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

Summary Report

April 10-11, 2019

Baltimore, Maryland

U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES

Clinical Laboratory Improvement Advisory Committee
April 10-11, 2018, Summary Report

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RECORD OF ATTENDANCE

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

Committee Members Absent
Dr. Keith Davis
Dr. Thomas Williams

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

Designated Federal Official
Dr. Reynolds Salerno, CDC

Executive Secretary
Ms. Nancy Anderson, CDC

Record of Attendance – cont'd

Centers for Disease Control and Prevention (CDC)

Ms. Natasha Griffith
Ms. Stacy Howard
Ms. Heather Stang

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

Ms. Julia Appleton, CMS
Ms. Lori Ashby, CMS
Ms. Sarah Bennett, CMS
Ms. Seraphina Brea, CMS
Dr. Joseph Chin, CMS
Ms. Cindy Flacks, CMS
Ms. Rachel Jacobs, CMS
Mr. Shyam Kalavar, FDA
Ms. Penny Keller, CMS
Ms. Linda Lebovic, CMS
Dr. Carl Li, CMS
Dr. Jinong Li, FDA
Dr. Shari Miura Ling, CMS
Dr. James Rollins, CMS
Ms. Tennille Rogers, CMS
Ms. Melissa Singer, CMS
Dr. Xiufen Sui, CMS
Ms. Debra Sydnor, CMS
Dr. Katherine Szarama, CMS
Ms. Kathleen Todd, CMS
Ms. Felicidad Valcarcel, CMS
Ms. Regina Van Brakle, CMS
Ms. Harriet Walsh, CMS
Dr. Zivana Tezak-Fragale, FDA

In accordance with the provisions of Public Law 92-463, the meeting was open to the public. Approximately 100 public citizens attended one or both days of the meeting. The meeting was also available by webcast.

CLINICAL LABORATORY IMPROVEMENT ADVISORY COMMITTEE (CLIAC) BACKGROUND

The Secretary of Health and Human Services is authorized under Section 353 of the Public Health Service Act, as amended, to establish standards to assure consistent, accurate, and reliable test results by all clinical laboratories in the United States. The Secretary is authorized under Section 222 to establish advisory Committees.

The Clinical Laboratory Improvement Advisory Committee (CLIAC) was chartered in February 1992 to provide scientific and technical advice and guidance to the Secretary and the Assistant Secretary for Health pertaining to improvement in clinical laboratory quality and laboratory medicine. In addition, the Committee provides advice and guidance on specific questions related to possible revision of the 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. Members are selected by the Secretary from authorities knowledgeable in the fields of microbiology, immunology, chemistry, hematology, pathology, and representatives of medical technology, public health, clinical practice, and consumers. In addition, CLIAC includes three ex officio members, or designees: the Director, Centers for Disease Control and Prevention; the Commissioner, Food and Drug Administration; the Administrator, Centers for Medicare & Medicaid Services; and such additional officers of the U.S. Government that the Secretary deems are necessary for the Committee to effectively carry out its functions. CLIAC also includes a non-voting liaison representative who is a member of AdvaMed and such other non-voting liaison representatives that the Secretary deems are necessary for the Committee to effectively carry out its functions.

Due to the diversity of its membership, CLIAC is at times divided in the guidance and advice it offers to the Secretary. Even when all CLIAC members agree on a specific recommendation, the Secretary may not follow their advice due to other overriding concerns. Thus, while some of the actions recommended by CLIAC may eventually result in changes to the regulations, the reader should not infer that all of the Committee's recommendations will be automatically accepted and acted upon by the Secretary.

CALL TO ORDER AND COMMITTEE INTRODUCTIONS

Dr. Ramy Arnaout, CLIAC Chair, welcomed the Committee and called the meeting to order. 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. All members then made self-introductions and financial disclosure statements relevant to the meeting topics. Dr. Arnaout acknowledged the importance of public participation in the advisory process and took a roll call of the members present.

