introduction

Dr. William Mac Kenzie

Deputy Director

Center for Surveillance, Epidemiology, and Laboratory Services (CSELS)

Office of Public Health Scientific Services (OPHSS)

Centers for Disease Control and Prevention

Dr. Mac Kenzie provided a brief overview of why the Institute of Medicine (IOM) Report Workgroup was formed. He related because of the desire to make recommendations that are effective, focused, and useful to the Department, the Committee, after exploring various options, decided to form a workgroup. The purpose was to discuss the major issues identified in the report, frame the discussion, and propose language for potential recommendations for CLIAC to consider. Dr. Mac Kenzie said this Workgroup chose to explore four topics from the IOM report.

CLIAC IOM Workgroup Charge

Addendum 11

Monica E. de Baca, MD, FCAP, FASCP

Medical Laboratory Associates

Dr. De Baca provided an overview of the IOM Workgroup's progress. The Workgroup charge was to review key laboratory related IOM recommendations and provide background to the Committee to assist in potentially forming recommendations. She related the Workgroup chose four topics to consider in depth:

1. Guidelines for Safe Communication of Sub-critical (non-life threatening) Abnormal Laboratory Results
2. The Role of Autopsies in the Healthcare Quality Process
3. Pathologists as Integral Care Team Members
4. Interoperability and Standards as part of the Healthcare Quality Process

Dr. De Baca said the Workgroup's deliberations on the first two topics would be presented to the Committee at this meeting.

IOM Workgroup Update: Autopsies as a Quality Assurance Tool

Addendum 12

Roger D. Klein, MD JD

Attending Pathologist

Department of Molecular Pathology

Cleveland Clinic Foundation

Dr. Klein began his presentation with a brief history of autopsies. He noted, in 1960, about 50% of hospital deaths underwent autopsy while today less than 10% result in autopsy. He remarked, in the past, autopsies were used to discover and understand disease, now they are used as a quality assurance tool. As a quality tool the chief emphasis is the difference between antemortem and postmortem diagnosis. Dr. Klein

discussed Goldman's classification criteria and the frequency of misdiagnosis. He said there are no objective data that support the use of autopsies as a quality assurance procedure to improve patient care and there are no studies that determine the error rates in autopsy diagnoses. Therefore, any theoretically positive effects of autopsies on the quality of care are unproven. He reviewed some of the reasons autopsies have declined in the past 50 years and indicated two important reasons were limited reimbursement and the elimination of the accreditation requirement for performing autopsies in a minimum percentage of hospital deaths. Dr. Klein reviewed the IOM report's conclusions on autopsies and the IOM recommendation. He described the Workgroup's vision of a potential study as well as its potential outcomes and discussed CLIAC's April 2016 proposed recommendation. Finally, Dr. Klein reviewed the Workgroup's proposed recommendation noting its similarity to the April 2016 proposed recommendation and reviewed the issues for Committee discussion.

Committee Discussion

- A member commented the goal of understanding the value of autopsies, reducing diagnostic error, and improving patient health outcomes is admirable but very difficult to accomplish. The member noted there a number of factors that complicate conducting a study, such as the current low rate of autopsies performed. The rate could theoretically be increased if families were encouraged to have an autopsy performed, if physician education was increased, and if reimbursement rates were increased. The member said there is currently disincentive within the system for institutions to engage in autopsies.
- A member asked for further clarification about the proposed study. Dr. Klein replied IOM recommended that a small number of institutions perform all autopsies and also mentioned performing studies. He asked for ideas on how to design studies to demonstrate improvement in patient outcomes due to autopsies. The member replied autopsies should be a learning tool. Dr. Klein responded that he agreed with treating physicians that an autopsy is not a useful tool. If an autopsy is used for learning, then we need to measure whether something is being learned and if what is being learned benefits patients. He said there is value in performing autopsies from an epidemiological standpoint and from a public health standpoint in terms of improving the accuracy of the cause of death on the death certificate.
- One member commented learning and the accuracy of death certificates could be measured. The member added there may be surrogate markers that could be used for outcome studies.
- Dr. Mac Kenzie commented that understanding the cause of death is essential since it can help to inform funded programs.
- The Chair noted the main question seemed to be whether it is possible to study if autopsies improve outcomes. It would seem the use of HHS funds could be useful for learning and improving autopsies and for standardization in how death certificates are filled out. The studies could give insight into care. However, unless an autopsy is performed on all deceased, there will not be broad scale improvement.
- Another member commented autopsies are important for diagnosis. However, clear guidelines must be provided if a study is to be pursued in order to get the expected result. The member agreed autopsies are important epidemiologically.

- A member commented this issue highlights many of the problems that are currently inherent in the American medical system. One is the need to create a non-punitive culture and another is tort reform.
- One member commented on the accuracy of death certificates and said it is frightening that health care funding decisions are based on the information derived from them. On many death certificates the cause of death is too broad, a more detailed statement would further the goal of improving patient outcomes. The member noted the concept of having clear guidelines of when an autopsy should be performed has been discussed for years and that some of the most informative autopsies have been when the clinical team thought they knew why the patient had died. The member added to increase the value of a study the clinical teams need to be involved. Regional autopsy centers would improve the autopsy but there would be logistical problems. Dr. Klein responded the IOM was not proposing regional centers, they were proposing to fund centers to perform autopsies on a representative proportion of their deaths.

The Committee concluded the discussion on autopsy as a quality assurance tool and made the following recommendation:

- ❖ The CLIAC supports the IOM recommendation that Department of Health and Human Services (HHS) provide funding for a designated subset of health care systems to conduct routine postmortem examinations on appropriately defined categories of patient deaths (for example, those listed in the College of American Pathologists Guidelines for Non-Forensic Autopsies). These funds should be directly linked to proposals for data acquisition, including standardization of autopsy procedure and reporting (including death-certificates), with the expressed goal of understanding the value of autopsies for improving individual and health system outcomes.

IOM Workgroup Update: Communication of Test Results

Addendum 13

Hardeep Singh, MD, MPH

Chief, Health Policy, Quality and Informatics Program
Houston VA HSR&D Center Excellence

Dr. Singh discussed the Workgroup topic ‘Communication of Test Results.’ He related the Workgroup developed two proposed recommendations for the Committee to consider. The first proposed recommendation addressed communication and follow-up of ‘actionable’ laboratory test results to providers and patients. He noted there are many definitions of ‘actionable’ among which are abnormal, critical, life-threatening, and sub-critical. He related that 7% to 62% of abnormal laboratory results are lost to follow-up. Current information technology has made the job of communication easier yet there are still problems in follow-up of results. One is shared responsibility between the different people involved in generating and receiving a test result (e.g., laboratories, providers, institutions) and the lack of a policy indicating who is responsible for follow-up. He said

what is needed is a highly reliable system that can communicate test results to providers and patients. However, currently we have a system that leaves patients vulnerable to lack of follow-up.

He said the Workgroup visualized a two-step approach. The first step would be the development of a national policy or standard on results' communication. He reviewed the Workgroup's first proposal and noted an example of guidance for the framework is the Veterans Health Administration (VHA) policy on communicating test results. The second step would be institutional self-assessment, that is, how an institution will assess how well they're doing in their test results notifications to patients. He reviewed the Workgroup's second proposal noting the Workgroup believes both proposals are necessary, that national as well as local guidance is needed. He noted the ONC SAFER Guide *Test Results Reporting & Follow-up* could be used as a guidance tool for developing the local guidance document.

Committee Discussion

- At the Chair's request, Dr. Singh provided an overview of the VHA policy on communicating test results.
- A member asked if the VHA document covered how to document attempts to reach the patient, whether abnormal results are handled differently from abnormal results, and other high-risk situations. Dr. Singh responded the VHA document addresses those situations. He noted the VHA document is a high-level policy document associated with the ONC SAFER implementation guidance.
- Another member remarked the crucial part of the two proposals is the risk assessment. The member noted the risk assessment has to be individualized.
- One member commented the term 'life-threatening' needed to be defined.
- A member noted there are already measures in place for reporting critical results.

The Committee discussed the Workgroup's proposed recommendation and made the following recommendation:

❖ Recommendation 1a

CMS should convene a multidisciplinary group* to

- Generate a report describing a process for health care institutions to improve safe communication and follow-up of diagnostic test results to providers and/or patients with clear guidelines on timelines for communicating those results.
- Provide an implementation and evaluation plan for the process.
- Examples of guidance for the report include 2015 VHA policy on communicating test results.
- A similar project was the CDC's *Core Elements of Hospital Antibiotic Stewardship Programs*.

*may include, but is not limited to, representatives from CMS, FDA, CDC, diagnostic industry representatives, relevant approved accrediting organizations, informaticians, human factors engineers, laboratory directors/professionals, clinician end-users, patient/consumer representatives, health IT developers/vendors, and other relevant professional organizations.

