

Clinical Laboratory Improvement Advisory Committee



Summary Report

April 14-15, 2021

Atlanta, Georgia

U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES

Clinical Laboratory Improvement Advisory Committee April 14-15, 2021 Summary Report

Table of Contents

❖ Record of Attendance

❖ Clinical Laboratory Improvement Advisory Committee (CLIAC) Background

❖ Call to Order, Recognition of Outgoing Members, and Committee Member Introductions

❖ Agency Updates and Committee Discussion

- Centers for Disease Control and Prevention (CDC)
- Centers for Medicare & Medicaid Services (CMS)
- Food and Drug Administration (FDA)
- CLIAC Recommendations Update
- Laboratory Response Network (LRN) Overview

❖ Presentations and Committee Discussion

Clinical Laboratory Medicine in the Age of COVID-19

- **Clinical Laboratory Perspectives on Laboratory Developed Tests**
 - Introduction to Topic
 - Challenges and Opportunities Surrounding Laboratory Developed Tests as an Essential Component of the Pandemic Response
 - Moving Mountains: (R)Evolution of LDT Regulation in the Face of COVID-19
- **Application of Regulations during the COVID-19 Pandemic**
 - CMS Regulatory Changes during COVID-19 Pandemic
 - FDA Regulatory Changes during COVID-19 Pandemic
 - Lessons Learned from SARS-CoV-2 Testing Regulatory Flexibilities
- **The Clinical Laboratory's Role in Identifying Health Inequities during the COVID-19 Response**
 - The Expansion of Point-of-Care Testing During the COVID-19 Pandemic FDA
 - Overview of Point-of-Care Testing and Home Collection and Testing
- **Future CLIAC Topic Discussion**

❖ Acronyms

❖ Nomination Information

❖ Adjourn

CLIAC APRIL 14-15, 2020 MEETING AGENDA

Addendum 1

CLIAC MEETING TRANSCRIPT

Addendum 2

RECORD OF ATTENDANCE

Committee Members Present

Dr. Valerie Ng, Chair
Dr. Birthale Archie
Dr. Marc Couturier
Ms. Heather Duncan
Dr. Mary Edgerton
Dr. Susan Gross
Dr. Lee Hilborne
Dr. Steven Hinrichs
Dr. Jordan Laser
Dr. Thomas Lorey
Dr. Lavinia Middleton
Ms. Carole Moss
Dr. Nirali Patel
Dr. Michael Pentella
Dr. Katherine Perez
Ms. Jennifer Rhamy
Dr. Gregory Sossaman
Dr. R.W. (Chip) Watkins
Dr. Thomas Williams
Dr. Donna Wolk
Mr. Andy Quintenz, AdvaMed (Liaison Representative)

Ex Officio Members

Dr. Collette Fitzgerald, CDC
Ms. Monique Spruill, CMS
Dr. Timothy Stenzel, FDA

Designated Federal Official

Dr. Reynolds Salerno, CDC

Executive Secretary

Ms. Nancy Anderson, CDC

In accordance with the provisions of Public Law 92-463, the meeting was open to the public. The meeting was a full virtual Zoom webcast, and approximately 160 public citizens attended one or both days of the meeting.

CLINICAL LABORATORY IMPROVEMENT ADVISORY COMMITTEE (CLIAC) BACKGROUND

The Secretary of Health and Human Services (HHS) 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 revisions of the Clinical Laboratory Improvement Amendments of 1988 (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. The Secretary selects members 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 carry out its functions effectively. CLIAC also includes a non-voting liaison representative who is a member of AdvaMed and other non-voting liaison representatives that the Secretary deems necessary for the Committee to carry out its functions effectively.

As a result of the different perspectives among its members, 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 the Committee's advice because of other overriding concerns. Thus, while some of the actions recommended by CLIAC may result in changes to the CLIA regulations or may lead to other actions taken by HHS, all of the Committee's recommendations may not be accepted and acted upon by the Secretary.