Dr. Arnaout stated that the agenda topics would include updates from the CDC, CMS, the FDA, and the CLIAC liaison to the CDC Office of Infectious Diseases (OID) Board of Scientific Counselors (BSC). In addition, there would be presentations and discussions on the Personnel Regulations Workgroup Report, the Nontraditional Workflow Workgroup Report, and the Next Generation Sequencing Workgroup Report.

AGENCY UPDATES AND COMMITTEE DISCUSSION

Centers for Disease Control and Prevention (CDC) Update *Addendum 3*

Collette Fitzgerald, PhD
Associate 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 DLS's work in four priority goal areas: quality laboratory science, highly competent laboratory workforce, safe and prepared laboratories, and accessible and usable laboratory data. She highlighted the publication of the CLIA proficiency testing (PT) proposed rule, noting the extended comment period ending on June 4, 2019. She also described the three recent CLIAC workgroups, emphasizing that this was the first time that more than one workgroup was convened between CLIAC meetings. Dr. Fitzgerald informed the members of the Diagnostic Error Scoping Review Project being performed by DLS, a structured literature review focused on summarizing and reporting clinical laboratory practices, challenges, and opportunities that support accurate and timely diagnoses, reduce diagnostic errors, and promote multidisciplinary collaborations to improve health care quality and patient safety. She noted that CDC will be coordinating with the Eagleson Institute and the American Biological Safety Association to lead the 16th International Symposium on Biosafety in Atlanta, GA in 2020. Dr. Fitzgerald announced the signed charter for the Tri-Agency Task Force for Emergency Diagnostics, formed to improve the implementation of Emergency Use Authorization assays. She reported that DLS is exploring the utility of opioid-related testing data for large commercial laboratories that provide referral testing services, noting the Council of State and Territorial Epidemiologists release of a position statement to help states to identify non-fatal overdose cases. She closed with a review of DLS laboratory training courses, including the current status and future activities of the Workforce Assessment of Laboratory Communities (WALC) project.

Centers for Medicare & Medicaid Services (CMS) Update *Addendum 4*

Karen Dyer MT (ASCP), DLM
Director
Division of Clinical Laboratory Improvement and Quality (DCLIQ)
Quality, Safety and Oversight Group (QSOG)
Centers for Medicare & Medicaid Services (CMS)

Ms. Dyer began with the current laboratory enrollment in the CLIA program, including the number of accredited laboratories and certifications among the self-selected laboratory types. She reviewed laboratory director citations and distribution of the top five deficiencies cited for laboratory directors. She mentioned the PT proposed rule publication and the CLIA fee increase notice. Ms. Dyer informed the members on the goals of the Tri-Agency Task Force for Emergency Diagnostics, the planned histopathology guidance, and a potential Request for Information on histopathology and microbiology. She provided information on cytology surveys noting that many issues identified have not changed since the impetus of CLIA, and CMS will continue in-depth cytology surveys and engagement of stakeholders. Ms. Dyer noted the Federal

Monitoring Survey Assessments that led to process improvements for the regional offices including standardization of worksheet and summary reports. Ms. Dyer closed with the introduction of the new CLIA Communications Listserv, which will allow CMS to disseminate information to laboratories and laboratory professionals.

Food and Drug Administration (FDA) Update ***Addendum 5***

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

Dr. Tobin began his presentation by providing updates on the applicants selected for the FDA Innovation Challenge: Devices to Prevent and Treat Opioid Use Disorder. He updated the Committee on the publication of a final guidance on the coordinated development of antimicrobial susceptibility test (AST) devices, which outlines a framework for how drug and device developers can partner to facilitate the timely development and availability of AST diagnostic devices. Dr. Tobin noted that, following the CLIAC recommendation from November 2018, the FDA implemented breakpoint change protocols to promote timely integration of updated AST interpretive criteria in device labeling. He concluded with an update on the FDA's reissuance of the revised CLIA waiver draft guidance, which was published in November 2018. The updated guidance is focused on study design aspects related to meeting the statutory criteria for waiver.