Recommendation 1b

CMS should recommend health care institutions create an interdisciplinary team comprised of clinical and diagnostic health care professionals, health IT, and other safety/human factors experts. This team should conduct periodic institutional self-assessments to address areas of risk and improvement related to safe communication and follow-up of diagnostic results.

Examples of guidance include *Test Results Reporting & Follow-up* ONC SAFER Guide. Additional guidance could be obtained from the report in Recommendation 1a

Future CLIAC Topic Suggestions from the Committee

- Big data
- Ensuring patient safety in the era of emerging technology
- Artificial intelligence affecting future care
- How do we modernize CLIA 88 to fit into the age of modern technology
- Next-Gen sequencing: competency and PT testing
- The role of laboratory testing in the era of telemedicine
- Initiation of the CLIA certification process (who initiates?)
- Concerns from CMS and accreditation organizations about repetitive failures (e.g. top 10 deficiencies, and what are they doing to address those issues)
- What are important issues to HHS and the three CLIA agencies and how can CLIAC address those concerns
- Addressing vulnerabilities in existing CLIA regulatory framework (structure or implementation) in view of
 - Emerging patient safety risk,
 - Emerging payment models,
 - Emerging technologies,
 - Emerging health care delivery systems
- Addressing patient-centeredness in laboratory studies
- Laboratory Medicine Best Practices updates and latest recommendations
- Continued follow-up of CLIAC recommendations
- IQCP follow-up: has the goal of improving patient care been met?

ACRONYMS

[Addendum 14](#)

BACKGROUND INFORMATION

[Addendum 15](#)

NOMINATION INFORMATION

[Addendum 16](#)

PUBLIC COMMENTS

[Addendum 17](#)

[Addendum 18](#)

[Addendum 19](#)

ADJOURN

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

❖ **Recommendation on Safety:**

CLIAC proposes that the voluntary Laboratory Associated Incident Reporting System (proposed by the CDC Blue Ribbon Panel recommendation in 2012) protect the privacy and confidentiality of reporting individual(s) and larger entities, e.g. via anonymity. The system should borrow from the principles of existing event-reporting systems and focus on incidents, near-misses, and mitigation measures that affect the safety of laboratory professionals. Finally, it should foster a non-punitive culture for reporting.

❖ **Recommendation on Autopsy:**

The CLIAC supports the IOM recommendation that Department of Health and Human Services (HHS) provide funding for a designated subset of health care systems to conduct routine postmortem examinations on appropriately defined categories of patient deaths (for example, those listed in the College of American Pathologists Guidelines for Non-Forensic Autopsies). These funds should be directly linked to proposals for data acquisition, including standardization of autopsy procedure and reporting (including death-certificates), with the express goal of understanding the value of autopsies for improving individual and health system outcomes.

❖ **Recommendation on Communication of Test Results:**

Recommendation 1a

CMS should convene a multidisciplinary group* to

- Generate a report describing a process for health care institutions to improve safe communication and follow-up of diagnostic test results to providers and/or patients with clear guidelines on timelines for communicating those results.
- Provide an implementation and evaluation plan for the process.

- Examples of guidance for the report include 2015 VHA policy on communicating test results, http://www.va.gov/vhapublications/ViewPublication.asp?pub_ID=3148.
- A similar project was the CDC's *Core Elements of Hospital Antibiotic Stewardship Programs*, <http://www.cdc.gov/getsmart/healthcare/implementation/core-elements.html>.

*may include, but is not limited to, representatives from CMS, FDA, CDC, diagnostic industry representatives, relevant approved accrediting organizations, informaticians, human factors engineers, laboratory directors/professionals, clinician end-users, patient/consumer representatives, health IT developers/vendors, and other relevant professional organizations.

Recommendation 1b

CMS should recommend health care institutions create an interdisciplinary team comprised of clinical and diagnostic health care professionals, health IT, and other safety/human factors experts. This team should conduct periodic institutional self-assessments to address areas of risk and improvement related to safe communication and follow-up of diagnostic results.

Examples of guidance include *Test Results Reporting & Follow-up* ONC SAFER Guide, <https://www.healthit.gov/safer/guide/sg008>.

Additional guidance could be obtained from the report in Recommendation 1a

Dr. Ramy Arnaout announced the spring 2017 CLIAC meeting dates as April 12-13, 2017, and adjourned the Committee meeting.

I certify this summary report of the November 2-3, 2016 CLIAC meeting is an accurate and correct representation of the meeting.

Dr. Ramy Arnaout, CLIAC Chair

Dated: January 19, 2017