CALL TO ORDER, RECOGNITION OF OUTGOING MEMBERS, AND COMMITTEE INTRODUCTIONS

Addendum 3
Addendum 4

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), Office of Public Health Scientific Services (OPHSS), CDC, welcomed the Committee and the members of the public. Dr. Salerno expressed gratitude to the CLIAC members and laboratory community for their ongoing efforts in responding to the COVID-19 pandemic. Dr. Valerie Ng, CLIAC Chairperson, welcomed the Committee and reviewed the process for public comments, quorum requirements, and the process for official CLIAC recommendations. Dr. Salerno recognized CLIAC outgoing members, Dr. Marc Couturier, Dr. Steve Hinrichs, Dr. Jordan Laser, Dr. Thomas Lorey, Dr. Katherine Perez, and Dr. Thomas Williams, for their contributions to the Committee. Dr. Salerno also thanked Ms. Regina Van Brakle for her service to CLIAC as the interim CMS ex officio. Dr. Salerno introduced Ms. Monique Spruill, who will serve as the new CMS ex officio, and introduced Ms. Heather Duncan as a new committee member. All members then made self-introductions and financial disclosure statements relevant to the meeting topics. Dr. Ng stated that the agenda topics would include updates from the CDC, CMS, and FDA, including updates on recent CLIAC recommendations and an overview of the Laboratory Response Network (LRN). She then introduced the meeting's theme, Clinical Laboratory Medicine in the Age of COVID-19.

AGENCY UPDATES AND COMMITTEE DISCUSSION

Centers for Disease Control and Prevention (CDC) Update

Addendum 5

Collette Fitzgerald, PhD
Deputy Director for Science
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. Fitzgerald updated CLIAC on CDC's Laboratory and Testing Task Force priority areas and activities, including the National SARS-CoV-2 genomic surveillance to track and analyze SARS-CoV2 variants. She provided an overview of CDC's COVID-19 response and the Division of Laboratory Systems' (DLS) work to support the COVID-19 response. Under laboratory testing and reporting guidance, she highlighted new and updated laboratory guidance posted on [CDC's COVID-19 webpage](#). Dr. Fitzgerald discussed activities related to partnership, communication, and outreach, emphasizing the critical importance of CDC's partnership with other organizations. She noted the calls with the Tri-agency Task Force for Emergency Diagnostics, the American Clinical Laboratory Association (ACLA) and large commercial laboratories, the Association of Public Health Laboratories (APHL), the Council for State and Territorial Epidemiologists (CSTE), as well as ongoing calls with CDC's federal partners at FDA and CMS. She highlighted laboratory communication exchange opportunities using the Clinical Laboratory Outreach Communication System (LOCS), the Clinical Laboratory Partners Forum, and the Clinical Laboratory COVID-19 Response calls. Dr. Fitzgerald provided an overview of policy activities related to the COVID-19 response,

including various information sharing and accountability requests and policy engagement activities through legislative monitoring and tracking. She provided an overview of CDC's Data Modernization Initiative. Dr. Fitzgerald concluded by updating on [CDC OneLab](#), an initiative to strengthen interconnections between clinical, public health, and CDC laboratory education and training professionals to collectively support rapid, large-scale responses. She described the OneLab goal to establish a sustainable learning community to equip the laboratory workforce with necessary tools, resources, and networks. Dr. Fitzgerald provided a summary of CDC's COVID-19 related training, job aids, virtual reality courses, and the CDC's Laboratory eLearning Course Syndication Program. She also announced that CDC DLS is working on OneLab Reach, a rapid education and capacity building hub, as a new learning management system specific for COVID-19 laboratory education and training resources.

Centers for Medicare & Medicaid Services (CMS) Update

Addendum 6

Ms. Monique Spruill

Director

Division of Clinical Laboratory Improvement and Quality (DCLIQ)

Center for Medicaid and State Operations (CMSO)

Centers for Medicare & Medicaid Services (CMS)

Ms. Spruill began by describing the reorganization of the five branches within the Division of Clinical Laboratory Improvement and Quality (DCLIQ): two policy branches and three operations branches. She provided the current laboratory enrollment in the CLIA program and gave statistics on the numbers of facilities with each of the CLIA certificate types. She highlighted that the public health pandemic resulted in an increase in Certificate of Waiver sites, primarily physician offices, pharmacies, and assisted living facilities. Ms. Spruill summarized changes to the [CMS CLIA website](#), including the available CMS brochures, the new CLIA pay banner that allows online payment of certificate fees, and the Certification Quick Start Guide. She highlighted several recent CMS memos posted on the CMS website that provide guidance to surveyors and laboratories. Next, Ms. Spruill stressed the importance of CMS partner engagement with accreditation organizations, state agencies, and state surveyors, and provided an overview of the [CLIA Communications Listserv](#). She described how CMS plans to utilize various approaches to evaluate existing CLIA regulations to align with current laboratory practices and improve laboratory testing quality and optimize oversight. Ms. Spruill explained that CMS will take a data-driven approach to identify widespread issues and opportunities to increase clinical laboratory excellence.

Food and Drug Administration (FDA) Update

Addendum 7

Timothy Stenzel, MD, PhD

Director

Office of In Vitro Diagnostics and Radiological Health (OIR)

Office of Product Evaluation and Quality (OPEQ)

U. S. Food and Drug Administration (FDA)

Dr. Stenzel began his presentation discussing the key milestones associated with the FDA's COVID-19 response. He highlighted COVID-19 testing milestones that included the first Emergency Use Authorization (EUA) for the CDC diagnostic assay in February 2020, the first screening authorization in July 2020, the first over-the-counter (OTC) home collection kit, and home testing EUAs in December 2020, and the first OTC serial screening assay for routine testing of asymptomatic individuals authorized in March 2021. Dr. Stenzel emphasized the

growing COVID-19 testing menu with over 350 EUAs granted as of March 31, 2021, and an additional 150 received for review. Dr. Stenzel announced that the BioFire® Respiratory 2.1 (RP2.1) was the first COVID-19 diagnostic test granted marketing authorization using the De Novo premarket review pathway, a regulatory pathway for low to moderate-risk devices of a new type. He reiterated that this full authorization did not impact the review of EUA submissions and noted that draft guidance is currently being cleared to address how current EUA holders can receive full authorization once the public health emergency is no longer declared. Dr. Stenzel continued his briefing by detailing how FDA has monitored viral mutations and variants and their impact on COVID-19 tests since early summer 2020. He emphasized that FDA now has a website to keep the community informed of specific mutations and variants. He acknowledged that, over the last year, FDA engaged the public and test developers by hosting over 50 virtual town halls, answering FAQs on the FDA website, and responding to over 185,000 inquiries. He concluded by describing the non-SARS-CoV-2 work that continues to take place at FDA, including the first CLIA waiver for a point-of-care test that detects *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in female vaginal swabs and male urine specimens. He also noted the Medical Device User Fee Amendment (MDUFA) V is currently being discussed to focus on device safety. The critical feedback received from stakeholders is that people want to engage with the FDA more and test developers desire real-world evidence to support regulatory decisions.

CLIAAC Recommendations Update

Heather Stang, MS, MT and Lisa Kalman, PhD

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

Addendum 8

Addendum 8a

Ms. Stang presented updates on eight recommendations from the April 2019 CLIAAC meeting related to forming a CLIAAC workgroup and Next Generation Sequencing (NGS) activities. Ms. Stang explained that formation of the new CLIA Regulations Assessment Workgroup had been paused to allow the agencies to focus on the pandemic. However, CDC, CMS, and FDA are now actively engaged in forming this new workgroup to focus on the total testing process evaluation. Ms. Stang also discussed two CLIAAC recommendations for surveys and information gathering from organizations already performing NGS. She described the request for information (RFI) published in the Federal Register in May 2020 to solicit public input on the personnel and the retention of NGS data in clinical and public health laboratories. Ms. Stang noted two additional CLIAAC recommendations about NGS guidelines or guidance documents developed by the government and professional organizations. She introduced the NGS Best Practices Forum which will provide an opportunity for an open discussion among organizations to share accomplishments, priorities, and challenges for NGS. Ms. Stang continued by highlighting the CDC and APHL NGS Quality Initiative and the comprehensive plan to implement an NGS Quality Management System (QMS) in CDC and public health laboratories. She promoted the availability of over 80 customizable, ready to implement products, including guidance documents, SOPs, and forms are available on the [NGS Quality Initiative webpage](#).

Dr. Kalman continued the CLIAC recommendations summary by providing an update on the development of electronic reference materials for NGS. She briefly described the Genetic Testing Reference Materials Program (GeT-RM) created in 2004 by the CDC to increase the availability of reference manuals for genetic testing. She noted that CLIAC recommended expanding the GeT-RM program regarding its scope and sample types and suggested including the creation and curation of NGS data sets used by laboratories for validating bioinformatic pipelines. Dr. Kalman provided an overview of a two-stage project to address this CLIAC recommendation. The first stage involved developing a list of expert-curated, clinically important variants that can be used to create multi-variant electronic reference materials by *in silico* “mutagenesis” of laboratory-generated NGS files. The project is currently at the second stage that involves pilot testing to determine if the variants added can be detected by clinical laboratories. Dr. Kalman indicated a manuscript would describe the pilot study and acknowledged the participants in both stages of the project.

Laboratory Response Network (LRN) Overview

Addendum 9

Julie Villanueva, PhD

Chief, Laboratory Preparedness and Response Branch

Division of Preparedness and Emerging Infections

National Center for Emerging and Zoonotic Infectious Diseases

Centers for Disease Control and Prevention

Dr. Villanueva began by providing an overview of the Laboratory Response Network (LRN) and its role in response to biological threats and emerging infectious diseases. She explained the LRN was established under the Presidential Decision Directive 39 and it became operational in August 1999 with the primary objective to ensure an effective laboratory response to bioterrorism. She noted the LRN’s mission to provide rapid laboratory response to biological (LRN-B) and chemical (LRN-C) threats and inform critical decisions about public health and safety. Dr. Villanueva illustrated the LRN-B and LRN-C tiered structures, including testing capabilities and laboratory network facility types and partners and informed CLIAC of the LRN’s role in detecting biological threats, including the response to the September 2001 anthrax attacks. She discussed the LRN’s role in detecting endemic disease agents, such as *Francisella tularensis*, *Yersinia pestis*, and naturally acquired *Bacillus anthracis*. Dr. Villanueva also discussed emerging infectious diseases and the essential role played by the LRN in responding to Ebola virus disease by developing an RT-PCR assay. She explained the many resources available for laboratory response activities and highlighted some of the challenges, such as the lack of clinical information that could delay ordering the correct diagnostic tests. Dr. Villanueva concluded by discussing the future of the LRN and the competitive selection of research proposals to detect existing and novel pathogens.

Committee Discussion

- A Committee member inquired if Dr. Fitzgerald had reached out to veterinary diagnostic laboratories to promote the OneLab initiative. Dr. Fitzgerald responded that she would check with the DLS Training and Workforce Development Branch to find out if veterinary partners were included.
- Another member asked if CMS could eliminate paper forms and replace them with a web format for submitting information. Ms. Spruill responded that CMS is working on a seamless system for updating certificates and making payments online.

- A member asked CMS and FDA what is being done to escalate the capabilities of having rapid diagnostic tests for distribution to home care. Dr. Stenzel suggested the FDA has been authorizing many tests and many different formats, including home collection and rapid tests for screening both symptomatic and asymptomatic individuals in home and congregate settings. The FDA has opened up a new pathway to allow those tests to be authorized. He noted that the FDA's current thought is that workers should be tested at least once a week if testing is performed by a molecular test but twice a week if using an antigen test. Ms. Spruill added that another division at CMS has oversight of nursing homes and she would take the comment back to the other division.
- A CLIAC member asked what the government is doing now to provide rapid diagnostic tests like other countries. Dr. Stenzel replied that several efforts are being taken to address the need for rapid diagnostic testing. He indicated that the National Institutes of Health (NIH) had started a home testing study in North Carolina and Tennessee.
- A member asked if any federal partners have been collecting outcome data that might show the impact of government decisions made during the pandemic and if that information can be used to inform the CLIAC CLIA Regulatory Assessment workgroup discussions. Dr. Ng commented that she had seen several letters submitted for public comment that address this issue. Dr. Stenzel added that since EUA denials are not made public, the CLIAC members and others are not aware of all the things done by the FDA to protect the public. He added that FDA receives pre-market and post-market data through complaint handling, medical device reporting, and the FDA email box. Dr. Stenzel noted that the FDA has seen several data integrity issues, and it is a challenge to identify data integrity issues and solutions.
- Dr. Salerno commented on a Committee member's observation and stated that a tremendous amount of outcome data could be used to critically evaluate the government's decisions in response to the pandemic. He noted that help is needed from the community to understand that outcome data and connect it to the regulatory systems.

PRESENTATIONS AND COMMITTEE DISCUSSION

Clinical Laboratory Medicine in the Age of COVID-19

Clinical Laboratory Perspectives on Laboratory Developed Tests

Introduction to the Topic

Valerie Ng, MD, PhD

Chair, Clinical Laboratory Improvement Advisory Committee

Chair

Department of Laboratory Medicine and Pathology

Alameda Health System/Highland Hospital

[Addendum 10](#)

[Addendum 10a](#)

Dr. Ng introduced the topics and presenters for the sessions and reviewed questions for the Committee to consider during their deliberations.

Challenges and Opportunities Surrounding Laboratory Developed Tests as an Essential Component of the Pandemic Response *Addendum 11*

Matthew J. Binnicker, PhD, D(ABMM)

Director of Clinical Virology, Mayo Clinic, Rochester, MN

Vice Chair of Practice, Department of Laboratory Medicine and Pathology

Professor of Laboratory Medicine and Pathology

President, Pan American Society for Clinical Virology

Dr. Binnicker described Mayo Clinic's response to COVID-19 and recognized the work of the Clinic's COVID-19 Rapid Response Team. He discussed the many initial challenges that Mayo Clinic faced during the pandemic, including access to validation material, supplies, and equipment, transportation issues, complexities with the EUA process, and questions surrounding test utilization and interpretation. Dr. Binnicker demonstrated why a laboratory-developed test (LDT) was essential to the Mayo Clinic response by providing early access to testing for patients in local communities. He highlighted some opportunities and lessons learned, noting how widespread testing during the early phase of an outbreak is necessary to prevent broad community transmission. He emphasized that an LDT developed by clinical laboratories near the patient population can meet this early testing need. Dr. Binnicker suggested creating a Center of Excellence Network for a pandemic response that could be used to leverage essential partnerships between public health, industry, clinical laboratories, and the federal, state, and local government. He highlighted the roles of each partner to rapidly expand testing capabilities during an outbreak. Dr. Binnicker concluded his presentation with a proposal that laboratories apply to become certified testing sites before an outbreak to provide broad testing capabilities early in the outbreak.

Moving Mountains: (R)Evolution of LDT Regulation in the Face of COVID-19 *Addendum 12*

Dara L. Aisner, MD, PhD

Associate Professor of Pathology

Director, Colorado Molecular Correlates Laboratory

University of Colorado

University of Colorado Anschutz Medical Campus

Dr. Aisner discussed her experience with implementing an LDT and working with the FDA for EUA approval of a test for SARS-CoV-2 during the COVID-19 pandemic. She described the challenges with the EUA process and the confusion laboratories had in understanding that EUA submissions were not needed for SARS-CoV-2 LDTs as described in the FDA's "Policy for Diagnostic Tests for Coronavirus Disease – 2019 during the Public Health Emergency." Dr. Aisner provided three EUA scenarios and the obstacles encountered, including slow EUA reviewer response time, variability in reviewer expertise, and changing EUA policies as the pandemic timeline progressed. She emphasized lessons learned, noting that testing performed at a local level using an LDT is more flexible and can decrease the time needed to implement testing over that required when using a commercial kit. Dr. Aisner transitioned her presentation to the broader issue of LDT use, indicating that there are estimated to be over 100,000 LDTs in the U.S., including many for cancer diagnosis. She suggested that cancer should be considered a pandemic and receive the same considerations for LDT flexibility as demonstrated during the COVID-19 pandemic. Dr. Aisner proposed several solutions to address the needed flexibility for LDT use, including the use of the EUA process instead of the FDA premarket approval (PMA) or 510(k) clearance processes, utilizing academic laboratory community expertise for reviewing assays, establishing professional credentialing

to qualify a person for developing and performing testing, and modifying existing infrastructure to include the modernization of CLIA. She concluded with an overview of the Genomics Organization for Academic Laboratories, a consortium of 28 academic laboratories that collaborate, share resources, and understand and minimize sources of variability in NGS by having standing non-disclosure agreements in place.

Public Comments

[*Addendum PC1*](#)

[*Addendum PC2*](#)

[*Addendum PC3*](#)

[*Addendum PC4*](#)

Committee Discussion

- Dr. Stenzel thanked the presenters and recognized the value of stakeholder feedback throughout the pandemic. He noted the February 29, 2021 guidance that allows LDTs to be implemented after notification to the FDA but without an EUA, which spurred the use of many tests. He explained that currently proposed LDT legislation contains grandfather clauses that will allow most LDTs on the market to be exempt from FDA review. Also, this legislative proposal provides an outline for an LDT precertification process that would allow test developers to proceed with the development of multiple LDTs under a single application. He indicated that if the current draft legislation is passed, the FDA will not be required to review as many tests. Dr. Stenzel stated that the FDA supports a legislative solution to LDTs, and stakeholders should contact Congress rather than the FDA with their views and concerns. Considering the needs of public health during the ongoing pandemic, the FDA is not encouraging full authorization submissions as the priority has been, and continues to be, the review of EUA applications. During a public health emergency, if there is an EUA in place, there is no need for a full authorization. He also clarified that the Office of In Vitro Diagnostics and Radiological Health does not review the majority of transplant-related tests. The FDA's Center for Biologics Evaluation and Research is the appropriate contact for those.
- A Committee member asked if the declaration of a public health emergency mandates the FDA to enforce the LDT review directives, and then inquired if the U.S. President can waive the FDA's requirements for LDT review during a public health emergency. Dr. Stenzel replied that during the past six pandemics, the FDA has followed the EUA provisions and reviewed and authorized many LDTs. He stated that in August 2020, HHS Secretary Azar released a statement that HHS would no longer require LDT review by the FDA before use of the test during the COVID-19 public health emergency.
- Another member asked about the current LDT environment. Dr. Stenzel noted that 40 years ago, when the FDA decided they would not actively review LDTs, the environment was drastically different from today. Now laboratories have numerous LDTs in their inventory, and their complexity has increased. There is currently a dichotomy between requirements for manufacturer kit authorization versus what a laboratory needs to do for an LDT. The playing field is not level.
- Several members commented on the increase in non-clinical laboratories developing LDTs during the COVID-19 pandemic and emphasized the need to oversee these types of new testing sites.

- A member commented that professional groups are currently active in LDT oversight and noted concerns with patient access to testing, agility, and rapid deployment under a more FDA-centric model. The member noted additional legislation in U.S. Congress that focuses on the modernization of CLIA.
- A member described the board certification process for laboratory directors in molecular microbiology and molecular diagnostics, noting that perhaps anyone in a laboratory with such a board certification could be qualified to launch LDTs during a public health emergency. The member also emphasized the increase in new laboratories during the COVID-19 pandemic and instances where the quality of laboratory testing was missing and stressed the need for a system to mitigate the risk.
- Several members suggested developing a national registry of laboratories or academic centers qualified to proceed with LDT development and testing without receiving an EUA for those tests. The members indicated the registry should include a pre-registration process to determine qualifications, including personnel qualifications, and demonstrated competency in LDT development. Members of this registry should demonstrate competency in the total testing process, not just test development.
- Another member added that laboratory accreditation organizations could create an inspection checklist to pre-qualify laboratories for LDT development. The checklist could include metrics such as the complexity of testing being performed in that laboratory, personnel qualifications, and proficiency testing performance utilizing the proposed LDT methodology. These laboratories could proceed with LDT development without FDA review.
- Several members reflected on the broad range of LDTs being developed, noting the differences between developing an LDT based on a current test but using a different specimen type versus the complex process of creating a de novo LDT.
- A member suggested the modernization of CLIA to include changes to address LDTs and ensure the quality of the tests being developed.
- Two members suggested using medical practices like obstetrics and gynecology and trauma unit certifications as a model for developing an LDT national registry.
- A member suggested a study to identify how other medical fields have addressed the issue of balancing expertise, professional responsibility, and accountability.
- A member inquired about the number of EUAs that have been submitted by laboratories new to clinical testing. Dr. Stenzel referenced the New England Journal of Medicine publication "[Covid-19 Molecular Diagnostic Testing — Lessons Learned](#)" and noted that most of the early applications from LDT developers had issues with performance or validation and design. Of the over 3,000 EUAs received, most applicants had not previously submitted an EUA or applications for 510(k) clearance or pre-market approval.

Application of Regulations during COVID-19

CMS Regulatory Changes during the COVID-19 Pandemic

Addendum 13

Ms. Monique Spruill

Director

Division of Clinical Laboratory Improvement and Quality (DCLIQ)

Center for Medicaid and State Operations (CMSO)

Centers for Medicare & Medicaid Services (CMS)

Ms. Spruill began by describing the initial steps CMS took as part of the Tri-agency Taskforce for Emergency Diagnostics, including CMS, FDA, and CDC. The taskforce worked to facilitate the availability of diagnostic tests approved by the FDA for EUA. Ms. Spruill described initiatives that affected laboratories applying for a CLIA certificate, pathologists, surveyors, proficiency testing programs, and accrediting organizations. She described the challenges CMS faced with pop-up laboratories and how CMS handled them. She detailed the changes made to the CLIA regulations via the interim final rule. Ms. Spruill described the temporary enforcement discretion CMS used regarding EUA tests, surveillance testing, temporary testing sites, individualized quality control plans, expired reagents and test kits, and extending CLIA certificate expiration dates. She concluded by providing a list of linked documents used for guidance for the pandemic.

FDA Regulatory Changes during the COVID-19 Pandemic

Addendum 14

Timothy Stenzel, MD, PhD

Director

Office of In Vitro Diagnostics and Radiological Health (OIR)

Office of Product Evaluation and Quality (OPEQ)

U. S. Food and Drug Administration (FDA)

Dr. Stenzel began by acknowledging the different agencies and partners that collaborated with the FDA during the pandemic. He described the guidance provided by the FDA that addressed LDTs, serology tests, molecular diagnostic tests, and the effects of viral variants on tests. Dr. Stenzel concluded his presentation with a discussion about the FDA definitions of surveillance, screening, and diagnostic tests, how FDA is streamlining authorization for screening tests, and points to consider when setting up a testing program.

Lessons Learned from SARS-CoV-2 Testing Regulatory Flexibilities

Reynolds M. Salerno, PhD

Addendum 15

Director, Division of Laboratory Systems

Center for Surveillance, Epidemiology, and Laboratory Services

Centers for Disease Control and Prevention

Dr. Salerno highlighted the lessons learned by CDC and its CLIA partners CMS and FDA since the start of the pandemic. He stressed the importance of partnerships across various federal agencies, as well as external partnerships with public health, professional organizations, and clinical and public health laboratories. Dr. Salerno discussed how the pandemic has exemplified the relationships among a variety of healthcare groups, including those that do not typically interact with public health, and he noted the importance of integration across healthcare, public health, and the broader testing community. He provided

an overview of several CLIA and FDA regulatory flexibilities presented in the CMS and FDA presentations. Some of the flexibilities proved beneficial to the laboratory community, including the CMS allowance of remote review and laboratory result reporting, and the allowance of CLIA certificates to be extended to temporary testing locations. Dr. Salerno also highlighted some of the challenges that laboratories had encountered. These included required reporting of test results to public health departments and CDC where, in some cases, processes and systems for electronic transmission of results did not exist. In addition, some of the mandated demographic data elements for reporting are not routinely part of laboratory test records. Dr. Salerno shared concerns over the increase in point-of-care and Certificate of Waiver sites and the specific expectations of the tests authorized for use in point-of-care settings. He addressed the confusion surrounding screening versus surveillance testing and discussed the various ways CDC communicated with laboratories. After reiterating the lessons learned from this pandemic related to the importance of partnerships and improved communication, which will hopefully help the laboratory community be better prepared for the next public health emergency, he closed with four questions for the Committee to consider for their discussion.

Public Comments

[*Addendum PC5*](#)

[*Addendum PC6*](#)

Committee Discussion

- A member asked each presenter what resources were still needed to support the pandemic response in each of their areas. Dr. Stenzel stated that additional staff to assist with FDA reviews of COVID and other tests were still needed. Dr. Salerno concurred that more CDC and public health personnel were needed in addition to a more integrated health information exchange system. Ms. Spruill replied that better engagement with stakeholders and laboratories, and the ability to develop and provide information using clear, consistent communication would be helpful. A Committee member agreed with the presenters' comments and also suggested a pandemic-specific communications office and better web communications from government agencies. Another member suggested improving the interoperability of systems for communicating laboratory data and suggested using the employer's uniform resource identifier (URI) when teleworking and reporting laboratory results to comply with CLIA regulations and still protect the worker's personal information.
- A Committee member commented on a concern that there is no proficiency testing available for sequencing. Additionally, clinicians that order a sequencing test sometimes want to know if a variant is present even if it does not affect patient care, but this adds a burden to the laboratory.
- Multiple members remarked that the modernization of the CLIA regulations is needed and that the pandemic has helped illustrate gaps.
- Multiple Committee members agreed that remote access for different activities worked well and should continue to be allowed even after the pandemic ends. Several Committee members cautioned that data protection and quality must be considered before making any permanent change to the CLIA regulations.
- A Committee member suggested that hospitals be included in groups discussing laboratory challenges with COVID-19. Dr. Salerno clarified that the Tri-agency Taskforce on Emergency Diagnostics has FDA, CDC, and CMS participants only.

However, in 2018, CDC, APHL, CSTE, and ACLA signed a Memorandum of Understanding on surge laboratory testing during a public health emergency. He agreed that the membership should be expanded to include representation so that the entire clinical laboratory system could support surge testing during a public health emergency

The Committee deliberated, voted, and approved the following recommendations on the topic of Laboratory Data Exchange during COVID-19:

Recommendation: CLIAC recommends that the Assistant Secretary for Preparedness and Response (ASPR) coordinate a national process to obtain and allocate critical diagnostic clinical laboratory testing resources to manage a public health emergency. Key features of the process include transparency about resource allocation and clearly defined approaches for both public health and clinical laboratories. Public health officials and clinical laboratory representatives need to collaborate to provide information to guide resource decisions. Processes, decisions (with justifications), and data provided by the public health and clinical laboratories and by responsible authorities (for example, public health and elected officials) should be made public.

Expansion of Point-of-Care, Self-Collection, and Self-Testing

The Expansion of Point-of-Care Testing During the COVID-19 Pandemic

Nancy Anderson, MMSc, MT(ASCP)

[*Addendum 16*](#)

Senior Advisor for Clinical Laboratories

[*Addendum 16a*](#)

Center for Surveillance, Epidemiology, and Laboratory Services

Centers for Disease Control and Prevention

Ms. Anderson opened her presentation by illustrating the increase in the number of each CLIA certificate type since 1993. She described the laboratory types that were issued a Certificate of Waiver between January 2020 and March 2021 and the trends for some laboratory types by month. Ms. Anderson reviewed the requirements for Certificates of Waiver and gave a brief history of CLIAC discussions about waived testing. She concluded her presentation by providing links to guidance and other resources available for laboratories and other testing sites that perform waived testing and a list of questions for the Committee to discuss.

FDA Overview of Point-of-Care Testing and Home Collection and Testing

Timothy Stenzel, MD, PhD

[*Addendum 17*](#)

Director

Office of In Vitro Diagnostics and Radiological Health (OIR)

Office of Product Evaluation and Quality (OPEQ)

U. S. Food and Drug Administration (FDA)

Dr. Stenzel described the types of tests developed to increase access to COVID-19 testing and presented a timeline of when each of the test types were first issued an EUA. He discussed what information FDA recommends test developers include for EUA point-of-care tests and a link to applicable templates on the FDA website. The templates provide details of the FDA-recommended information that should be included in an EUA request for a

molecular, serological, or antigen test. Dr. Stenzel discussed the advantages of at-home testing and home specimen collection for COVID-19 compared to a point-of-care test. He closed with recommendations given to test developers for submitting EUA applications for both home collection and at-home testing.

Public Comments

Addendum PC7

Committee Discussion

Multiple Committee members commented and discussed various issues regarding point-of-care tests, self-collection, and at-home testing including:

- Providing inexpensive, readily available, at-home tests to those who cannot afford clinical testing and health equity.
- Providing reimbursement to clinicians for their interpretation of the results of at-home tests for individuals. It was noted that a different part of CMS handles reimbursement than the division that administers the CLIA program.
- Tracking discordant results, particularly for at-home tests and identifying who would be responsible for the tracking.
- Continuing or discontinuing the use of at-home tests when disease incidence is low because many more false positives would occur in this situation, which would require further testing.
- Educating the public and those who provide testing in alternate venues (e.g., nursing homes) about at-home and point-of-care testing. A member suggested that education be provided to those who perform testing in non-traditional venues to ensure quality testing regardless of the setting.
- Clarifying the oversight and regulation of on-demand or walk-up testing when a physician has not been consulted or is not on-site to write a prescription. Dr. Stenzel explained that such oversight and regulation is outside the purview of the FDA, and that state and local laws vary with respect to when prescriptions are required.
- Analyzing gaps and providing guidance on telehealth and offering clinical expertise when using an at-home test.
- Engaging with patients whose primary language is not the same as the language of the test's instructions, and those who do not have computers or smartphones.
- Ensuring that specimens are collected correctly for at-home and point-of-care testing, and whether or not that may be accomplished through more education.
- Educating the public about the appropriate use of COVID-19 tests, such as to meet travel or work-related requirements, and following potential exposure etc.

Future CLIAC Topics

Topics suggested by Committee members included:

- The role of Center for Biologics Evaluation and Research (CBER) within FDA that regulates biological products for human use under applicable federal laws, including the Public Health Service Act and the Federal Food, Drug and Cosmetic Act.
 - The relationship between CBER and the Office of In Vitro Diagnostics and Radiological Health (OIR) with transfusion medicine and blood bank testing at the core.
 - The qualifications needed for an immunohematology technical supervisor in CLIA as many Specialists in Blood Banking Technology do not meet current requirements.
- The need for guidance on CLIA validation for next-generation sequencing.
- Continued discussions on health information exchange systems.
- Increased oversight of CLIA-waived and point-of-care testing.
- The role of the laboratory in addressing health disparities.

ACRONYMS

[*Addendum 18*](#)

NOMINATION INFORMATION

[*Addendum 19*](#)

ADJOURN

Drs. Ng and Salerno acknowledged the staff that assembled the meeting agenda and thanked the CLIAC members and partner agencies for their support and participation.

I certify this summary report of the April 14-15, 2021 CLIAC meeting is an accurate and correct representation of the meeting.

Dr. Valerie Ng, CLIAC Chair

Date