Public Comments
Addendum PC1

CDC OID Board of Scientific Counselors (BSC) Update ***Addendum 6***

Sheldon Campbell, MD, PhD
Committee Liaison to CDC Board of Scientific Counselors
Office of Infectious Diseases (OID)
Clinical Pathologist
Pathology and Laboratory Medicine Service
VA Connecticut Healthcare System

Dr. Campbell presented updates relevant to CLIAC from the December 2018 BSC meeting. The BSC discussed the recent outbreaks of acute flaccid myelitis (AFM) and the formation of the AFM task force. The task force, including stakeholders from neurology, infectious diseases, and the laboratory community, academia, and public health, is seeking to understand the epidemiology pathogenesis, treatment, and management of this condition. Dr. Campbell provided an update on several activities of both the Food Safety Modernization Act Surveillance Working Group and the Infectious Disease Laboratory Working Group.

Committee Discussion

- A member asked Ms. Dyer if CMS would consider modernizing their current practices and accepting electronic signatures, or copies of signed attestation statement forms, rather than requiring that the physically signed attestation form be in the laboratory. This could prevent some citations. Ms. Dyer responded that they will take that issue under consideration.
- Another CLIAC member inquired as to what happens after laboratory director citations are issued. Ms. Dyer responded that a corrective action plan must be initiated by the laboratory.

PRESENTATIONS AND COMMITTEE DISCUSSION

CLIA Personnel Regulations Workgroup

CLIA Personnel Regulations Workgroup Report ***Addendum 7***
Addendum 7a

Lee Hilborne, MD, MPH
Director, Center for Patient Safety and Quality
Professor of Pathology and Laboratory Medicine
UCLA School of Medicine

After a brief introduction by Ms. Karen Dyer, Dr. Hilborne thanked the CLIA Personnel Regulations Workgroup members and stated the charge of the workgroup. As part of their charge, the workgroup received nine questions to answer. Dr. Hilborne explained the questions and the workgroup's discussions and agreements for each of the questions. He noted that as the workgroup discussed the questions, they also considered other pertinent personnel issues, including military training and experience, the Doctorate of Clinical Laboratory Science (DCLS) degree, and the recognition of histotechnologists and pathology assistants as laboratory personnel. Dr. Hilborne closed with a list of potential CLIAC topics that the workgroup suggested for future meetings.

Public Comments
Addendum PC2 ***Addendum PC3*** ***Addendum PC4*** ***Addendum PC5***
Addendum PC6

Committee Discussion
The Committee discussed the workgroup's agreement for each question summarized in the CLIA Personnel Workgroup presentation and report, and discussed several recommendations. In addition to the discussions on the workgroup agreement, other relevant comments follow.

- Appropriate educational background to meet CLIA personnel requirements:
  - Require a minimum number of credit hours that include a clinical laboratory component and remove the specific list of degrees from the regulations.
  - Two pathways could be considered for meeting CLIA personnel qualification requirements: one based on a degree named in the regulations, and another based on having appropriate credit hours of courses with clinical laboratory components.

    - CMS should consider allowing certification agencies to serve as a primary-source verification for laboratory personnel education and training.
    - Individuals with nursing degrees should qualify based on having satisfied educational requirements for courses with a clinical laboratory science component.
- The appropriate laboratory training and experience:
    - Training and experience should be commensurate with personnel roles and responsibilities listed in the CLIA regulations, and should include clinical laboratory experience.
    - Consider whether technical supervisor qualifications should be uniform across specialties rather than having specialty-specific requirements.
- The CLIA regulations statement "possessing qualifications that are equivalent to board certification:"
    - Both the laboratory director and the technical supervisor requirements include reference to being board eligible. Since it is not possible to determine equivalency, this option should be removed from the regulations wherever it appears.
- Clarification is needed to indicate the requirement for 20 continuing education hours for a laboratory director must relate to their clinical laboratory director responsibilities.
- The amount of time the laboratory director needs to be on site:
    - Opinions varied on the ability of all laboratory directors to make on-site visits every six months.
    - It was acknowledged that many laboratory director duties can be performed remotely.
- In addition to the future topics proposed by the CLIA Personnel Workgroup, the Committee discussed future CLIAC topics, including:
    - Explicitly including qualification pathways for Veteran's Administration and military training, the Doctorate in Clinical Laboratory Science (DCLS) as an acceptable doctoral degree, and consideration of areas where the only route for qualification includes a doctorate level scientist.
    - Communication of significant and critical results as it relates to diagnostic accuracy.
    - Reclassification of automated blood bank platforms as moderate complexity when used for transfusion.

