

# Clinical Laboratory Improvement Advisory Committee



## **Summary Report**

**November 7 - 8, 2018**

**Atlanta, Georgia**

U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES

# **Clinical Laboratory Improvement Advisory Committee November 7 - 8, 2018, Summary Report**

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## **RECORD OF ATTENDANCE**

### **Committee Members Present**

Dr. Ramy Arnaout, Chair  
Dr. Sheldon Campbell  
Dr. Marc Couturier  
Dr. Keith Davis  
Dr. Susan Gross  
Dr. Lee Hilborne  
Dr. Bradley Karon  
Dr. Jordan Laser  
Dr. Sharon Massingale  
Dr. Lavinia Middleton  
Ms. Helen Mills  
Dr. Valerie Ng  
Dr. Katherine Perez  
Ms. Bonnie Rubin  
Dr. Gregory Sossaman  
Ms. Cynthia Wilkerson  
Dr. Thomas Williams  
Dr. Donna Wolk  
Mr. Andy Quintenz, AdvaMed (Liaison Representative)

### **Committee Members Absent**

Dr. Steven Hinrichs

### **Ex Officio Members**

Ms. Karen Dyer, CMS  
Dr. Collette Fitzgerald, CDC  
Dr. Peter Tobin, FDA

### **Designated Federal Official**

Dr. Reynolds Salerno, CDC

### **Executive Secretary**

Ms. Nancy Anderson, CDC

*Record of Attendance – cont'd*

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

Dr. J. Rex Astles	Dr. William Mac Kenzie
Ms. Diane Bosse	Dr. Bereneice Madison
Ms. Monica Brady	Ms. Leslie McDonald
Dr. Allison Brown	Ms. Anja Minnick
Ms. Juley Cetoute	Ms. Graylin Mitchell
Ms. Jasmine Chaitram	Dr. Atis Muehlenbachs
Dr. Bin Chen	Ms. Desiree Mustaquim
Dr. Nancy Cornish	Mr. James Nowicki
Ms. Jennifer Driggers	Dr. Jean Patel
Dr. Marie Earley	Dr. Cau D Pham
Ms. Sonnet Gaertner	Ms. Ami Putman
Ms. MariBeth Gagnon	Mr. Manjula Gama-Ralalage
Ms. Leona Grant	Ms. Meredith Reagan
Ms. Natasha Griffith	Mr. Matthew Rubinstein
Dr. Sukwan Handali	Ms. Slavica Mijatovic-Rustempasic
Ms. Brittnee Hawkins	Dr. Adeeba Saboor
Mr. Peter Hicks	Dr. Paramjit Sandhu
Ms. Stacy Howard	Dr. Shahram Shahangian
Ms. Jodi Jackson	Ms. Theresia Snelling
Dr. Kahaliah Joseph	Ms. Heather Stang
Ms. Brenda Johnson	Ms. Hong Tao
Dr. Alana Vivolo-Kantor	Mr. Riley Wells
Dr. Lisa Kalman	Ms. Kellie White
Dr. Cecilia Kato	Dr. Laurina Williams
Mr. Jonathan Lipscomb	Dr. Yang Xia
Dr. Ira Lubin	

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

Ms. Sarah Bennett, CMS	Dr. Timothy Stenzel, FDA
Ms. Cindy Flacks, CMS	Ms. Felicidad Valcarcel, CMS
Ms. Penny Keller, CMS	Ms. Regina Van Brakle, CMS
Ms. Tennille Rogers, CMS	Dr. Chelsea Virgile, FDA

In accordance with the provisions of Public Law 92-463, the meeting was open to the public. Approximately 100 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 ensure 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, 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.

Because of 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 because of other overriding concerns. Thus, while some of the actions recommended by CLIAC may eventually result in changes to the regulations, not all of the Committee's recommendations will be automatically accepted and acted upon by the Secretary.

## **CALL TO ORDER AND COMMITTEE INTRODUCTIONS**

Dr. Reynolds Salerno, Designated Federal Official (DFO), Clinical Laboratory Improvement Advisory Committee (CLIAC), and Director of the Division of Laboratory Systems (DLS), Center for Surveillance, Epidemiology, and Laboratory Services (CSELS), CDC, welcomed the Committee and the members of the public. He acknowledged the importance of public participation in the advisory process and took a roll call of the members present. Dr. Ramy Arnaout, CLIAC Chair, 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. Salerno acknowledged the death of Dr. Toby Merlin. Dr. Merlin served as a CLIAC member from 1998 to 1999 and then as CLIAC Chair from 1999 to 2003, when he left his position as CLIAC Chair and began his CDC career as the Associate Director for Laboratory Medicine in the Division of Laboratory Systems. Dr. Salerno spoke of Dr. Merlin's work with CLIAC and with CDC, and expressed CLIAC's gratitude for his contributions.

Dr. Arnaout reminded the Committee that CLIAC seeks suggestions for candidates to the Committee at any time. Suggestions for consideration can be provided by emailing [CLIAC@cdc.gov](mailto:CLIAC@cdc.gov). Each slate of nominees is carefully selected in an effort to ensure that the Committee meets the required balance of stakeholders with respect to laboratory medicine, pathology, public health, clinical practice, and consumers. The HHS policy stipulates that Committee membership be balanced in terms of professional training and background, points of view represented, and the Committee's function. Appointments shall be made without discrimination on the basis of age, race, ethnicity, gender, sexual orientation, gender identity, HIV status, disability, and cultural, religious, or socioeconomic status. Nominees must be U.S. citizens, and cannot be full-time employees of the U.S. Government.

Dr. Salerno stated that the agenda topics would include updates from the CDC, CMS, the FDA, and the CLIAC liaison to the CDC Office of Infectious Diseases (OID) Board of Scientific Counselors (BSC). In addition, there would be presentations and discussions on the role of the laboratory in improving diagnoses, CLIA personnel requirements, the role of the laboratory in the opioid crisis, and an antibiotic resistance activities update.

## **AGENCY UPDATES AND COMMITTEE DISCUSSION**

### **Centers for Disease Control and Prevention (CDC) Update**

*Addendum 01*

#### **Collette Fitzgerald, PhD**

Associate Director for Science

Division of Laboratory Systems (DLS)

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

Centers for Disease Control and Prevention (CDC)

Dr. Fitzgerald updated CLIAC on DLS's work in four priority goal areas: quality laboratory science, highly competent laboratory workforce, safe and prepared laboratories, and accessible and usable laboratory data. She highlighted the distribution of the "Ready? Set? Test!" educational products and the online training course outcome evaluation. She discussed the charge and tasks for the Next Generation Sequencing and the Nontraditional Workflow Model workgroups recommended at the April 2018 CLIAC meeting and the timelines for each workgroup. Dr. Fitzgerald informed the members of the development of a new CLSI guidance document for decontamination of laboratory equipment. She covered the progress on CLIAC's recommendation #1 related to interoperability from the April 2018 meeting, and closed by discussing DLS laboratory training courses now available.

### **Centers for Medicare & Medicaid Services (CMS) Update**

*Addendum 02*

#### **Karen Dyer MT (ASCP), DLM**

Director

Division of Clinical Laboratory Improvement and Quality (DCLIQ)

Quality, Safety and Oversight Group (QSOG)

Centers for Medicare & Medicaid Services (CMS)

Ms. Dyer began by noting QSOG personnel leadership changes. She continued with the current laboratory enrollment, including the number of accredited laboratories, and the top 10 standard and condition level deficiencies. Ms. Dyer discussed how CMS is addressing these deficiencies, and she described the federal monitoring surveys and principles of documentation used to provide oversight of state agencies and guidance for surveyors. She summarized the most frequent inquiries received by the laboratory excellence mailbox. She finished by describing activities underway related to the CMS CLIA outreach program.

## **Food and Drug Administration (FDA) Update**

*Addendum 03*

### **Peter Tobin, PhD**

Division of Program Operations and Management  
Office of In Vitro Diagnostics and Radiological Health (OIR)  
Center for Devices and Radiological Health (CDRH)  
U. S. Food and Drug Administration (FDA)

Dr. Tobin began his presentation by describing the CDRH reorganization and OIR staffing changes. He updated the Committee on several final guidances aimed to increase consistency and transparency in how the FDA makes benefit-risk decisions for device submissions. He also covered guidances related to the appropriate use of voluntary consensus standards, FDA recognition of LOINC codes, next generation sequencing, and genetic variant databases. Dr. Tobin provided an update on the Breakthrough Device Program and described an innovation challenge for opioid prevention and treatment devices. He concluded by discussing the increase in the number of Dual 510(k) and CLIA Waiver applications.

## **Committee Discussion – Agency Updates**

- The agencies commented on the evaluation metrics for the activities discussed during their updates.
- The Chair suggested the agencies consider developing a dashboard or some type of graphic to monitor the success of key activities and laboratory metrics.
- The agencies mentioned their outreach activities for educational products, including social media, websites, and promotion through professional partners.
- Committee members supported outreach through professional organizations and electronic platforms.
- FDA commented that the dual submission process has decreased review times.

## **CDC Office of Infectious Diseases (OID) Board of Scientific Counselors (BSC) Update**

*Addendum 04*

### **Sheldon Campbell, MD, PhD**

CLIAC Liaison to CDC Office of Infectious Diseases (OID) Board of Scientific Counselors (BSC)  
Clinical Pathologist  
Pathology and Laboratory Medicine Service  
VA Connecticut Healthcare System

Dr. Campbell presented updates relevant to CLIAC from the May 2018 BSC meeting. The OID structure and budget information for fiscal year 2018 and proposed budget for fiscal year 2019 was reviewed. The BSC discussed CDC's high containment (BSL-4) laboratory initiative, including results from a study done in 2014, the cost of a new BSL-4 laboratory, and use for the current laboratory when it is retired. Dr. Campbell continued with information regarding the flu season and shortages of antiviral drugs and diagnostic test kits. He summarized information about global HIV and tuberculosis efforts, the



development of a detection assay for malaria, and CDC training for new public health workers. He next discussed the Infectious disease Laboratory Working Group report and a presentation from CDC Director, Dr. Robert Redfield. He concluded with information from the National Center for Emerging and Zoonotic Infectious Diseases and CDC's antimicrobial resistance activities.

### **Committee Discussion**

- Dr. Campbell responded to questions about the BSC's discussion of immunizations rates and HIV point-of-care testing.

## **PRESENTATIONS AND COMMITTEE DISCUSSION**

### **The Role of the Laboratory in Improving Diagnoses**

#### **Introduction to Topic**

*Addendum 05*

**Reynolds M. Salerno, PhD**

Director

Division of Laboratory Systems (DLS)

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

Centers for Disease Control and Prevention (CDC)

Dr. Salerno provided statistics pertaining to diagnostic errors and their contribution to patient deaths. He stated that because laboratory test results often inform medical treatments, the laboratory clearly has a role in improving diagnoses. He concluded with three questions for the committee to consider when discussing information presented in the session.

#### **The National Academy of Medicine Report on Diagnostic Errors: Implications for Laboratory Practice**

*Addendum 06*

**Michael Laposata, MD, PhD**

Professor and Chairman

Department of Pathology

University of Texas Medical Branch

Dr. Laposata described the problem and extent of medical errors in the United States. He detailed the diagnostic process and discussed where diagnostic errors can occur. He continued by depicting a number of examples specifically focused on misdiagnoses related to laboratory test ordering and/or result interpretation, and he proposed possible solutions including better teamwork, education, and health information technology. He concluded his presentation giving his perspectives on goals to improve diagnosis and reduce diagnostic errors.

## **From Lab Benches to Primary Care Trenches: Recognizing, Mitigating, and Preventing Diagnostic Errors** *Addendum 07*

**Gordon D. Schiff, MD**

Associate Director – Center for Patient Safety Research and Practice  
Brigham and Women's Hospital Div. General Medicine;  
Safety Director – Harvard Center for Primary Care  
Academic Improvement Collaborative;  
Associate Professor of Medicine Harvard Medical School

Dr. Schiff began his presentation by describing the diagnostic system and explaining how diagnostic errors occur, including an example that examined issues around test ordering that can lead to mistakes. He then described errors when test results are transmitted from the laboratory to the clinician and the patient, and discussed his research in this area. Dr. Schiff discussed errors that can occur during the testing process, and specifically discussed how linking the pharmacy and the laboratory could reduce errors. He finished his presentation by discussing ideas to implement a culture of diagnostic safety in the medical system.

### **Public Comments**

There were no public comments on this topic.

### **Committee Discussion**

CLIAC discussed the following as related to diagnostic error and the laboratory:

- Aspects of information technology (IT), including electronic health records, test ordering systems, and infrastructure that contribute to effective information management.
- Costs required to customize laboratory IT, including computer infrastructure, incentivizing change (especially with respect to laboratory medicine), and payment issues related to such costs.
- The need to change the culture to allow personnel to admit mistakes without fear of reprisal.
- The importance of incentives for pathologists to specialize in clinical laboratory medicine.
- The value of diagnostic improvement teams or programs within healthcare institutions, and the need to include laboratory representation in such.
- The need to better train pathologists and laboratory staff to be comfortable consulting about appropriate test utilization in light of the laboratory's role in practicing medicine.
- The power of CMS to prod hospital administrations to move forward on issues through regulations or other incentives.
- Lessons that can be learned using pharmacy as an example.
- The usefulness of report cards and evaluation metrics as a system for tracking diagnostic errors and in demonstrating the value of the laboratory.
- The need to emphasize the importance of the laboratory perspective and include

laboratory representation on the work group organized by the Agency for Healthcare Research and Quality, the Federal Interagency Work Group on Improving Diagnostic Safety and Quality.

### **Recommendations: The Role of the Laboratory in Improving Diagnoses**

**Recommendation 1:** CLIAC requests the active participation of laboratory medicine in the workings of the Federal Interagency Workgroup on Improving Diagnostic Safety and Quality. Diagnostic errors related to the total testing process lead to over 50,000 deaths each year. Inspired by the success of the CMS role in antimicrobial resistance stewardship, CLIAC recommends that healthcare centers be required (for example by CMS, or as suggested by the Federal Interagency Workgroup on Improving Diagnostic Safety and Quality) to have an independent multidisciplinary diagnostic improvement program that includes laboratory professionals as co-equal stakeholders. The program should focus on the total testing process (including the traditional pre-analytical, analytical, and post-analytical steps) and emphasize the cognitive elements of test selection and ordering, results interpretation, and communication (both to the care team and to patients), to promote safety, improve patient outcomes, and decrease diagnostic errors.

**Recommendation 2:** CLIAC recommends that the Federal Interagency Workgroup on Improving Diagnostic Safety and Quality develop and/or centralize, with an emphasis on the cognitive processes surrounding test ordering, interpretation, and communication and the actions taken as a result thereof:

- High-yield approaches to monitoring for diagnostic error
- Effective best practices and research priorities for reducing diagnostic error
- High-impact information-management processes related to decision support for improving diagnostic performance
- Recommendations for incentivizing diagnostic performance improvement
- Develop resources for improving diagnostic performance analogous to those developed for antibiotic stewardship (including through communicating with e.g. the National Quality Forum)

Quantify the “total value” of laboratory diagnostics (including delineating the stakeholders, what budgets, and what units other than dollars - e.g. QALYs - are expended based on correct or incorrect decisions involving the total laboratory process)

### **CLIA Personnel Requirements**

#### **CMS Presentation**

**Karen Dyer MT (ASCP), DLM**

Director

Division of Clinical Laboratory Improvement and Quality (DCLIQ)

Quality, Safety and Oversight Group (QSOG)

Centers for Medicare & Medicaid Services (CMS)

*Addendum 08*

*Addendum 08a*

**Sarah F. Bennett, MT (ASCP)**

Division of Clinical Laboratory Improvement and Quality (DCLIQ)  
Quality, Safety and Oversight Group (QSOG)  
Centers for Medicare & Medicaid Services (CMS)

**Cindy Flacks, MPH, M.T., ASCP**

Division of Clinical Laboratory Improvement and Quality (DCLIQ)  
Quality, Safety and Oversight Group (QSOG)  
Centers for Medicare & Medicaid Services (CMS)

Ms. Dyer provided an overview of the CMS Request for Information issued in early 2018 that included questions about CLIA personnel requirements. She summarized the comments CMS received, and described the plan to move forward. Ms. Bennett and Ms. Flacks presented additional background, and introduced nine questions for CLIAC’s consideration. The topics related to CLIA personnel covered necessary educational background, training, experience, supervision, laboratory director and technical consultant qualifications, and gross examination review.

**Public Comments**

*Addendum PC1*

*Addendum PC9*

*Addendum PC17*

*Addendum PC2*

*Addendum PC10*

*Addendum PC18*

*Addendum PC3*

*Addendum PC11*

*Addendum PC19*

*Addendum PC4*

*Addendum PC12*

*Addendum PC20*

*Addendum PC5*

*Addendum PC13*

*Addendum PC21*

*Addendum PC6*

*Addendum PC14*

*Addendum PC22*

*Addendum PC7*

*Addendum PC15*

*Addendum PC8*

*Addendum PC16*

**Committee Discussion**

- Committee members expressed concern that the personnel issues were too complicated to reach a recommendation in the time allotted at the meeting and proposed forming a CLIAC workgroup to provide input that would not only respond to the CMS questions, but would look toward future laboratory personnel needs.
- A member suggested time at this meeting be spent deciding what should be considered by the workgroup.
- Due to the complexity of the topic, a member asked CMS for more information about laboratory director deficiencies.
- Much of the discussion involved how to best determine qualifications needed for the various CLIA personnel categories (e.g. curriculum-based, competency-based, degree-based).
- After discussing the question on requirements for gross examination review, the Committee commented that having policies in place would be sufficient and preferable to a time-based requirement.

### **Recommendation: CLIA Personnel Requirements**

CLIAC recommends formation of a working group to advise the Committee on how to respond to the personnel questions asked by CMS. In particular, the working group should address: (1) the educational requirements necessary for laboratory personnel, including possible use of competency exams/other key performance indicators, and leveraging the cumulative experience of existing accreditation bodies; and (2) the following issues related to requirements for clinical laboratory directors, supervisory positions, and technical consultants: supervisory experience for laboratory directors and technical supervisors, documentation/verification of training, experience, and supervisory activities, qualifications “equivalent to board certification,” continuing medical education requirements as a function of degree, on-site requirements, and other clinical laboratory experience. CLIAC further recommends that CMS report to the workgroup and to CLIAC as to the breakdown of specific deficiencies related to laboratory directors, to assist the Committee in providing advice regarding the role/qualifications of laboratory directors.

### **Ethics and the Laboratory**

**Dr. Ramy Arnaout**

CLIAC Chair

Dr. Arnaout briefly discussed the topic of ethics and the laboratory. He asked the Committee to consider the laboratory community’s responsibility to help ensure that new technology provides valid results before it is offered to the public and promoted.

### **Committee Discussion**

- The laboratory community must be diligent in advancing truthful and accurate descriptions of the capabilities of various technologies.
- Use social media to share legitimate science.
- Regulatory agencies need to watch for laboratories that are not performing well.
- There is a lack of structure around the evaluation of technology in laboratory medicine.
- Data for new technology should be available for review.
- Laboratory scientists should come forward if something does not seem right and no data supporting the testing are available.
- Must not confuse the validity of new technology with the personal assessment of its proponents.

## **Role of the Laboratory in the Opioid Crisis**

### **Introduction to Topic**

*Addendum 09*

#### **Jasmine Chaitram, MPH**

Associate Director for Laboratory Preparedness  
Chief, Informatics and Data Science Branch  
Division of Laboratory Systems (DLS)  
Center for Surveillance, Epidemiology, and Laboratory Services (CSELS)  
Centers for Disease Control and Prevention

Ms. Chaitram introduced the topic, reviewed opioid crisis statistics, and introduced the three speakers and the questions for CLIAC consideration.

### **The Opioid Epidemic: What labs have to do with it?**

*Addendum 10*

#### **Ewa King, PhD**

Associate Director of Health  
RIDOH State Health Laboratories  
President, Association of Public Health Laboratories (APHL)

Dr. King began by reviewing opioid overdose trends. She summarized the differences and similarities of opiates and opioids, described how opioids work, including an overview of the physiological and psychological effects, and provided examples of opiates, semi-synthetic opiates, and opioids. Dr. King stated the opioid epidemic is actually driven by synthetic opioids, the most prominent one being fentanyl. She described designer opioids, for which there is no medical use, indicating that they are created to mimic the effects of the original drug while circumventing existing legal restrictions; she spoke about carfentanil, an analog of fentanyl, and its potency. Dr. King reviewed toxicology testing in the forensic laboratory, provided an overview of preliminary testing and confirmatory testing, described the three categories of laboratories where toxicology testing takes place, and reviewed overdose surveillance by laboratories. She described the current issues in toxicology testing, noting the scope of testing is not standardized and, therefore, some drugs are not being detected. Dr. King finished her presentation with a review of the barriers to a standardized approach to toxicology testing, and an overview of new public health initiatives.

### **Minnesota Department of Health – A Response to the Substance Abuse Crisis**

#### **Jason Peterson, MS**

*Addendum 11*

Chemical Threat Preparedness Coordinator  
Minnesota Department of Health

Dr. Peterson discussed the Minnesota Drug Overdose and Substance Abuse Pilot Surveillance System (MNDOSA). He reviewed the data on Minnesota opioid overdoses, and indicated that the MNDOSA program has chosen to analyze a large range of drugs across all classes since the state is continuing to experience a problem with all drug types.

He reviewed the program's objectives, said that the project is driven by clinicians at several pilot hospitals, explained how reports are produced, and discussed the MNDOSA flow chart for laboratory specimen submission, emphasizing that results are used for surveillance purposes only. Dr. Peterson reviewed the statistics, as of November 1, 2017, and said the suspected drugs vary across all categories. He discussed the in-house developed analytical method, provided an example of a multi-drug run, and noted that the CLIA regulations were followed for test validation. He presented some of the results, and stated the laboratory was looking for both primary compounds and metabolites. Dr. Peterson ended his presentation with a review of the current challenges, noting that, because there are so many drugs and they change, targeting specific opioids is difficult. Thus, the laboratory is moving away from a target test to a targeted/non-targeted test.

### **Substance Abuse: A Clinical Laboratory Perspective**

*Addendum 12*

**Leland F. McClure, MSci, PhD, F-ABFT**

Medical Science Liaison Director  
Corporate Medical Affairs  
Quest Diagnostics

Dr. McClure presented Quest's experience as a large diagnostic laboratory that provides testing for drugs-of-abuse. He discussed the national overdose epidemic and reviewed drug misuse and overdose deaths, indicating that laboratory data is foundational to healthcare, and laboratories are the first touch point clinicians have for guidance. He discussed the contributing factors to prescription drug misuse, and reviewed the screening tools available to clinicians. He noted that patient behavior can confound monitoring of prescription drug use, and that CDC had produced a guideline in response to this. He discussed clinical drug monitoring, presented information on drug-testing terminology, explaining the difference between presumptive drug testing and definitive drug testing, and reviewed the drug-testing process and drug-abuse testing versus prescription-drug monitoring. Dr. McClure indicated that Quest maintains a large database for test results. A large study of benzodiazepine and opiate use, taken from these data, was published last year in the *Journal of Addiction Medicine*. He also said that Quest produces a yearly report titled *Health Trends<sup>TM</sup>*, and he reviewed the portion of the report related to the opioids. In closing, Dr. McClure said drug testing should be risk relevant for the patient population and tailored to what is medically necessary for patients.

### **Public Comments**

*Addendum PC23*

## **Committee Discussion**

- Discussions in Congress that would require laboratory developed tests (LDT) to go through the FDA clearance process could delay the implementation of new tests for drugs.
- FDA clearance of a test does make it more legally defensible. However, FDA clearance is not relevant in forensic testing when patients are no longer living.
- There are no FDA-cleared definitive methods for drug testing.
- Tests cannot be developed quickly enough to address the drug trends.
- There is a need for provider education. Laboratory leadership needs to be more involved in education on opioid addiction and drug testing.
- Laboratories need more published guidelines and decision support tools related to opioids.
- The CDC National Center for Environmental Health (NCEH) is involved in developing new standards associated with opioid-related testing. They oversee the public health Laboratory Response Network of Chemical Laboratories (LRN-C). CDC is working with the LRN-C to help develop their testing algorithms.
- A laboratory reference system for drugs should mimic the reference system set up for infectious diseases.
- A payment system for testing needs to be addressed.
- Items to consider in order to address drug testing on a national level:
  - Standardization of the immunochemistry platform in all of the nation's hospitals.
  - All laboratories should use the same cut-off points for testing.
  - "Presumptive positive" should never be entered in a patient's electronic medical record. Test results must always be confirmed since false positives and false negatives are common.
  - There is a need for large reference laboratories.
- Discussion is needed on how laboratory medicine fits into helping to address the social determinants of health that seem to be key components of managing the opioid crisis.

## **Recommendation: the Opioid Crisis**

CLIAAC recommends that CDC, CMS, and FDA convene a blue-ribbon panel (e.g. with input from the Council for State and Territorial Epidemiologists) on laboratory engagement in controlling the opioid crisis. The panel should address the following, with emphasis on standardization of scope of testing (list of analytes), different methodologies, no clear reference laboratory system, inadequate capacity (especially in the forensic area), inadequate capability to test for novel analogs -"designer opioids":

1. How can information on the clinical and analytic properties of presumptive and definitive (confirmatory) drug testing methods be best communicated with providers who order and utilize these tests?
2. How can a list of analytes be standardized (e.g. nationally vs. by region), especially given the rapid change in usage patterns?
3. What incentives and regulatory approaches may improve access to definitive (confirmatory) drug testing?
4. What approaches to laboratory-based surveillance and reporting, leveraging preexisting systems for reporting public health concerns of communicable



- diseases, cancer, heavy metals, and HIV/AIDS (e.g. ECLRS, New York Department of Health) might improve our ability to monitor and address the epidemic of drug misuse?
5. Investigate the feasibility for Departments of Health to require clinical laboratories to report drugs-of-abuse toxicology results (a reference laboratory system).

## **Antibiotic Resistance Activities Update**

### **CDC Update: Antimicrobial Resistance**

*Addendum 13*

**Jean B. Patel, PhD, D(ABMM)**

Science Lead

Antibiotic Resistance Coordination and Strategy Unit

Division of Healthcare Quality Promotion

National Center for Emerging & Zoonotic Infectious Diseases

Centers for Disease Control and Prevention

Dr. Patel provided the CDC update on antimicrobial resistance. She began with a description of the new drug susceptibility program being launched within the Antibiotic Resistance (AR) Laboratory Network and discussed programs for treating and testing for carbapenemase-resistant *Enterobacteriaceae*, especially those infections caused by metallo- $\beta$ -lactamase-producing (MBL+) *Enterobacteriaceae*. She discussed the implementation of a pilot program in four of the regional laboratories that is focused on new drug susceptibility testing for MBL+ isolates. She reviewed the implementation of polymerase chain reaction testing for *Candida auris* colonization within the AR laboratory network, emphasizing that early detection is important. Dr. Patel said that CDC is also working with the World Health Organization's (WHO) Global AR Surveillance System Emerging Antimicrobial Resistance (GLASS-EAR) portal, into which new types of resistance can be reported. She noted the United States reports new types of resistance through Clinical and Laboratory Standards Institute (CLSI) documents. Dr. Patel closed her presentation by mentioning ongoing efforts to align susceptibility testing breakpoints between CLSI and EUCAST, the breakpoint-setting agency in Europe. Last, she alerted CLIAC of the publication of *Antibiotic Resistance Threats in the United States 2019*.

**Antimicrobial Resistance Surveillance Task Force Update**  
**Kelly Wroblewski, MPH, MT(ASCP)**

*Addendum 14*

Director  
Infectious Diseases  
Association of Public Health Laboratories

Ms. Wroblewski began her presentation with a brief overview of the Antimicrobial Resistance Surveillance Task Force (ARSTF). She related the ARSTF recommendation topic areas, and discussed the three areas most relevant to the CLIA regulations. Ms. Wroblewski ended her presentation with questions for the Committee to consider.

**Public Comments**

There were no public comments on this topic.

**Committee Discussion**

- The earlier comment about Congressional discussions on requiring FDA clearance for LDTs was re-emphasized. Such a requirement could potentially prevent the agile response to emerging and ongoing health concerns, including AR.
- Requiring the use of the most updated susceptibility testing breakpoints would impact both manufacturers and laboratories. It would require manufacturers to quickly revise their product breakpoints and labeling. Laboratories would be impacted due to the time it takes to transition their test systems to those that incorporate the updated breakpoints.
- Streamlined approaches to updating breakpoints would be beneficial to both laboratories and manufacturers.
- The FDA indicated they are working towards streamlining their process so antimicrobial susceptibility tests are available as soon as possible after a drug is approved for use.
- There should be standardization of multidrug resistance definitions.
- The 21<sup>st</sup> Century Cures Act gives the FDA the authority to designate a standards development organization for setting and revising breakpoints. CLSI is the organization recognized by the FDA. Breakpoints may be adopted by laboratories after CLSI has submitted a rationale document to the FDA, describing the basis for a breakpoint change.
- Concerns were expressed regarding the appropriate timeframe to expect laboratories to adopt new breakpoints once they have been established or updated.
- The question of who pays for work to support epidemiological needs was raised and discussed. There should be recognition, from a payment perspective, of the resources needed by clinical microbiology laboratories for this purpose.

## **Recommendations: Antibiotic Resistance Activities**

**Recommendation 1:** In support of antibiotic stewardship efforts by the president’s advisory council and others, CLIAC recommends that CMS require that clinical laboratories, in a timely fashion (e.g. within at most one year) and using reasonable effort, convert to contemporary antimicrobial resistance breakpoints in accordance with manufacturer’s instructions.

**Recommendation 2:** Recognizing the urgency imposed by the pace of emerging antimicrobial resistance, CLIAC recommends that the FDA update existing guidance to prioritize manufacturers’ timely integration of updated antimicrobial susceptibility breakpoints.

## **ACRONYMS**

*Addendum 15*

## **NOMINATION INFORMATION**

*Addendum 16*

## **CLIAC MEETING TRANSCRIPT**

*Addendum 17*

## **ADJOURN**

Dr. Ramy Arnaout and Dr. Ren Salerno 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 six Committee recommendations passed at this meeting:

### **❖ Recommendations on The Role of the Laboratory in Improving Diagnoses:**

**Recommendation 1:** CLIAC requests the active participation of laboratory medicine in the workings of the Federal Interagency Workgroup on Improving Diagnostic Safety and Quality. Diagnostic errors related to the total testing process lead to over 50,000 deaths each year. Inspired by the success of the CMS role in antimicrobial resistance stewardship, CLIAC recommends that healthcare centers be required (for example by CMS, or as suggested by the Federal Interagency Workgroup on Improving Diagnostic Safety and Quality) to have an independent multidisciplinary diagnostic improvement program that includes laboratory professionals as co-equal stakeholders. The program should focus on the total testing process (including the traditional pre-analytical, analytical, and post-analytical steps) and emphasize the cognitive elements of test selection and ordering, results interpretation, and communication (both to the care team and to patients), to promote safety, improve patient outcomes, and decrease diagnostic errors.

**Recommendation 2:** CLIAC recommends that the Federal Interagency Workgroup on Improving Diagnostic Safety and Quality develop and/or centralize, with an emphasis on the cognitive processes surrounding test ordering, interpretation, and communication and the actions taken as a result thereof:

- High-yield approaches to monitoring for diagnostic error
- Effective best practices and research priorities for reducing diagnostic error

- High-impact information-management processes related to decision support for improving diagnostic performance
- Recommendations for incentivizing diagnostic performance improvement
- Develop resources for improving diagnostic performance analogous to those developed for antibiotic stewardship (including through communicating with e.g. the National Quality Forum)

Quantify the “total value” of laboratory diagnostics (including delineating the stakeholders, what budgets, and what units other than dollars---e.g. QALYs---are expended based on correct or incorrect decisions involving the total laboratory process)

❖ **Recommendation on CLIA Personnel Requirements:**

CLIAAC recommends formation of a working group to advise the Committee on how to respond to the personnel questions asked by CMS. In particular, the working group should address: (1) the educational requirements necessary for laboratory personnel, including possible use of competency exams/other key performance indicators, and leveraging the cumulative experience of existing accreditation bodies; and (2) the following issues related to requirements for clinical laboratory directors, supervisory positions, and technical consultants: supervisory experience for laboratory directors and technical supervisors, documentation/verification of training, experience, and supervisory activities, qualifications “equivalent to board certification,” continuing medical education requirements as a function of degree, on-site requirements, and other clinical laboratory experience. CLIAAC further recommends that CMS report to the workgroup and to CLIAAC as to the breakdown of specific deficiencies related to laboratory directors, to assist the Committee in providing advice regarding the role/qualifications of laboratory directors.

❖ **Recommendation on The Role of the Laboratory in the Opioid Crisis:**

CLIAAC recommends that the CDC, CMS, and FDA convene a blue-ribbon panel (e.g. with input from the Council for State and Territorial Epidemiologists) on laboratory engagement in controlling the opioid crisis. The panel should address the following, with emphasis on standardization of scope of testing (list of analytes), different methodologies, no clear reference laboratory system, inadequate capacity (especially in the forensic area), inadequate capability to test for novel analogs-”designer opioids”:

1. How can information on the clinical and analytic properties of presumptive and definitive (confirmatory) drug testing methods be best communicated with providers who order and utilize these tests?
2. How can a list of analytes be standardized (e.g. nationally vs. by region), especially given the rapid change in usage patterns?
3. What incentives and regulatory approaches may improve access to definitive (confirmatory) drug testing?
4. What approaches to laboratory-based surveillance and reporting, leveraging preexisting systems for reporting public health concerns of communicable diseases, cancer, heavy metals, and HIV/AIDS (e.g. ECLRS, New York DoH), might improve our ability to monitor and address the epidemic of drug misuse?

5. Investigate the feasibility for Departments of Health (DoH) to require clinical laboratories to report drugs-of-abuse toxicology results (a reference laboratory system)

❖ **Recommendations on Antibiotic Resistance Activities:**

**Recommendation 1:** In support of antibiotic stewardship efforts by the president's advisory council and others, CLIAC recommends that CMS require that clinical laboratories, in a timely fashion (e.g. within at most one year) and using reasonable effort, convert to contemporary antimicrobial resistance breakpoints in accordance with manufacturer's instructions.

**Recommendation 2:** Recognizing the urgency imposed by the pace of emerging antimicrobial resistance, CLIAC recommends that the FDA update existing guidance to prioritize manufacturers' timely integration of updated antimicrobial susceptibility breakpoints.

Dr. Ramy Arnaout announced the spring 2019 CLIAC meeting dates as April 10-11, 2019, and adjourned the Committee meeting.

I certify this summary report of the November 7-8, 2018 CLIAC meeting is an accurate and correct representation of the meeting.

Dr. Ramy Arnaout, CLIAC Chair

Dated: