Clinical **L**aboratory **I**mprovement **A**dvisory **C**ommittee

Summary Report

April 12-13, 2023

Atlanta, Georgia (Virtual)

U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES

Clinical Laboratory Improvement Advisory Committee (CLIAC) April 12-13, 2023, Summary Report

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RECORD OF ATTENDANCE

Committee Members Present

Dr. Jordan Laser (Chair)
Dr. Birthale Archie
Dr. Esther Babady
Mr. Michael Black
Dr. Chester Brown
Dr. Kimberle Chapin
Dr. James Crawford
Ms. Heather Duncan
Dr. Mary Edgerton
Dr. Tanner Hagelstrom
Dr. Yael Heher
Dr. David Koch
Dr. Hung Luu
Ms. Carole Moss
Dr. Nirali Patel
Dr. Michael Pentella
Ms. Jennifer Rhamy
Dr. Mark Tuthill
Dr. R.W. (Chip) Watkins
Mr. Andy Quintenz, AdvaMed (Liaison Representative)

Ex Officio Members

Dr. Collette Fitzgerald, CDC
Mr. Gregg Brandush, CMS
Dr. Timothy Stenzel, FDA

Designated Federal Official

Dr. Reynolds Salerno, CDC

Executive Secretary

Ms. Heather Stang, 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 277 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 practice. 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 (CDC); the Commissioner, Food and Drug Administration (FDA); the Administrator, Centers for Medicare & Medicaid Services (CMS); 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 sometimes 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 different actions taken by HHS, all of the Committee’s recommendations may not be accepted and acted upon by the Secretary.

CALL TO ORDER AND COMMITTEE INTRODUCTIONS

Dr. Reynolds Salerno, Designated Federal Officer (DFO), Clinical Laboratory Improvement Advisory Committee (CLIAC), and Director of the Division of Laboratory Systems (DLS), Office of Laboratory Science and Safety (OLSS), CDC, welcomed the Committee and the members of the public. Dr. Salerno welcomed Dr. Jordan Laser as the new CLIAC Chair. On both meeting days, Dr. Laser, CLIAC Chairperson, welcomed the Committee and reviewed the process for public comments, quorum requirements, and official CLIAC recommendations. Dr. Salerno introduced the new Committee members, Dr. Esther Babady, Dr. Chester Brown, Dr. Tanner Hagelstrom, Dr. Yael Heher, and Dr. Hung Luu. All members made self-introductions and financial disclosure statements relevant to the meeting topics. Dr. Laser stated that the agenda topics would include agency updates from CDC, CMS, and FDA, an update on the new CLIAC Biosafety Workgroup, and an update on TRUU-Lab. In addition, the meeting would include presentations and discussions on reports from two CLIAC workgroups: the CLIA Regulations Assessment Workgroup and the CLIA Certificate of Waiver and CLIA Certificate for Provider-performed Microscopy Procedures Workgroup, and deliberation of the topic of the laboratory's role in advancing health equity.

AGENCY UPDATES AND COMMITTEE DISCUSSION

Centers for Disease Control and Prevention (CDC) Update ***Addendum 1***

Collette Fitzgerald, PhD
Deputy Director for Science
Division of Laboratory Systems (DLS)
Office of Laboratory Science and Safety (OLSS)
Centers for Disease Control and Prevention (CDC)

Dr. Fitzgerald updated CLIAC with information about CDC's new organizational structure as part of the reorganization and recommendations from the CDC Advisory Committee to the Director's Laboratory Workgroup. Dr. Fitzgerald then highlighted DLS activities in six areas: laboratory preparedness and response, laboratory quality and safety, health equity, laboratory informatics, laboratory training and workforce development, and partnership, communication, and outreach. She discussed the latest outbreaks of H5N1 bird flu and Marburg virus disease and how CDC has responded with guidance for laboratories in the United States. Dr. Fitzgerald informed the members about the CDC and the Association of Public Health Laboratories (APHL) Next Generation Sequencing Quality Initiative's recently completed quality management system, The Extension for Community Healthcare Outcomes (ECHO) Biosafety Project to address challenges in clinical and public health laboratories through the development of a community of practice. She announced that the Blood Culture Contamination Measure submitted to the National Quality Forum as a patient safety measure was endorsed in January 2023 as a national quality measure. She mentioned the current DLS health equity projects and explained that more detail would be provided during the CLIAC session on The Laboratory's Role in Advancing Health Equity. Dr. Fitzgerald updated CLIAC on the CDC-led Forum on Adoption of Standards for Laboratory Data Exchange and Interoperability, which is designed to help address CLIAC's recommendation in November 2021 related to the Systemic Harmonization and Interoperability Enhancement for Lab Data (SHIELD). This monthly forum includes participants from HHS agencies, healthcare-related software vendors, and professional groups, and the forum aims to provide a space for organizations to develop new relationships and discuss challenges and successes related to adopting laboratory data

standards. Dr. Fitzgerald provided updates on OneLab™ activities, including the launch of OneLab TEST on May 1, 2023, the release of a OneLab VR environment for free on the Oculus Store, and the new Career Pathways in Public Health Laboratory Science, a partnership with the Association for Public Health Laboratories that places college students in public health laboratories to gain valuable early career experience. Dr. Fitzgerald highlighted several partnerships, communication, and outreach activities, including the CDC Clinical Laboratory Partners Forum and DLS exhibiting activities. She closed the presentation by highlighting DLS's Medical Laboratory Professionals Week activities to honor laboratory professionals' contributions to public health and patient care.

Centers for Medicare & Medicaid Services (CMS) Update ***Addendum 2***

Gregg S. Brandush, RN, JD
Director
Division of Clinical Laboratory Improvement and Quality (DCLIQ)
Quality, Safety, and Oversight Group (QSOG)
Center for Clinical Standards and Quality (CCSQ)
Centers for Medicare & Medicaid Services (CMS)

Mr. Brandush began by giving an overview of the CMS DCLIQ leadership team, including two new positions, the Survey Technical Advisor and the State Oversight Technical Advisor. He provided the current laboratory enrollment in the CLIA program, including the increased number of Certificate of Waiver (CoW) sites, accounting for 80% of all CLIA-certified laboratories. He compared the number of laboratories by certificate type this year to last year and noted a decrease in the number of CoW laboratories. Mr. Brandush described CMS' goals for 2023, including improved processes and the use of data to ensure efficiency and effectiveness. He explained different CLIA modernization efforts, such as the proficiency testing rule implementation and the availability of electronic CLIA certificates. Mr. Brandush emphasized that the flexibilities implemented during the pandemic are still in place until new guidance that revises, rescinds, or keeps the flexibility in place is released. He provided an overview of the 2023 survey goals to promote quality and consistency. He described how CMS would analyze data to determine where changes can be made to ensure equitable allocation of resources and citation rates between regions. Mr. Brandush concluded his presentation with an overview of lessons learned from the public health emergency (PHE) and emphasized that using CLIA flexibilities allowed rapid expansion of temporary testing sites. He concluded by summarizing the Procedural Guidance for Clinical Laboratory Improvement Amendments (CLIA) Form CMS-116 Changes that Require a New Form CMS-116 or Written. Notification (UPDATED) memorandum.

Food and Drug Administration (FDA) Update ***Addendum 3***

Timothy Stenzel, MD, PhD
Director
Office of In Vitro Diagnostics
Office of Product Evaluation and Quality (OPEQ)
Center for Devices and Radiological Health (CDRH)
U. S. Food and Drug Administration (FDA)

Dr. Stenzel began his presentation with an update on the reauthorization of the Medical Device User Fee Amendments for fiscal years 2023 through 2027 (MDUFA V), which authorizes FDA to collect user fees for the review of device applications. He noted that CDRH accepts and initiates the review process for all new IVD premarket submissions and pre-submissions per

the performance goals established in the MDUFA V Commitment Letter. He explained that CDRH is working to clear the backlog of premarket submissions created due to the more than 6,000 COVID-19 submissions during the pandemic. Dr. Stenzel gave an update on tests for both COVID-19 and MPOX, including the number and description of the currently available tests. Next, he discussed the National Institutes of Health (NIH) Rapid Acceleration of Diagnostics (RADx) Independent Test Assessment Program (ITAP), established to accelerate regulatory review and availability of high-quality, accurate, and reliable over-the-counter (OTC) COVID-19 tests available to the public. He highlighted nine tests authorized after an ITAP evaluation by this collaboration between the FDA and the NIH RADx program. Dr. Stenzel noted that over 30 OTC COVID-19 diagnostic tests were authorized, and the FDA provides a List of Authorized At-Home OTC COVID-19 Diagnostic Tests, including links to home use instructions for each test. He summarized a policy update from September 2022 regarding COVID-19 test modifications, enforcement, and use of the traditional pathway for full authorization to ensure the availability of tests. Dr. Stenzel presented the Emergency Use Authorization (EUA) review priorities, explaining that CDRH will focus on diagnostic tests with significant public health benefits and may include new technologies that fulfill an unmet need. He listed several novel authorizations, including the first OTC test to detect both influenza and COVID-19 viruses. He briefly explained two guidances issued in March 2023 for the transition period when the PHE ends, resulting in the end of the EUA authorities for COVID-19. He stated that the guidances reflect FDA's awareness of the continued requirement for available tests and the need to facilitate the authorization process to move tests from EUA to fully authorized status. He added that the dual pathway for a 510(k) CLIA-waiver application is available and that Congress gave FDA authority to perform a Dual De Novo and CLIA-waived review for COVID diagnostic tests. In addition to the COVID guidances, Dr. Stenzel discussed a September 2022 guidance that established review priorities for MPOX, including an enforcement policy for some laboratory developed tests and serology tests and recommendations for diagnostic test validation. He ended his presentation with a description of the outreach opportunities both during the pandemic and currently ongoing. He shared that FDA granted authorization for a new test to improve the diagnosis of Alzheimer's Disease.

CLIAC Biosafety Workgroup Update ***Addendum 4***

Víctor De Jesús, PhD
Chief, Quality and Safety Systems Branch (QSSB)
Division of Laboratory Systems (DLS)
Office of Laboratory Science and Safety (OLSS)
Centers for Disease Control and Prevention (CDC)

Dr. De Jesús, the designated federal officer for the new CLIAC Biosafety Workgroup, provided an overview of the five CLIAC recommendations made between 2001 and 2019 that address laboratory safety. He highlighted the June 2022 CDC Town Hall Meeting on Laboratory Biosafety – Use of Laboratory Instruments that provided an overview and discussion on laboratory biosafety when using laboratory instruments to test human and biologic specimens and resulted in an agreement for CDC, CMS, and FDA to convene a workgroup to continue addressing the issues raised during the town hall. Dr. De Jesús thanked Dr. Michael Pentella for agreeing to serve as the chair, shared the workgroup charge, and explained upcoming steps. He closed the presentation by stating that the Committee will be updated as the process progresses.

Update on TRUU-LAB *Addendum 5*

Ila Singh, MD, PhD
Chief of Laboratory Medicine
Chief of Pathology Informatics
Texas Children's Hospital
Professor, Baylor College of Medicine

Dr. Singh began the presentation with real-life examples of the challenges due to the lack of standardized test names and how they directly affect patient health. She stated multiple reasons for the laboratory test name challenges, including that test names are usually chosen without consulting clinicians, without a style guide or guidance to refer to, and without consultation with other institutions. Dr. Singh provided an overview of the previous attempts at standardizing laboratory test names and stated that despite initiatives such as Logical Observation Identifiers Names and Codes (LOINC), there are still challenges to test naming. Dr. Singh explained that Test Renaming for Understanding and Utilization Laboratory (TRUU-Lab) initiative aims to gather healthcare providers, professional societies, industry groups, and federal liaisons to develop consensus naming guidelines for standardizing laboratory test names and to promote the adoption and implementation of the names and guidelines. She illustrated the comprehensive nature of the groups involved, including international partners who experience the same challenges as in the United States when naming laboratory tests. Dr. Singh discussed pilot surveys sent to primary care providers to assess intuitive name preferences given a short and specific prompt. She explained how the survey results illustrated why test names are challenging, including ambiguity, confusing abbreviations, different names for the same analyte, and character limits in previous versions of electronic medical records and laboratory information systems. She described how the TRUU-Lab initiative, in collaboration with the Brand Institute's Drug Safety Institute, currently surveys clinicians in different specialties about laboratory test names and explained the survey design used to minimize preconceptions. She presented the list of survey modules that have been completed; the data are being analyzed now, and the survey modules are in progress. Dr. Singh finished her presentation with the project's next steps to accomplish the goal of better laboratory test names.

PRESENTATIONS AND COMMITTEE DISCUSSION

CLIAC Workgroup Reports

CLIA Regulations Assessment Workgroup Report *Addendum 6* *Addendum 6a*

Gregory N. Sossaman, MD
System Chairman, Ochsner Health System
Department of Pathology and Laboratory Medicine
Ochsner Medical Center

Kimberle C. Chapin, MD, ABMM, FCAP
Medical and Scientific Affairs
Cepheid

Dr. Sossaman thanked the workgroup members and presented an interim report from the CLIA Regulations Assessment Workgroup. He provided an overview of the workgroup charge, membership, scope, and discussion topics. Dr. Sossaman then provided an overview of the

workgroup agreements regarding analytical testing specifications found in CLIA Subpart K – Quality Systems for Nonwaived Testing.

Public Comments
Addendum PC1 ***Addendum PC2*** ***Addendum PC3*** ***Addendum PC4***

Committee Discussion
The Committee discussed the workgroup agreements summarized in the CLIA Regulations Assessment Workgroup presentation and report. Relevant CLIAC member comments follow.

- In response to a member's question about home-collected specimen adequacy, Dr. Stenzel clarified that FDA has authority over home collection devices and home tests, and emphasized that FDA addresses adequacy controls on a case-by-case basis during the FDA review process.
- Several members discussed the workgroup agreement relating to the requirement for confidentiality of patient information under § 493.1231, mainly as applied to data transfer to referral laboratories or other entities. A member expressed concern that the workgroup agreement said ensuring patient confidentiality during data transfer must include cloud-based computing, which would infer that laboratories must implement cloud-based computing methods. The workgroup chairs clarified that cloud-based computing was discussed as an example of one data transfer mechanism.
- Members discussed electronic data analysis and suggested that a new standard related to data analysis is needed to address all data types that can be manipulated to generate a final laboratory test result.
- Several members discussed the workgroup agreement related to § 493.1232 for specimen identification and integrity. Members agreed that the requirements for having and following documented policies and procedures for specimen acceptance and rejection should not specify home collection but should be general and address all specimens collected outside the laboratory.
- Members discussed the regulations related to the phrase "reportable range," both in § 493.1251(b)(6) for procedure manuals and § 493.1253 related to the establishment or verification of reportable range. They agreed that many qualitative tests do not have reportable ranges, and there are challenges in applying these parts of the regulations.
- Several members discussed the use of the phrase "expected result" as a replacement for "reference intervals (normal values)" in §§ 493.1251 and 493.1253 of the CLIA regulations. Some members thought that using "expected result" would be confusing if the expected result was an abnormal value. Another member suggested including "expected result as defined by the methodology." One member commented that "normal values" should be replaced with "reference intervals."
- Members discussed the need to provide guidance in the CMS State Operations Manual (SOM) for control procedures for platforms that produce multiple results, such as multiplex cartridges, genetic panels, and similar tests. The members questioned whether two levels of controls were feasible or needed for every organism or genetic test performed using such technologies.
- Several members discussed the workgroup agreement that the cytology regulations at § 493.1274 for workload reporting should be clarified to account for the use of immunocytochemical tests. Members noted that the workload of a cytotechnologist is more diverse than when the law was passed in 1988, and agreed that the regulations should be reevaluated in recognition of the more diverse interpretive workload and practice context.

- The CLIAC members disagreed with the workgroup proposal to remove the requirement for an annual statistical laboratory evaluation for cytology at § 493.1274(c)(5).
- Multiple members discussed the workgroup agreement that the regulations related to the requirement for test records at § 493.1283(a) should be updated to include a requirement for specimen collection date and time. Several members provided various scenarios in which samples would not be processed or rejected if there was a requirement for a sample collection time. Other members agreed that there should be a requirement for specimen collection time.

The Committee deliberated, voted, and approved the following recommendations based on the CLIA Regulations Assessment Workgroup Report on the CLIA Subpart K – Quality Systems for Nonwaived Testing. CLIAC recommends that HHS consider modifying the CLIA Subpart K as follows:

Recommendation 1: CLIA Subpart K - Quality System for Nonwaived Testing should be updated to reflect past CLIAC recommendations related to remote and distributive testing from April 2022 and November 2022.

Recommendation 2: The definitions in the CLIA regulations or CMS State Operations Manual (SOM) should be updated to include terms related to the establishment of performance specifications for both qualitative and quantitative tests, including accuracy, precision, analytical sensitivity, and specificity. Information in the SOM should include published professional organization guidelines, as applicable.

Recommendation 3: Subpart K - Quality System for Nonwaived Testing, Analytic Systems should be generalized to address quantitative and qualitative test modalities.

Recommendation 4: The regulations on quality assessment at § 493.1200(b) should be clarified to address the recurrence of problems, “The laboratory's quality systems must include a quality assessment component that ensures continuous improvement of the laboratory's performance and services through ongoing monitoring that identifies, evaluates, resolves, and limits the likelihood of the recurrence of problems.”

Recommendation 5: A new standard related to data analysis is needed in Subpart K - Quality System for Nonwaived Testing under General Laboratory Systems, to encompass all data types that can be manipulated to generate a final laboratory test result.

Recommendation 6: Additional information relating to the confidentiality of patient information should be included in § 493.1231 that the laboratory must follow documented policies and procedures to ensure patient confidentially during data transfer to external referral laboratories, remote testing locations, or other entities. This may include cloud-based computing, such as storing confidential data, as appropriate. The laboratory must comply with other Federal laws, including but not limited to the HIPAA Final Security Rule.

Recommendation 7: The specimen identification and integrity regulations under § 493.1232 should be clarified to include a requirement that the laboratory must follow documented policies and procedures for specimen acceptance and rejection.

Recommendation 8: CLIAC recommends that CMS include information related to specimens collected outside of the laboratory's control in the SOM.

Recommendation 9: The use of "panic or alert values" should be replaced with "critical value" at §§ 493.1241(c)(1), 493.1251(b)(11), 493.1251(b)(13), and 493.1291(g).

Recommendation 10: The specimen labeling requirement at § 493.1241(c)(2) and § 493.1242(a)(3) should be updated to remove "patient name or unique patient identifier…" and include "at least two unique patient-specific identifiers."

Recommendation 11: The procedure manual requirement § 493.1251(a) should be updated to remove the reference to "Textbooks" and replace it with "resource materials reflecting the current standard of care." This change should also be made at § 493.1253(b)(2) to include "…or other materials reflecting the current standard of care."

Recommendation 12: Additional information is needed under the procedure manual requirements under § 493.1251(b) to include information related to data analysis. For example, § 493.1251(b)(3) should consist of data collection and analysis. Examples can be added to the SOM.

Recommendation 13: The SOM should be updated to include a definition of interfering substances as mentioned in § 493.1251(b)(9).

Recommendation 14: The current use of "Reference intervals (normal values)" should be replaced with "Reference intervals or expected results as appropriate to the test system" at §§ 493.1251(b)(10), 493.1253(b)(1)(ii), 493.1253(b)(2)(vi), 493.1282(b)(iii), and 493.1291(d).

Recommendation 15: The SOM should include examples of reference intervals or expected results as appropriate to the test system for both qualitative and quantitative tests.

Recommendation 16: The CLIA regulations under § 493.1252 or SOM should be updated to include new technologies or testing practices for each specialty or subspecialty, data exchange, analysis, and remote/distributive work requirements. The November 2022 CLIAC recommendation to modify the definition of a "test system" to include "…software algorithms, data exchange and analysis procedures, and other components needed to perform an assay or examination and generate test results and report" should be incorporated into this section.

Recommendation 17: The regulations related to test systems not subject to FDA clearance or approval at § 493.1253(b)(2) should be updated to replace "in-house" with "laboratory developed test" terminology.

Recommendation 18: The CLIA regulations and SOM should be updated to include harmonized definitions for the terms used in § 493.1253(b)(i-vii) so they apply to qualitative and quantitative tests.

Recommendation 19: The SOM should be updated to include more guidance related to calibration verification procedures under § 493.1255(b). This should include clarification between the analytical measurement range and the reportable range.

Recommendation 20: The requirement for including at least a minimal (or zero) value, a mid-point value, and a maximum value near the upper limit of the range to verify the laboratory's reportable range of test results for the test system at § 493.1255(b)(2)(ii) is problematic for qualitative assays. The regulations should be clarified for qualitative assays, or the current regulations should be modified to include “as applicable to the test system.” Also, many test systems do not have a “zero” value. The regulations should be updated to remove the reference to a “zero” value.

Recommendation 21: The SOM should be updated to include more guidance on control procedures under § 493.1256 for platforms producing multiple results, such as multiplex cartridges, genetic panels, etc.

Recommendation 22: The SOM should be updated to include guidance for tests where two levels of quality control are not beneficial.

Recommendation 23: The specification for thin layer chromatography under § 493.1256(d)(4) should be removed from the CLIA regulations and included in the SOM.

Recommendation 24: The specialty and subspecialty sections starting § 493.1261 through § 493.1278 should be updated to address outdated regulations and update the regulations to incorporate changes in technology.

- Generalized statements should be developed for each specialty and subspecialty section to account for new test technologies and the need for remote test analysis and reporting of test results.
- A crosswalk should be performed in these sections with the general considerations section.
- The SOM should include information specific to each specialty or subspecialty.

Recommendation 25: The regulations related to immunohematology at § 493.1271(c) should be updated to change “inspected” to “tested.” Also, the CLIA regulations at § 493.1271(c)(2) should be updated to “Alarm system testing must be documented.”

Recommendation 26: The regulations related to cytology at § 493.1274 should be reevaluated in recognition of the more diverse interpretive workload and practice context.

Recommendation 27: The SOM should be updated to clarify the comparison of test results requirements described under § 493.1281. The update should include the following:

- Information on what is considered as the same test using different methodologies or instruments.
- Examples of what is considered when something is regarded as the same analyte, e.g., different specimen types, different analytic targets (troponin I versus T or HS troponin), different analytic or therapeutic ranges, tests with different sensitivities, and qualitative versus quantitative tests.

Recommendation 28: The regulations related to the requirement for test records at § 493.1283 should be updated to include patient confidentiality requirements.

Recommendation 29: The regulations related to the requirement for test records at § 493.1283(a) should be updated to include a requirement for specimen collection date and time in accordance with laboratory-specified requirements.

CLIA Certificate of Waiver and Certificate for Provider-performed Microscopy Procedures Workgroup Report *Addendum 7* *Addendum 7a*

Heather Duncan, MPH, MT
Director of Laboratory Operations
ECU Health Medical Center

Ms. Duncan thanked the workgroup members and presented the final report from the CLIA Certificate of Waiver and Certificate for Provider-performed Microscopy (PPM) Procedures Workgroup. She provided an overview of the workgroup charge, membership, and discussion topics. She briefly highlighted the PPM project that was initiated by CMS in 2020. Ms. Duncan continued by summarizing the workgroup discussions related to the questions outlined in the workgroup report. She concluded with the workgroup agreements about routine inspections and competency assessments.

Committee Discussion
The Committee discussed the workgroup agreements summarized in the CLIA Certificate of Waiver and Certificate for Provider-performed Microscopy Procedures Workgroup report. Relevant CLIAC member comments follow.

- A member suggested the development of a checklist to tailor the CLIA competency assessment requirements for personnel performing PPM procedures.
- One Committee member requested clarification on the CLIA regulations for moderate complexity testing and how they apply to sites under a CLIA Certificate for PPM Procedures. Mr. Brandush commented that PPM sites are required to follow the CLIA regulations at Subpart K – Quality System for Nonwaived Testing as stated in § 493.1235. He added that the CLIA regulations do not include PPM-specific competency requirements. Mr. Brandush confirmed that CMS does not regularly inspect CLIA Certificate of PPM Procedures sites unless there is a complaint.
- Several members commented that physicians performing PPM procedures should not be required to perform competency assessments. One member added that a medical affairs department is often responsible for communicating scientific and clinical information and ensuring the competency assessment is conducted in their facility. Members agreed that all laboratory staff need regular competency assessment and training. Therefore, the same should be required for personnel who perform PPM procedures.

The Committee deliberated, voted, and approved the following recommendations based on the CLIA Certificate for Provider-performed Microscopy Procedures topic:

Recommendation 30: CLIAC recommends that more information is needed about CLIA Certificate for Provider-performed Microscopy Procedure sites and suggests the expansion of the CMS PPM Project.

Recommendation 31: CLIAC recommends that CLIA regulations be modified to implement routine inspection for CLIA Certificate for Provider-performed Microscopy sites.

Recognition of Outgoing CLIAC Members ***Addendum 8***

Reynolds Salerno, PhD
Director
Division of Laboratory Systems (DLS)
Office of Laboratory Science and Safety (OLSS)
Centers for Disease Control and Prevention (CDC)

Dr. Salerno recognized the CLIAC outgoing members, Dr. Birthale Archie, Ms. Carole Moss, and Ms. Jennifer Rhamy, for their contributions to the Committee.

The Laboratory's Role in Advancing Health Equity

Update on DLS Activities ***Addendum 9***

Víctor De Jesús, PhD
Chief, Quality and Safety Systems Branch (QSSB)
Division of Laboratory Systems (DLS)
Office of Laboratory Science and Safety (OLSS)
Centers for Disease Control and Prevention (CDC)

Dr. De Jesús began by explaining that health equity is a guiding principle for the CDC's Division of Laboratory Systems' most recent strategic framework. It also supports CDC's incorporation of health equity in its CORE (Cultivate, Optimize, Reinforce, Enhance) strategy. He updated the Committee on DLS activities to promote health equity, including increasing the number of new Electronic Test Orders and Results (ETOR) systems between public health laboratories, healthcare providers, and systems to support the medically underserved. He also described a current DLS initiative aimed at adding a laboratory outreach component to the Million Hearts® Quality Improvement, Preventing Health Attacks and Strokes Project. Finally, he discussed a collaboration to identify barriers to laboratory fellowship and internship participation and pursuit of laboratory careers, and a study to identify practices to increase equitable point-of-care (POC) testing in public health emergencies. Dr. De Jesús concluded his presentation by introducing the topic presentations and providing an overview of the questions for CLIAC deliberation.

Prevalence and Incidence of End-Stage Kidney Disease in the United States, 2000–2019

Alain Koyama, ScD ***Addendum 10***
Epidemiologist ***Addendum 10a***
Division of Diabetes Translation
National Center for Chronic Disease and Health Promotion
Centers for Disease Control and Prevention

Dr. Koyama began his presentation by providing background on end-stage kidney disease (ESKD), specifically focusing on the disparities of two ESKD risk factors, hypertension, and diabetes. He explained that although the prevalence and incidence of diabetes and the incidence of ESKD have been decreasing, health resources for ESKD are still essential to examine. He explained that the Morbidity and Mortality Weekly Report (MMWR) on the *Reported Cases of End-Stage Kidney Disease — United States, 2000–2019,* investigated the incidence and prevalence of ESKD each year by specific demographics. Dr. Koyama described the methods used to collect the data and discussed the findings, noting that the prevalence and incidence of cases are increasing over the 20 years studied. He stated that

there were limitations to the study due to using data based on reports to CMS, obtaining the ESKD cause from the physician's assessment, and misclassification of race or ethnicity. He concluded by stating that ESKD will continue to burden the healthcare system. Future directions include improving care and management of ESKD risk factors and addressing the disparities observed in preventing and treating ESKD, hypertension, and diabetes.

Implementation of the CKD-EPI 2021 eGFR Equation Re-fit without Race Co-efficient

M.J. Lewis
Senior Project Director
CKDintercept
National Kidney Foundation

Addendum 11
Addendum 11a

Jonathan Genzen, MD, PhD
Professor, University of Utah
Chief Medical Officer, ARUP Laboratories

Ms. Lewis began by introducing the National Kidney Foundation's CKDintercept program, which aims to improve primary care testing, recognition, and management of chronic kidney disease (CKD). She presented published data showing that 37 million adults have chronic kidney disease. Still, almost 90% are unaware of their condition, and less than 30% of those with diabetes and only about 10% of those with hypertension had received the guideline-concordant assessment, comprised of eGFR and urine albumin-to-creatinine ratio. Ms. Lewis described the efforts of the National Kidney Foundation (NKF) and the American Society of Nephrology task force to reassess the inclusion of race in the estimation of glomerular filtration rate (eGFR). Ms. Lewis promoted the *New Creatinine- and Cystatin C–Based Equations to Estimate GFR without Race* 2021 publication in The New England Journal of Medicine. She explained that the NKF's Laboratory Engagement Initiative (LEI), comprised of pathologists and laboratory leadership from across the United States, created guidance documents and tools to facilitate laboratory implementation of the task force recommendations. Ms. Lewis highlighted several efforts to promote the use of the race-free eGFR equation, including the findings from NKF surveys to demonstrate the implementation status.

Dr. Genzen continued the presentation by explaining the eGFR and how the 2009 CKD Epidemiology Collaboration (CKD-EPI) published eGFR rate is calculated. He described that the 2009 eGFR calculation contains adjustment factors for age, females, and the Black/African American population. Dr. Genzen explained the timeline for developing and publishing the 2021 CKD-EPI Creatinine and 2021 CKD-EPI Creatinine-Cystatin C equations. He provided an overview of the 2022 College of American Pathologists (CAP) five-question survey to assess awareness and adoption of the 2021 CKD-EPI equations. This survey was provided to clinical laboratories enrolled in the first event of the 2022 CAP general chemistry proficiency testing module. Dr. Genzen highlighted that the survey was distributed to 6,000 clinical laboratories and was completed by 4,300 laboratories. He concluded with an overview of the guidance documents and tools available to assist laboratories with implementing the race-free eGFR equation.

Health Disparities in Hemodialysis-Associated Staphylococcus aureus Bloodstream Infections —United States, 2017–2020 ***Addendum 12*** ***Addendum 12a***

Shannon Novosad, MD, MPH
Medical Officer
Dialysis Safety Team
Division of Healthcare Quality Promotion
National Center for Emerging and Zoonotic Infectious Diseases
Centers for Disease Control and Prevention

Brian Rha, MD, MSPH
Medical Epidemiologist
Dialysis Safety Team
Division of Healthcare Quality Promotion
National Center for Emerging and Zoonotic Infectious Diseases
Centers for Disease Control and Prevention

Dr. Novosad began by providing background information on the population with end-stage kidney disease (ESKD) in the United States. She provided data showing that bloodstream infections (BSIs) are the leading cause of morbidity and mortality in patients on hemodialysis, with *Staphylococcus aureus* being the most common pathogen. Dr. Novosad noted that ESKD prevalence had been shown to vary by race and ethnicity and that compared to non-Hispanic white persons, ESKD prevalence is four-fold higher in Black persons and more than two-fold higher in Hispanic persons. Dr. Novosad added that there are general disparities in ESKD and disparities related to inequities in six key areas of social determinants of health. She continued by introducing the study's primary objective, which was to characterize markers of disparities in burden and risk for *Staphylococcus aureus* bloodstream infections in patients on hemodialysis.

Dr. Rha continued the presentation by discussing the methods and results of a study. He stated that the National Safety Network (NHSN) and the Emerging Infections Program (EIP) provided BSI surveillance data from dialysis patients. He explained that both surveillance programs are in the CDC's Division of Healthcare Quality and Promotion and were included to help address the limitations of each surveillance data set. He provided an overview of the general approach of the study: first, to calculate rates of *Staphylococcus aureus* BSIs in hemodialysis patients using each of these data sets, and then, to assess for associations between dialysis-associated *Staphylococcus aureus* BSI and markers of health disparities, such as race and ethnicity, and markers of social determinants of health, such as socioeconomic factors and measures of social vulnerability. Dr. Rha explained that the findings from analyzing the NHSN data showed that over 5,000 out of 114,822 reported dialysis BSIs were due to *Staphylococcus aureus*. He highlighted that the EIP data showed that the central venous catheters (CVC) vascular access type is strongly associated with *Staphylococcus aureus* BSIs. He added that race, ethnicity, and socioeconomic factors played a role in the burden of dialysis BSIs. Dr. Rha concluded that many dialysis patients are minorities, and the importance of using culturally and language-appropriate patient education to improve understanding of infection prevention.

Public Comments
Addendum PC5 ***Addendum PC6***

Committee Discussion

- A CLIAC member inquired about the scoping review currently conducted by DLS to identify promising practices associated with increased, equitable access to POC testing during public health emergencies or outbreaks. The member asked if the study would evaluate how the closure of acute care hospitals in rural areas would impact access to POC testing. After the meeting, Dr. De Jesús and the DLS Evaluation Office responded that the study sample reflects only sites with CoW as of January 28, 2022. It includes some hospitals, but most hospitals are certified to conduct moderately complex diagnostic testing, so only a small sample of hospitals will likely be included in this CoW analysis; it may not include acute care hospitals in rural areas.
- One member requested clarification on the scoping review process and whether it included a review of data from grey literature. The member added that the NIH RADx program has funded studies and programs related to POC testing during public health emergencies and suggested those studies may provide valuable data. After the meeting, Dr. De Jesús and the DLS Evaluation Office responded that the current scoping review focuses on research questions related to approaches to increase equitable access to POC testing during public health emergencies or outbreaks evaluated in the literature over the past five years. Dr. De Jesús added that based on preliminary results from the title/abstract review for the full scoping review, 109 peer-reviewed publications and 46 grey literature reports met the inclusion criteria. Regarding the grey literature, many reports were identified from the NIH RADx program and its partners.
- A member noted that recent studies indicate that two independent variants of the Apolipoprotein L1 (APOL1) gene, G1, and G2, have been associated with a greater risk of developing non-diabetic ESKD in African Americans. The member asked if APOL1 testing was considered in the Morbidity and Mortality Weekly Report (MMWR) publication on the Reported Cases of End-Stage Kidney Disease — United States, 2000–2019. Dr. Koyama responded that genetic testing was not included in the publication but noted that genetic epidemiology studies indicate that APOL1 should be included as a genetic risk score.
- A member inquired if the race-free eGFR surveys stratified the adoption of the race-free eGFR equation by size and type of laboratories. Dr. Genzen responded that the survey results had shown greater adoption of the race-free eGFR equation in larger systems such as hospital and academic medical center settings. He stated that, based on survey results, there had been a lower adoption rate in physician office laboratories. Dr. Genzen noted that physician office laboratories are not necessarily the largest enrollee in the CAP general chemistry proficiency testing module and may not have received the survey.
- Another member asked if there were any plans to assess the impact of using the race-free eGFR equation. Ms. Lewis responded that the NKF had not conducted any follow-up surveys or publications but is focusing on increasing awareness of the new equation. Dr. Genzen added that the collaboration between professional societies has been invaluable in raising awareness.
- A CLIAC member inquired if implementing the race-free equation would require an update in the laboratory information system which could hinder adoption. Dr. Genzen agreed that some institutions might lack information technology support to implement,

validate, and verify the new equation. He added that there is an opportunity for electronic health record vendors to help their customers implement this equation.

- A member requested clarification on the MMWR-reported relationship between the type of vascular access and the populations at risk for bloodstream infections and if data are available for the type of vascular access by race and ethnicity, poverty, crowding, and education. Dr. Novosad responded that the data come from several sources, including the U.S. Renal Data System (USRDS) and EIP. Dr. Rha added that the multivariable analyses accounted for vascular access type.
- Another member added that a BSI comparison to the oncology population with catheters would be beneficial. Dr. Novosad responded that a comparison to other groups with long-term catheters, such as oncology patients, has not been performed but may assist in identifying underlying differences in the patient populations and how they might contribute.
- The same member asked how long the catheters were in place in the MMWR studies and noted that in apheresis, *Staphylococcus aureus* BSIs frequently originate from catheter placement. Dr. Novosad stated that granular-level data on catheter duration were not available.
- One member inquired if the *Staphylococcus aureus* BSI was identified using a single draw from a catheter or a peripheral draw. The member noted that many people are colonized with *Staphylococcus aureus,* and culture contamination from skin flora is challenging. Dr. Novosad responded that the blood draw source was not specified.
- A member noted the 2023 National Academies of Sciences, Engineering, and Medicine publication entitled Using Population Descriptors in Genetic and Genomics Research with recommendations that provide a framework for using such population descriptors in future genetics and genomics studies. The member urged that race should be in the appropriate context whenever used as a population descriptor.
- In response to the question, "How can the clinical laboratory contribute towards closing racial/ethnic inequities in chronic kidney disease?" the CLIAC members discussed the need for a CLIAC workgroup to address the laboratory's role in advancing health equity.
- In response to the question, "Recognizing that the laboratory community has made significant strides in implementing the CKD-EPI 2021 eGFR race-free equation, how do we engage to further advance the implementation of the race-free equation?" the CLIAC members discussed:
    - The need for additional promotional and educational activities to advance the use of the CKD-EPI 2021 eGFR race-free equation;
    - The need for implementation guides for sites, such as smaller POC testing facilities, to assist with IT support and interoperability challenges related to implementation; and
    - The need to determine if some laboratory test devices are not harmonized and capable of performing testing based on the CKD-EPI 2021eGFR race-free equation.

The Committee deliberated, voted, and approved the following recommendations on the topic of the laboratory's role in advancing health equity:

Recommendation 32: CLIAC recommends the formation of a workgroup to determine how the clinical laboratory can contribute to health equity and population health and to closing racial/ethnic inequities in disease conditions with substantive disparities in incidence, prevalence, and outcomes. The scope is to be chronic kidney disease and its contributing

factors, including social determinants of health, including examining barriers to closing these inequities.

Recommendation 33: CLIAC recommends that the FDA evaluate instruments that cannot implement the CKD-EPI 2021 eGFR race-free equation, standardize the creatinine methods, and report back to CLIAC during the November 2023 meeting.

Recommendation 34: CLIAC recommends that the CDC's Division of Laboratory Systems work with partners, such as professional organizations, community groups, and others, to provide outreach and training related to the CKD-EPI 2021 eGFR race-free equation.

Future CLIAC Topics

Topics suggested by Committee members included

- Expansion of agency training efforts beyond public health and into clinical testing sites such as community centers and rural hospitals and efforts to increase access to care.
- Efforts to address delayed response to abnormal laboratory test results or alerts that delay patient treatment or harm.
- Need to update the CLIA histocompatibility regulations to allow for virtual crossmatch.
- Update the efforts to address the CMS CLIA top 10 deficiencies.
- Diverse and equitable solutions to identify sepsis quickly.
- Continued discussions on the laboratory workforce to stay abreast of the shortage crisis.

CLIAC APRIL12-13, 2023 MEETING AGENDA

Addendum 13

CLIAC MEETING TRANSCRIPT

Addendum 14

NOMINATION INFORMATION

Addendum 15

ADJOURN

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

I certify that this summary report of the April 12-13, 2023, CLIAC meeting accurately and correctly represents the meeting.

Dr. Jordan Laser, CLIAC Chair Date