Recommendations: CLIA Personnel Regulations

CLIAC recommends that HHS consider modifying CLIA personnel requirements as follows:

Recommendation 1: Biological science degrees such as biology, chemistry, medical technology, and clinical/medical laboratory science are acceptable degrees for laboratory personnel. Other degrees (such as those in the humanities, physical sciences, and others) may not have the requisite science coursework, and candidates for positions should be considered based on a minimum number of hours of courses with laboratory components with relevance to clinical laboratory testing (which could also come from post-degree curricular work).

Recommendation 2: The degree in physical science should be removed from the CLIA regulations because it is too broad and may not include relevant laboratory science coursework.

Recommendation 3: All personnel should have training and experience in their areas of responsibility as listed in CLIA for their appropriate test complexity as shown in the table below.

CLIA Section	Role	Complexity
493.1407(e)	*Laboratory director*	*Moderate*
493.1413(b)	*Technical consultant*	*Moderate*
493.1425(b)	*Testing personnel*	*Moderate*
493.1445(e)	*Laboratory director*	*High*
493.1451(b)	*Technical supervisor*	*High*
493.1495(b)	*Testing personnel*	*High*

Recommendation 4: Remove the statement "possess qualifications that are equivalent to those required for such certification" from relevant sections noted below.

CLIA Section	Role	Complexity	CLIA Section	Role	Complexity
493.1405(b)(1)(ii)	*Director*	*Moderate*	*493.1449(h)(1)(ii)*	*Technical Supervisor*	*High (Diagnostic Immunology)*
493.1411(b)(1)(ii)	*Technical Consultant*	*Moderate*	*493.1449(i)(1)(ii)*	*Technical Supervisor*	*High (Chemistry)*
493.1443(b)(1)(ii)	*Director*	*High*	*493.1449(j)(1)(ii)*	*Technical Supervisor*	*High (Hematology)*
493.1443(b)(6)	*Director*	*High (Oral Pathology)*	*493.1449(k)(1)(ii)(A) & (B)*	*Technical Supervisor*	*High (Cytology)*
493.1449(b)(2)	*Technical Supervisor*	*High*	*493.1449(l)(1)(i)(B)*	*Technical Supervisor*	*High (Histopathology)*
493.1449(c)(1)(ii)	*Technical Supervisor*	*High (Bacteriology)*	*493.1449(l)(2)(i)(B)(1), (2) &(3)*	*Technical Supervisor*	*High (Dermatopathology)*
493.1449(d)(1)(ii)	*Technical Supervisor*	*High (Mycobacteriology)*	*493.1449(l)(3)(i)(B)(1) & (2)*	*Technical Supervisor*	*High (Ophthalmic Pathology)*
493.1449(e)(1)(ii)	*Technical Supervisor*	*High (Mycology)*	*493.1449(m)(1)(ii) & (2)*	*Technical Supervisor*	*High (Oral Pathology)*
493.1449(f)(1)(ii)	*Technical Supervisor*	*High (Parasitology)*	*493.1449(n)(1)(ii)*	*Technical Supervisor*	*High (Radiobioassay)*
493.1449(g)(1)(ii)	*Technical Supervisor*	*High (Virology)*	*493.1449(q)(1)(ii)*	*Technical Supervisor*	*High (Immunohematology)*

Pre 2/2/1992 specifications

CLIA Section	Role	Complexity
493.1406(b)(1)	*Director*	*Moderate*
493.1406(b)(2)(iii)	*Director*	*Moderate*
493.1406(b)(3)	*Director*	*Moderate*

Recommendation 5: Throughout section 493, subpart M, specify that the laboratory experience described under the experience route should be "clinical laboratory experience."

Recommendation 6: Regarding board certification, current and future HHS approved doctoral boards should be reviewed to ensure that they include a clinical component that addresses laboratory management and administration. (Current approved boards may be found at https://www.cms.gov/regulations-and-guidance/legislation/clia/certification_boards_laboratory_directors.html.)

Recommendation 7: As a prior education requirement, 20 CME or CE credit hours specifically addressing laboratory practice commensurate with laboratory director responsibilities (CFR493.1405 and 1443) should be required for both moderate and high complexity laboratory directors except those certified by the American Board of Pathology, the American Board of Osteopathic Pathology, the American Board of Dermatology, or other boards approved by HHS.

Recommendation 8: Regarding residency education, Clarify 493.1443(b)(2)(i) by emphasizing that the requisite laboratory training must be "clinical" laboratory training: "have at least one year of clinical laboratory training during medical residency or fellowship…."

Recommendation 9: Laboratory directors should make at least two (reasonably spaced) on-site visits to each laboratory they direct per year. On-site visits are not meant to substitute for execution of director responsibilities, and are meant to supplement regular interactions between off-site directors and the laboratory (e.g. by telephone or other telepresence).

Recommendation 10: Clear documentation of laboratory director on-site visits should demonstrate that the laboratory is in continuous compliance with current laws and regulations including but not limited to the assessment of the physical environment for safe laboratory testing.

Recommendation 11: Consider modifying CLIA requirements for technical consultants at 493.1411 (b)(4)(i-ii) to add the option that individuals with an associate degree in chemical, biologic, or medical technology and two years of laboratory training and experience would qualify as a technical consultant.

Recommendation 12: Consider modifying CLIA requirements for provider-performed microscopy procedures to add certified registered nurse anesthetist (CRNA) and clinical nurse specialist (CNS) to the definition of mid-level practitioner.

Nontraditional Testing Workflow Model Workgroup

Nontraditional Testing Workflow Model Workgroup Report *Addendum 8*
Addendum 8a

Valerie Ng, MD, PhD
Professor and Interim Chair Department of Laboratory Medicine
University of California, San Francisco
Chief, Laboratory Medicine Service and Chief of Staff Elect
San Francisco General Hospital

After a brief introduction by Ms. Nancy Anderson, Dr. Ng thanked the workgroup members and stated the charge for the workgroup. She explained and provided examples of the nontraditional testing workflow model, and emphasized gaps in the model where there is increased risk that could affect patient management. Dr. Ng summarized the discussions around each of the seven questions, and explained the main aspects of the testing process where concerns were identified by the workgroup (e.g., database validation, data security, potential lawsuits, and surveyor challenges).

Public Comments
Addendum PC7 *Addendum PC8* *Addendum PC9* *Addendum PC10*

Committee Discussion
The Committee discussed the workgroup presentation and report, commented on several topics, and developed and voted upon recommendations. Relevant comments include:

- Artificial intelligence and advanced technologies continue to change the practice of medicine. The regulatory agencies should start addressing the impact of these new technologies on the current CLIA regulations and anticipate where changes may need to be considered.
- The way in which terms including “laboratory,” “test,” and “specimen” are defined by CLIA affects how the regulations are interpreted. Clear definitions are needed.
- Determining the ultimate responsibility and accountability for testing in a distributive model is challenging. All contributors to the process should be held accountable for their parts of the process.
- Two scenarios could exist. One would be that each laboratory or facility involved in the process would be required to be CLIA-certified; the other would hold one laboratory responsible for the entire testing process. An example of the first would be a scenario where a specimen is sent to a facility with a CLIA certificate and then part of the process takes place at other facilities, all of which are responsible to be certified and meet the CLIA regulations. In the second scenario, a specimen or data is sent to a second facility without a CLIA certificate for a part of the process, with the sending facility taking responsibility for the non-CLIA certified laboratory testing processes.
- Varying testing algorithms, data transfer standards, end-method verification, proficiency testing, and digital data are all issues that need to be considered.
- Is it the intent of the CLIA definition that states “materials derived from the human body” should include both biological material (e.g., DNA) and data derived from it (e.g., sequencing data), or just biological material?

- It would be challenging for a bioinformatics company to meet specific CLIA requirements for certification.

Recommendations: Nontraditional Testing Workflow Model

The rise of big data and machine learning have led to geographically decentralized information flows, and the necessity for extensive and novel controls (samples/data with known results). In response to these trends, CLIAC recommends that:

Recommendation 1: HHS issue proposed regulations that reflect that the word "materials" in the CLIA-88 definition of a clinical laboratory shall include all data derived from a patient specimen, including images, genetic and protein sequence(s), –omics data, and other data.

Recommendation 2: Any site that performs an activity that involves such data (provided that the activity is related to the diagnosis, prevention, or treatment of any disease or impairment of, or the assessment of, the health of human beings) shall be considered a "laboratory," if that site is not an extension of an existing CLIA-certified laboratory.

Recommendation 3: HHS develop guidance to allow distributive proficiency testing (PT) models, including analytes that are currently subject to CLIA-required PT, to assure quality across the whole testing cycle.

Recognition of Outgoing Members

Addendum 9

Dr. Reynolds Salerno recognized Ms. Helen Mills and Dr. Sheldon Campbell for their contributions to the Committee. A special presentation was provided that highlighted the CLIAC accomplishments during Dr. Ramy Arnaout's term as CLIAC Chair.

Next Generation Sequencing Workgroup

Next Generation Sequencing Workgroup Report

Addendum 10
Addendum 10a

Jordan Laser, MD
Medical Director, Pathology and Laboratory Medicine
Department of Pathology
Long Island Jewish Medical Center

After a brief introduction by Dr. Collette Fitzgerald, Dr. Laser thanked the workgroup members and stated the charge for the Next Generation Sequencing (NGS) Workgroup. He provided a word cloud of the overarching responses for each of the twelve NGS discussion questions. Dr. Laser explained the top conclusions for each question, and mentioned current guidance documents and other resources available, if any, and what resources are still needed.

Public Comments

Addendum PC11 ***Addendum PC12*** ***Addendum PC1***

Committee Discussion

The Committee discussed the workgroup presentation and report, commented on several topics, and developed and voted upon recommendations. Relevant comments include:

- CLIA does not have specific requirements for molecular testing; there may be a need to update the regulations to address new disciplines, such as molecular laboratory testing. Alternatively, there may be ways to make updates within the existing CLIA regulations.
- NGS is a method and not a specific test. It is challenging to set regulations around a methodology, including defining what should be required for quality control and quality assurance.
- Support from the laboratory to healthcare providers is critical with respect to NGS.
- Minimum standards are needed for defining and establishing performance characteristics for NGS.
- NGS data sharing, storage, retention, and quality control should be considered.
- The incorporation of standards for interoperability and data usage in clinical genetic and genomic testing is needed. Logical Observation Identifiers Names and Codes (LOINC®) may not be sufficient for NGS interoperability and data exchange alone. The Systematized Nomenclature of Medicine (SNOMED) should be incorporated. The Systemic Harmonization & Interoperability Enhancement for Laboratory Data (SHIELD) program could address this issue and the use of current and future interoperability standards.
- There are gaps in CLIA related to qualified testing personnel for NGS, including bioinformaticians.
- A complete review of the CLIA regulations is needed to define all areas where updates are needed to address issues such as those noted by the three workgroups.
- Information from the three workgroups should be synthesized and a new workgroup formed, or the same three workgroups used, to focus on where updates to the CLIA regulations are needed.
- Several additional proposed recommendations and future CLIAC topics were raised and it was suggested that the November 2019 CLIAC meeting continue these discussions.

Recommendations: Next Generation Sequencing

Recommendation 1: CLIAC recommends that HHS thoroughly update the CLIA regulations to address issues related to new biomarker testing and other new technologies. This update may include a new section, revising existing sections, or other alternatives. This update should take account of the reports by the Personnel Regulations, Non-Traditional Workflow Models, and NGS workgroups presented to CLIAC. For NGS, such issues include but are not limited to, e.g., the definition, role, and responsibilities of bioinformaticists; quality control, e.g. moving from a simple requirement for positive- and negative controls to controls more appropriate for NGS; establishment and verification of performance specifications, including the availability and sharing of samples; proficiency testing; reporting; delivery of data to patients, e.g. FASTQ vs. BAM vs. VCF-formatted NGS files; measurement, e.g. of NGS testing volumes; and data sharing, e.g. repositories and incentives and/or requirements for contribution to them.

Recommendation 2: CLIAC recommends creation of a new CLIAC workgroup with the charge of advising on how CLIA might specifically be updated, integrating and reflecting the reports by the Personnel Regulations, Non-Traditional Workflow Models, and NGS workgroups presented to CLIAC, ideally incorporating members from each of these groups (for continuity).

Recommendation 3: CLIAC recommends that CMS, CDC, and FDA encourage professional societies and others (e.g. CLSI) to develop and/or update NGS guidelines. Specific fields of interest include, but are not limited to, oncology, inherited conditions, and microbiology applications of NGS. Recommended topics for guidelines include but are not limited to:

A) Revalidation of (i) analytical targets (e.g. additional genes or additional variant types); (ii) The bioinformatics pipeline (e.g. sequencing software updates, updates/changes in software in pipeline etc.)
B) Data retention (e.g. file types, duration, intent)
C) Data sharing (e.g. to patients, between organizations, between providers)

Recommendation 4: CLIAC recommends that CMS, CDC, and FDA create guidelines or best practices related to clinical and public-health NGS. These could be based on or in partnership with guidelines already established by the government, professional societies, or other groups (e.g. CLSI).

Recommendation 5: CLIAC recommends HHS support the incorporation of standards for interoperability and data usage in clinical genetic and genomic testing and NGS across the laboratory subspecialties.

Recommendation 6: CLIAC recommends expanding the CDC GeT-RM program with regard to scope and type (e.g. wet samples and data files). Focus should be on the three major categories of oncology, inherited conditions, and microbiological applications. Expansion could also include the creation/curation of NGS data sets to be used by laboratories while validating/revalidating bioinformatic pipelines.

Recommendation 7: CLIAC recommends CDC create and send a survey to laboratories and other organizations that perform NGS to collect data on bioinformaticians. Specifically, this survey should collect: job descriptions and educational and training requirements, as well as the availability, hiring, roles, responsibilities, salaries, and turnover of individuals who work in roles related to bioinformatics. This survey would support the CLIAC Workgroup responsible for creating suggestions about personnel changes to CLIA.

Recommendation 8: CLIAC recommends that CDC carry out a survey of clinical laboratories to define the specific use cases for long-term storage (i.e., beyond diagnosis delivery) of NGS data, and for keeping archival software (including versioning), hardware (including e.g. tapes, drives, or disks), and environment/platform, to be able to re-run data under original settings.

ACRONYMS *Addendum 11*

NOMINATION INFORMATION *Addendum 12*

ADJOURN

Drs. Arnaout 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 10-11, 2019 CLIAC meeting is an accurate and correct representation of the meeting.

Dr. Ramy Arnaout, CLIAC Chair Dated: